10º Simpósio da Fundação 🔊 🗟 🖾 🖽

Aquém e Além do Cérebro Behind and Beyond the Brain

Casa do Médico - Porto • 26 a 29 de março de 2014

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Interações mente-matéria *Mind-matter interactions*

O livro "Aquém e Além do Cérebro" contém as atas do 10º Simpósio da Fundação Bial, realizado na Casa do Médico, de 26 a 29 de março de 2014, tendo como membros da Comissão Organizadora os Senhores Professores Fernando Lopes da Silva, Dick Bierman, Miguel Castelo-Branco, Alexandre Castro-Caldas, Axel Cleeremans, Rui Mota Cardoso, Mário Simões e Caroline Watt. Os textos estão disponíveis em www.bial.com.

The book "Behind and Beyond the Brain" includes the texts of the Bial Foundation's 10th Symposium, held at Casa do Médico, from the 26th to the 29th March 2014, having as members of its Organizing Committee the following Professors: Fernando Lopes da Silva, Dick Bierman, Miguel Castelo-Branco, Alexandre Castro-Caldas, Axel Cleeremans, Rui Mota Cardoso, Mário Simões and Caroline Watt. The texts are available at www.bial.com.

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SESSÃO DE ABERTURA OPENING SESSION

DISCURSO DO PRESIDENTE DA FUNDAÇÃO BIAL

Luís Portela

20 Anos de Fundação Bial. 30 Anos de Prémio Bial. 20 Anos de Bolsas de Investigação Bial. 10ª Edição do Simpósio Aquém e Além do Cérebro.

É com satisfação que os recebemos nesta sessão de abertura do X Simpósio da Fundação Bial, comemorativa do nosso vigésimo aniversário.

Foi em 1993 que o Conselho de Reitores das Universidades Portuguesas aceitou o convite dos Laboratórios Bial para constituírem e administrarem em conjunto uma instituição independente, sem fins lucrativos, tendo em vista promover a investigação do ser humano, tanto sob os aspetos físicos como sob o ponto de vista espiritual.

A Fundação Bial veio a ser constituída em 1994, assumindo a gestão do Prémio Bial, que já existia desde 1984 e que é atualmente um dos maiores prémios europeus na área da saúde, distinguindo excelentes profissionais de diversas nacionalidades.

Ainda em 1994 foi lançado o primeiro concurso de bolsas de investigação científica, abrangendo a Psicofisiologia e a Parapsicologia. Nestes vinte anos, foram apoiados 461 projetos - que representam 31% do total dos solicitados -, envolvendo mais de mil investigadores de 27 países diferentes. Cerca de metade das bolsas foram atribuídas na área da Psicofisiologia e a outra metade à Parapsicologia.

Resultaram até agora dos projetos por nós apoiados 671 artigos em publicações indexadas, das quais 460 em Psicofisiologia e 211 envolvendo a Parapsicologia. O fator de impacto médio destas publicações é de 3,2. Cerca de 70 artigos foram publicados em publicações com um fator de impacto superior a 5.

Estes resultados podem ser vistos num poster que está presente na galeria aqui ao lado, da autoria de Paula Guedes, Assunção Júdice, Sylvie Marinho e Helena Topa. Estas quatro autoras construíram no último ano – pela iniciativa e sob a orientação da Professora Maria de Sousa – um centro de documentação e uma base de dados *online* sobre os projetos apoiados pela Fundação Bial, que está agora acessível ao público.

O Centro de Documentação – repositório documental da Fundação – integra as referências e, em alguns casos, os próprios ficheiros eletrónicos, dos livros das várias edições do Prémio Bial, dos Simpósios "Aquém e Além do Cérebro" e das Bolsas de Investigação Científica. A Base de Dados inclui informação relativa aos projetos apoiados, o que torna mais fácil avaliar a sua produtividade, ficando também o público em geral com um acesso facilitado aos resultados do trabalho dos nossos bolseiros.

Percebe-se agora claramente que a produção científica foi crescendo ao longo dos anos, especialmente na última década. Também é clara a interligação crescente a nível dos projetos entre a Psicofisiologia e a Parapsicologia, sugerindo um cada vez maior interesse numa aproximação multidisciplinar.

A construção do Centro de Documentação e da base de dados foi uma forma de comemorarmos o nosso vigésimo aniversário, que entendemos reforçar com a publicação em livro da coleção de sumários dos resultados dos projetos apoiados pela Fundação Bial. Temos gosto em lhes oferecer um exemplar deste livro, na pasta do simpósio.

De hoje até ao dia 29, tem lugar a 10^a edição dos nossos Simpósios Aquém e Além do Cérebro. Como habitualmente, procuramos aqui reunir um significativo número dos nossos bolseiros – neste caso cerca de 100 – que nos apresentam os resultados preliminares ou definitivos dos seus projetos de investigação.

Teremos 48 posters em exibição na galeria aqui ao lado. Trinta dos autores desses projetos terão, na tarde de quinta-feira, dois minutos cada para os convidar a visitá-los. Doze outros foram selecionados para apresentações orais de dez minutos, na tarde de sexta-feira. Os nossos bolseiros estarão disponíveis para discutir com todos os participantes os resultados dos seus trabalhos, sobretudo nessas duas tardes, após as apresentações orais.

O tema deste simpósio – Interação mente-matéria – parece apropriado e atual. Apropriado, dado o interesse científico de muitos dos nossos bolseiros. Atual, por ser algo que hoje motiva o interesse de muita gente e dos próprios órgãos de comunicação social.

Teremos ao longo destes quatro dias cerca de 20 palestrantes de grande relevo, que estamos certos nos proporcionarão belos momentos de aprendizagem e de saudável convívio. Os nossos agradecimentos a todos os intervenientes. Gostaria, aliás, de agradecer a presença de todos os presentes, e em especial a do Senhor Ministro Nuno Crato, que já nos deu a honra de estar connosco como palestrante numa edição anterior, e que hoje aqui preside a esta sessão comemorativa do nosso vigésimo aniversário. Uma palavra de simpatia para a presença dos Senhores Secretários de Estado, do Presidente do CRUP e dos Senhores Bastonários.

Mas permitam-me ainda que lembre, com profunda gratidão e muita saudade os nossos administradores iniciais, Professores Nuno Grande e Manuel Baganha, a quem muito devemos no percurso que fizemos. Enaltecendo, naturalmente, o trabalho que os Professores Maria de Sousa e Daniel Bessa, que lhes sucederam, têm feito nos últimos anos, a quem igualmente estamos muito gratos.

Os nossos agradecimentos também aos membros da Comissão Organizadora deste Simpósio, em especial ao seu presidente Prof. Fernando Lopes da Silva, aos restantes membros dos nossos órgãos sociais, à Ordem dos Médicos – que sempre aqui nos acolhe tão bem -, ao Conselho de Reitores das Universidades Portuguesas, aos Conselhos Científicos das Faculdades de Medicina e, finalmente, à Presidência da República, que desde sempre patrocinou a Fundação Bial. O nosso reconhecido agradecimento aos Presidentes Mário Soares, Jorge Sampaio e Aníbal Cavaco Silva.

Ainda um abraço especial aos Professores Alexandre Castro-Caldas e Rui Mota Cardoso, membros da Comissão Organizadora do Simpósio há muitos anos e que não participarão na organização do próximo por razões profissionais e pessoais. Um grande e grato abraço aos dois.

Na atual conjuntura, a comemoração do nosso aniversário assume esta forma simples e algo espartana. Mas, temos muito gosto em lhes anunciar que procuraremos ao longo dos próximos anos dar continuidade às iniciativas que temos realizado. Pensamos que não será possível alargar o seu âmbito como desejaríamos, mas procuraremos incrementar a sua qualidade.

Assim, é com satisfação que lhes anuncio que a Fundação Bial vai promover um novo pacote de bolsas, cobrindo as mesmas áreas e com características semelhantes às anteriores. O regulamento e a documentação para concurso estarão disponíveis a partir de amanhã no nosso espaço *www.bial.com* e o prazo de entrega das candidaturas terminará em 31 de agosto próximo. Sublinho que não apoiaremos projetos de patologia ou de terapêutica, mas apenas Psicofisiologia e Parapsicologia. Foi criada uma plataforma *online* de submissão de candidaturas e de gestão das bolsas, fornecendo funcionalidades eletrónicas aos investigadores e aos avaliadores envolvidos no processo.

A Prof.^a Maria de Sousa selecionou para a contra-capa do livro comemorativo dos nossos 20 anos uma frase de Freeman Dyson, que eu gostaria de vos ler: *"Humans need beliefs in order to live, and great scientists are no exception. Great scientists produce right theories and wrong theories, and believe in them with equal conviction. Science is not concerned only with things that we understand. The most exciting and creative parts of science are concerned with things that we are still struggling to understand. Wrong theories are not an impediment to the progress of science. They are a central part of the struggle".*

A Fundação Bial deseja contribuir para a aprendizagem, a compreensão e o esclarecimento nas áreas da Psicofisiologia e da Parapsicologia, apoiando aqueles que dão o melhor do seu esforço para que a investigação científica proporcione conhecimento e sabedoria que permitam ao ser humano viver melhor, na utilização de todas as suas potencialidades e no respeito pelas Leis Universais.

Em março de 2016 esperamos encontrar-nos aqui no nosso XI Simpósio. Muito obrigado pela vossa presença e pela vossa atenção. Votos de um excelente simpósio.

DISCURSO DO BASTONÁRIO DA ORDEM DOS MÉDICOS

José Manuel Silva

Boa noite. Um agradecimento muito particular ao Doutor Luís Portela pela gentileza que teve em convidar a Ordem dos Médicos para, nesta casa da Ordem dos Médicos e na presença do Presidente da Seção Regional do Norte que aqui saúdo, o Dr. Miguel Guimarães, participar nesta sessão de abertura do 10º Simpósio da Fundação Bial. E é com muito prazer e orgulho que o fazemos, não só por a jornada decorrer na Casa da Ordem dos Médicos, mas também por esta íntima associação, de há muitos anos, entre a Ordem dos Médicos, a Bial e a Fundação Bial.

Cumprimento naturalmente, na pessoa do Doutor Luís Portela e do Senhor Ministro Nuno Crato, todos os membros da mesa. Permitam-me uma saudação particular ao Secretário de Estado do Ministro da Saúde, Dr. Fernando Leal da Costa, naturalmente o nosso superior hierárquico e de todos os médicos, ainda por cima médico e aqui também na casa de todos os médicos.

E gostaria de dizer apenas que é um orgulho para o país termos um laboratório como a Bial e uma Fundação como a Fundação Bial.

A história da Bial é uma história de êxito. Quase que poderíamos dizer que é uma história de êxito à americana, mas não; é uma história de êxito à portuguesa, porque em Portugal o êxito é muito mais difícil e, portanto, tem de facto muito mais valor, uma vez que é preciso arrostar com muito mais dificuldades e com muito menos apoios.

Eu quero desejar que se mantenha a aposta na investigação que, sobretudo num país pequeno, é absolutamente essencial para a afirmação desse mesmo país e é um dos pilares essenciais - a investigação e a inovação - para a sustentabilidade futura de Portugal como país independente. E que a Bial continue a ser um exemplo desta aposta na investigação e na inovação, mesmo naquela que aparentemente é mais atrevida, é mais surpreendente, mas que tem a capacidade de ligar aquilo que para alguns será talvez um pouco esotérico - mas que eu acredito que não o é -, à metodologia da rigorosa investigação científica. Parabéns à Bial, parabéns à Fundação Bial, parabéns ao Doutor Luís Portela e muito êxito em mais este 10º Simpósio e, sobretudo, muito êxito para o futuro.

Muito obrigado pelo convite e parabéns.

DISCURSO DO PRESIDENTE DO CONSELHO DE REITORES DAS UNIVERSIDADES PORTUGUESAS

António Rendas

Muito obrigado, muito boa noite a todos. Eu queria começar por felicitar a Fundação Bial, na pessoa do Doutor Luís Portela, por esta obra notável que ele tem vindo a fazer ao longo de várias décadas e que se materializa hoje na 10^a edição deste Simpósio, que tem muito dele próprio e, portanto, queria transmitir-lhe em meu nome pessoal, e em nome do Conselho de Reitores, o enorme privilégio que tem sido para nós fazer uma coisa, que em Portugal às vezes não se faz e devia-se fazer, que é deixar os outros trabalhar.

A nossa posição no CRUP não tem nenhum mérito; nós somos pura e simplesmente agentes daquilo que o Doutor Luís Portela nos pede com aquela persistência, mas também com aquela emoção que sabemos que está patente na lógica da sua forma de estar. O CRUP tem enorme gosto em poder ajudar modestamente na viabilização das personalidades que felizmente têm colaborado, graças também à sua forma de estar e à qualidade de tudo aquilo que faz, não só na Fundação, mas também na própria Bial. Portanto, modestamente também, muitos parabéns e que estes 10, mais 20, mais 30 anos se possam ir prolongando ao longo do tempo e que seja possível ao Conselho de Reitores e às Universidades - e neste caso à comunidade das ciências da saúde, com todas essas pontes que vai criando -, continuar a beneficiar da forma generosa como tem sempre intervido na sociedade portuguesa.

Queria, como é lógico, cumprimentar o Senhor Ministro da Educação e Ciência, Prof. Nuno Crato, com muita consideração e amizade, o Senhor Secretário de Estado da Inovação, Investimento e Competitividade, Dr. Pedro Gonçalves, o Senhor Secretário de Estado Adjunto do Ministro da Saúde, Dr. Fernando Leal da Costa, também com amizade e consideração, o Senhor Bastonário e o Prof. Fernando Lopes da Silva, que é também um companheiro, que eu me vou habituando a encontrar nos momentos certos. Ainda há pouco quando cheguei estava a perguntar-lhe se ele continua a fazer aquilo de que gosta, porque há muitas pessoas que estão, neste momento, a fazer aquilo de que não gostam, e eu incluo-me nesse grupo. É bom que haja pessoas como o Prof. Fernando Lopes da Silva que têm essa capacidade de poder fazer coisas de que gostam e eu tenho a certeza de que planeou este Simpósio exatamente com a competência e com o gosto que sempre põe na sua maneira de estar.

É muito curioso porque cheguei há pouco de Lisboa e ontem estive com o Senhor Ministro da Educação e Ciência e com o Secretário de Estado da Inovação nas comemorações dos 25 anos do IBET. O IBET é uma instituição sem fins lucrativos que está ligada à Universidade Nova de Lisboa - é o Instituto de Biologia Experimental e Tecnológica. Vou só levar 2 minutos porque o Senhor Ministro fez ontem uma citação e eu, como procuro ser bom aluno, fui às fontes e vou dizer uma coisa que acho que talvez seja útil, sendo uma reflexão conjunta em relação a todas estas nossas preocupações, em relação à investigação científica em Portugal. O Senhor Ministro na sua intervenção citou - e eu pedi ao Prof. Miguel Seabra a origem - algo que tinha sido publicado recentemente pela DGEEC, Direção-Geral de Estatísticas da Educação e Ciência, sobre a produção científica portuguesa entre 1990 e 2012. Claro que depois quando se tenta esmiuçar não é bem assim, é entre 2008 e 2012, comparando Portugal com a Europa a 15 e a Europa a 27. É muito curioso ver onde é que nós estamos bem e onde é que nós estamos mal. Onde é que estamos bem? Acima dos 15 ou dos 27 estamos bem nas ciências agrárias, nas engenharias, nas neurociências, excluindo a psicologia e a psiquiatria, na imunologia, na física e nas ciências aeroespaciais. Onde é que estamos atrás, muito próximo do Luxemburgo, da Grécia e da Espanha, etc.? Estamos atrás na Psicologia, na Psiquiatria, na Farmacologia, na Medicina Clínica, nas Geociências e na Microbiologia. Eu, que tenho muitas afinidades com todas elas, fiquei muito preocupado com as Geociências, porque se queremos ter uma plataforma marítima, vai ser complicado fazer isto sem Geocientistas e, portanto, há aqui um caminho muito interessante a percorrer.

Claro que isto é baseado em citações, é um trabalho da Thomson muito honrado, mas qual é a minha mensagem final, e peço desculpa por ter ocupado um pouco do vosso tempo, nós precisamos de um Portugal transparente e equilibrado. Ainda há pouco estávamos a falar do interior e do litoral e não é possível que haja, na realidade, capacidade competitiva do país se tudo isto não for relativamente melhor. Não chega só termos solistas, temos de ter orquestras. E acho que a melhor homenagem que nós podemos prestar ao Doutor Luís Portela é reconhecer a enorme capacidade que ele tem de, sendo um magnífico solista, ter também uma grande orquestra.

Muitas felicidades para este Simpósio e procurarei acompanhar com muita admiração toda a sua obra. Muito obrigado.

DISCURSO DO SECRETÁRIO DE ESTADO ADJUNTO DO MINISTRO DA SAÚDE

Fernando Leal da Costa

Muito obrigado, muito boa noite a todos. Sigo o exemplo do Senhor Bastonário e, na sua pessoa e na pessoa do Senhor Ministro, cumprimento os restantes membros da mesa. Mas também, tal como ele fez, não deixarei de dirigir-lhe um cumprimento especial, ao qual queria também associar um cumprimento especial ao Senhor Vereador Dr. Manuel Pizarro, um abraço fraterno por ter aqui um médico, a quem além do mais eu tive o gosto de suceder e, portanto, é provavelmente na sala aquele que melhor compreenderá as minhas angústias e dificuldades. Ainda vou ter de falar com ele para depois perceber como é que é a vida depois da vida, uma vez que o tema deste congresso em parte poderia também ser a vida depois da morte, mas essas matérias mais parapsicológicas eu deixarei para depois.

Há pouco, quando vinha para aqui, estive a falar com outros colegas e, obviamente, achei curioso ter que admitir, como Secretário de Estado Adjunto do Ministro da Saúde, nas funções que agora desempenho e sendo médico, que vinha à Ordem dos Médicos, ainda bem, a um congresso em que a parapsicologia tem obviamente um lugar de destaque.

É uma posição de coragem desde há longos anos do Doutor Luís Portela; é a demonstração clara de que é um homem de vistas largas, é uma pessoa que compreende que a ciência não tem que necessariamente ter fronteiras e, desse ponto de vista, deixa-nos a todos com uma extrema curiosidade de saber como é que o Doutor Luís Portela tem sabido tão bem lidar com este cruzamento de várias fontes do conhecimento. Depois, obviamente, saudar a escolha das neurociências que são, por excelência, muito atrativas do ponto de vista da investigação. Mas, como dizia há pouco o Professor Rendas, infelizmente as áreas da Psicologia e da Psiquiatria ainda estão um pouco aquém daquilo que nós gostaríamos de ter enquanto investigadores e, desse ponto de vista, reuniões como esta são seguramente altamente encorajadoras para levar a uma maior cooperação entre aquilo que são as ciências da neurofisiologia e as ciências afins. Obviamente que as palavras do Senhor Bastonário foram muito simpáticas, mas eu, como é óbvio, não sou superior hierárquico de médico algum, tenho apenas a ingrata tarefa de, neste momento, representar de alguma forma o Patronato, o que nos tempos que correm nem sempre é necessariamente muito agradável. No entanto, também estou certo de que é relativamente fácil, através daquilo que são as pontes comuns que nos unem a todos, nomeadamente a sede do conhecimento, estabelecer pontes de entendimento entre vários investigadores, não só médicos, mas também pessoas interessadas noutro tipo de investigação, como o congresso vai demonstrar.

E eu tenho sincera pena de não poder assistir aos trabalhos do congresso, o Doutor Luís Portela sabe que é verdade, porque já várias vezes falamos sobre isto. Mas, como sempre, ficarei a aguardar pela gentileza que costumam ter para comigo de me enviarem os Proceedings e, de alguma forma, aprender mais alguma coisa sobre estas matérias, sendo certo, devo dizer-vos, que durante algum tempo estes livros acabam por fazer a minha mesa de cabeceira, não porque sejam propriamente muito soporíferos, mas acima de tudo porque é o tipo de temática que nos dá alguma tranquilidade.

O conhecimento das neurociências e, acima de tudo, imaginarmos que ainda poderemos com algum treino, capacidade e, eventualmente, evolução, vir a ser capazes de fazer melhor com o nosso cérebro, é seguramente muito encorajador para quem está no Governo, a quem faltam muitas vezes capacidades de adivinhação, claramente capacidades de telecinesia e, acima de tudo, capacidades de teleportação, que hoje me teriam dado muito prazer. Não fosse o facto de, felizmente, e com alguma coragem também, continuar a atravessar a distância que é estritamente física entre Lisboa e Porto porque, como sabem, o Porto estará sempre no meu coração. Nesta matéria estejam à vontade, porque como penso que é do conhecimento geral até sou do Sporting e, portanto, não vale a pena ficarem preocupados.

E com isto termino agradecendo ao Doutor Portela este convite e o prazer de estar aqui convosco, com estes amigos, na certeza porém de que, continuadamente este é o 10º, continuaremos a ter reunióes destas e eu gostaria de continuar a poder vir a elas, provavelmente num tempo breve e futuro já como assistente, uma vez que, seguramente, todos os temas serão apetitosos. Muito obrigado.

DISCURSO DO MINISTRO DA EDUCAÇÃO E CIÊNCIA

Nuno Crato

Muito obrigado, muito boa noite. Eu esqueci-me de como se come bem no Porto e jantei bem, portanto, vou falar de pé para poder falar mais diretamente.

Senhor Doutor Luís Portela, Senhor Secretário de Estado da Inovação, Investimento e Competitividade, Senhor Secretário de Estado Adjunto do Ministro da Saúde, Senhor Presidente do Conselho de Reitores das Universidades Portuguesas, Senhor Bastonário da Ordem dos Médicos, Senhor Presidente da Comissão Organizadora deste Simpósio, demais autoridades presentes, minhas senhoras, meus senhores, colegas investigadores, é com enorme prazer que vos acompanho nas celebrações do 20º aniversário da Fundação Bial e do 90º da empresa Bial. E recordo também que aqui estive há 4 anos, com imenso prazer, a falar sobre um assunto que me dá muito prazer, que é a Matemática.

Na Bial, 20 anos são 20 anos de apoio à investigação, 90 anos de investimento, 90 anos de uma empresa que aposta no conhecimento.

Todos sabemos que o conhecimento está na base do desenvolvimento moderno mas, para transformar o conhecimento em melhores condições de vida, precisamos de empreendedores e de empresas. Empresas inovadoras que reconhecem os benefícios de integrar a investigação nas suas atividades, conscientes do valor acrescentado das novas tecnologias e das novas ideias, conscientes da importância das atividades de investigação e desenvolvimento.

A Bial é um exemplo. A Bial, desenvolvendo uma atividade intensa em conhecimento e tecnologia na área da saúde e indústria farmacêutica, faz parte das 1500 empresas mundiais que desenvolvem atividades de investigação e desenvolvimento de topo e é a empresa portuguesa que, de acordo com os dados recolhidos pelo primeiro Diagnóstico do Sistema de Investigação e Inovação 2013, maior número de patentes publicou no European Patent Office em 2008 e 2009. Este sucesso está obviamente associado ao facto da empresa olhar para a ciência como fator de competitividade e de ter integrado nos seus quadros jovens investigadores, jovens altamente qualificados. Ao fazê-lo acrescentou valor à empresa, aos seus produtos, aos seus projetos, acrescentou valor à economia, beneficiou as pessoas, acrescentou valor ao conhecimento, beneficiou a ciência. Esta é a estratégia de desenvolvimento. Ao adotá-la a empresa colocou o conhecimento ao serviço do crescimento económico e social, aproximou a ciência a um dos seus melhores e mais válidos objetivos: melhorar a qualidade de vida das pessoas.

Perante os desafios da descoberta científica e os desafios da integração produtiva, temos de fazer mais, podemos fazer mais, temos condições para produzir ainda mais ciência, para responder ainda melhor à curiosidade científica, iremos formar mais recursos humanos qualificados, conseguiremos aprofundar a inovação de base científica. Mas, para isso contribuem os nossos cientistas, contribuem as nossas universidades, contribuem os nossos laboratórios, contribuem as nossas unidades de investigação e contribui também uma cultura empresarial que queremos que aposte mais no conhecimento, que aposte mais nas gerações mais qualificadas.

Portugal é um dos países com mais baixa taxa de emprego de doutorados nas empresas - 2,6% em comparação com uma taxa de quase 35% em países como a Holanda ou a Bélgica.

A nossa ciência está consciente do enorme contributo que pode fornecer na cadeia de produção. As nossas empresas precisam dos nossos investigadores. As empresas portuguesas estão cada vez conscientes da importância das atividades de investigação e desenvolvimento - e o Governo tem estado a trabalhar, e os cientistas portugueses têm estado a trabalhar, e as unidades de investigação portuguesas têm estado a trabalhar, para que o sistema científico e tecnológico nacional se torne mais interativo com as empresas.

Estimulando a colaboração das empresas nacionais com o sistema científico, promovendo o investimento em investigação e desenvolvimento pelas empresas, estimulando através dos programas doutorais FCT, programas híbridos de transferência da investigação para a economia, atribuindo bolsas de doutoramento a empresas, revendo o sistema de incentivos fiscais que, para além de tornar elegíveis as despesas com auditorias a investigação e desenvolvimento e os custos com registo e manutenção de patentes, passou a considerar a 120% as despesas com contratação de doutorados. E, deixem-me confessar-vos, como fator estratégico a este título, gostaria de ver este benefício aumentado, gostaria de ver este benefício muito aumentado. Mas sobretudo, gostaria de ver muitas empresas tomarem o exemplo da Bial.

Sabemos que o país avançou muito, mas pode ir muito mais além. Sabemos que a inovação surge da união de esforços entre a investigação e o empreendedorismo; que a transformação de novas ideias em projetos, produtos e tecnologia, tem por base o conhecimento científico, a tecnologia moderna, a criatividade e a coragem para enfrentar o risco. Sabemos que a ciência tem sido, é e continuará a ser movida pela curiosidade, movida pelo espírito científico, movida pelo espírito de descoberta, mas sabemos também que precisamos de mais empresas e mais empreendedores que invistam no amanhã e que vejam a ciência como uma oportunidade para o futuro. Precisamos de empresas que integrem nos seus quadros os nossos jovens mais bem qualificados.

Em nome do Governo, deixo aqui os parabéns à Bial, à Fundação Bial e a todos que participam no nosso esforço científico, um esforço que é do País, para o País, um esforço para o benefício de todos.

Muito obrigado.

CONFERÊNCIA INAUGURAL OPENING CONFERENCE

APRESENTAÇÃO DO CONFERENCISTA PRESENTATION OF THE KEYNOTE SPEAKER

Fernando Lopes da Silva

As was announced initially the inaugural lecture would have been given by Professor Miguel Nicolelis who, unfortunately, was not able to come to Porto due to major unexpected events that started to unfold late last week, and have required his presence in São Paulo today and tomorrow. The major event is a scientific demonstration that he personally must give to FIFA officials – International Federation of Football Associations – and to members of the Brazilian government, including the President Dilma Rousseff tomorrow. He will then demonstrate his new creation, a robotic limb prosthesis, which can be directly controlled by the subject's own brain activity through a brain-machine interface. The crucial event is that these authorities want to see whether this new device will really work in practice, since the aim is to use it as showcase to the entire world during the opening football match of the FIFA 2014 Soccer World Cup on June 12, 2014, in São Paulo, Brazil. As Miguel Nicolelis self wrote to us "we are required to comply with all requests made by FIFA and the Brazilian government to assure that everything is fine. Failure is not an option." Nonetheless and unfortunately he has to fail the BIAL Symposium.

The audience here tonight may be content to join the 3 billion people who will watch on TV this robotized person moved by his own brain signals at this Football match. As you may imagine nothing rises so high nowadays than Soccer, not even BIAL. And Soccer with a scientific salt rises to stratospheric heights.

We are very fortunate, however, that Eberhard Fetz, who was invited to be the key-note speaker at the morning session tomorrow, agreed to be the key-note speaker at the opening of this 10th BIAL Symposium on the theme of "*Bidirectional interactions between the brain and implantable computers*".

Eberhard Fetz is Professor of Physiology, Biophysics and of Bioengineering, University of Washington, School of Medicine, Seattle (USA) and Head of the Neuroscience Division, Primate Research Center at the same University. He received his Ph.D. in physics from the MIT (Massachusetts Institute of Technology) in 1967. He came to the University of Washington for postdoctoral work in Neuroscience and has been on the faculty ever since.

Among several other honors Professor Fetz was appointed Fellow of the Wissenschaftskolleg zu Berlin, Berlin, and Visiting Professor, College de France in Neuroscience in 2002, in Paris.

He received the Alexander von Humboldt Foundation Research Award 2011 and the New York Academy of Sciences Aspen Brain Forum First Prize in Neurotechnology in 2010.

The citation of this prize states that "Dr. Fetz is a pioneer in the field of neural interfaces and a leading scientist in the field of neuroprosthetics and brain-computer interface research." His work can be considered, indeed, as the cradle of the whole field of Brain-Machine or Computer interfaces.

All began, back in 1969, when Eb Fetz discovered that the brain, at will, can control the activity of cortical neurons in variable patterns. This led to a very well known paper in Science entitled "operant conditioning of cortical unit activity". More recently, he developed a so-called "neurochip", an implantable recurrent brain-computer interface that can record activity of cortical cells during free behavior and convert this activity in real time to steer behavior.

We are anxious to listen to more of this.

BIDIRECTIONAL INTERACTIONS BETWEEN THE BRAIN AND IMPLANTABLE COMPUTERS

Eberbard Fetz *

Recent advances in brain-computer interfaces (BCI), also known as brain-machine interfaces, have demonstrated that brain signals can be tapped directly to allow subjects to control external devices, such as robotic arms or cursors on a computer screen (Carmena et al 2003, Donoghue 2002, Nicolelis 2003, Velliste et al 2008). These signals can be obtained from the scalp via electroencephalographic (EEG) recording, from the surface of the brain via electrocorticograms (ECoG) or from single or multiple neurons in the brain via intra-cortical microelectrodes. The invasiveness of each procedure is inversely proportional to the spatiotemporal specificity of the signals. The subject typically learns to optimize the signals for control of the external device through visual feedback of the ongoing consequences. Efforts are currently underway to provide other modalities of feedback about the controlled device through electrical stimulation of the brain (Bensmaia & Miller 2014).

In contrast, bidirectional brain-computer interfaces (BBCI) provide direct closed-loop activity-dependent stimulation without any external controlled device beyond the computer. The computer itself can be small enough to be carried around and operate continuously during free behavior. We have developed a head-fixed system called the "neurochip" which records activity of cortical neurons in freely behaving monkeys and delivers activity dependent stimulation to the brain, spinal cord or muscles (Mavoori et al 2005, Zanos et al 2011). Similar closed-loop BB-CIs have also been developed (Azin et al 2011), some of them operating via tethered cables (Moritz et al 2008, Rebesco et al 2010, Rolston et al 2010, Venkatraman et al 2009) or through telemetry (Delgado et al 1970, Rouse et al 2011) to provide connections to external computers. The advantage of continuous operation of the BBCI during free behavior

^{*} Department of Physiology & Biophysics and Washington National Primate Research Center, University of Washington, Seattle, USA.

is that the brain can learn to incorporate the artificial recurrent connection into normal behavior. When the loop time is sufficiently short, BB-CIs can also produce spike-timing dependent synaptic plasticity (SPTP) by spike-triggered stimulation.

We have demonstrated the ability of a BBCI to bridge a lost physiological connection and allow brain cells to control functional electrical stimulation (FES) of paralyzed muscles (Moritz et al 2008). The experimental setup is shown in Fig. 1A. The monkey first controlled the position of a cursor on the screen by generating normal torques about the wrist to place the cursor into the target. After the nerves to the muscles were blocked with an anesthetic the monkey quickly learned to control the cursor with activity of a motor cortical neuron. Interestingly, it did not matter whether the cell had any prior relation to the wrist; the activity of essentially all motor cortex cells can be volitionally controlled (Fetz & Baker 1973). Next, the cell activity was converted to electrical stimulation of the agonist muscle, which generated torques that again drove the curser (Fig. 1B). Thus the BBCI allowed the monkey to readily acquire new targets by cell-controlled FES. Bidirectional wrist torques could be produced by using two cells, one activating flexor muscles and the other extensors, or by using one cell and allowing increases and decreases of activity to stimulate a different muscle group. Since any motor cortex cell could be volitionally controlled, this paradigm expands the pool of potential control sources well beyond those neurons that might be originally related to the wrist. Indeed, neurons in many other cortical areas are also likely to be modulated by "top-down" volitional signals (Fetz 2007), making this a powerful paradigm for controlling FES. One might imagine that this strategy puts a considerable "cognitive load" on the brain to control these independent signals, but many experiments have now shown that the brain can quickly adapt to new contingencies. For example, humans required to activate six forearm muscles in unnatural combinations in order to acquire targets learned to do so in about 200 trials (Radhakrishnan et al 2008). Similarly, monkeys learned to control a population of motor cortical neurons in novel ways to drive a cursor into targets in two dimensions (Ganguly & Carmena 2009) or three (Jarosiewicz et al 2008). The remarkable ability of the brain to adapt to new contingencies provides a powerful mechanism to allow arbitrary neurons to control FES.



Figure 1. Brain-controlled functional electrical stimulation (FES) of muscle. a. Schematic shows cortical cell activity converted to FES during peripheral nerve block. b. Example of motor cortex cell activity controlling FES of paralyzed wrist extensors. Wrist torque targets for extension (red shading) and center hold (grey shading) were randomly presented. Monkeys learned to modulate smoothed cell rate to control proportional muscle stimulation. In this case FES was delivered to muscles EDC and ED4,5 at 50/sec, with current proportional to cell rate above a stimulation threshold. Pps indicates pulses per second. c. Histograms of cell rates while acquiring the extensor and center targets, illustrating cell activity used to control FES. Shading indicates target hold period and horizontal line denotes baseline cell rate. From (Moritz et al 2008).

While possible in principle, the FES of muscles through nerves is problematic because electrical stimulation recruits the motor units of a muscle in unnatural order, with large and rapidly fatiguing units recruited first. Also, finely controlled synergistic activation of multiple muscles via FES is challenging. A possible solution is to stimulate in the spinal cord, which evokes synergistic combinations of muscles and recruits motor units in natural order (Moritz et al 2007). Cortically controlled stimulation of spinal cord via BBCIs is a promising strategy to circumvent damaged corticospinal connections (Jackson et al 2006b, Jackson & Zimmermann 2012). In a recent case study of a monkey that had learned the target tracking task and was subsequently rendered paretic by a spinal cord injury, the monkey learned to control intraspinal stimulation by generating increases in cortical field potentials, allowing him to acquire targets again (Nishimura et al 2013b).

A second type of application for BBCIs is to induce synaptic plasticity. Spike-triggered stimulation of a cell's target neurons can strengthen the synaptic connections between them. A first demonstration involved an implanted BBCI that recorded cell activity at one motor cortex site and delivered spike-triggered stimuli at a neighboring site (Jackson et al 2006a). After operating for a day or more during free activity and sleep, the outputs evoked from the two sites changed, and suggested stronger connections from the recording to the stimulation site. These changes were obtained only when the delay between the spike and the stimulus was 50 ms or less, consistent with the effective window for STDP (Caporale & Dan 2008, Dan & Poo 2004, Markram et al 2011). The changes lasted for several days past the end of conditioning, indicating a remarkably robust effect. A similar phenomenon has also been demonstrated in rat cortex, where spike-triggered stimulation changed the inferred functional connectivity between sites (Rebesco et al 2010).

Cortical plasticity could also be produced by using a BBCI to deliver cortical stimuli triggered from EMG of forearm muscles (Lucas & Fetz 2013). The muscle served as a more easily recorded surrogate of cortical cells, whose activity was correlated with the muscle. This EMG-triggered stimulation was sufficient to produce similar cortical reorganization, although the effects did not last as long as with spike-triggered simulation, perhaps due to looser timing between the cortical and muscle activities.

More direct evidence of inducing STDP was obtained by changing the strength of synaptic connections between corticomotoneuronal (CM) cells and their target motoneurons (Nishimura et al 2013b). The spikes recorded from individual CM cells were used to trigger intraspinal stimuli at the site of the cells' target motoneurons during free behavior (Fig. 2). The strength of the CM cell's synaptic connection was measured by the size of the post-spike effects of the cell on its target muscles. These post-spike effects increased in size after a few hours of spiketriggered stimulation, and sometimes remained augmented for days after the end of conditioning. Again, the effective spike-stimulus delays that strengthened the connections were consistent with the STDP window. Interestingly, spike-triggered stimuli delivered at zero delay decreased the strength of the connection. At zero delay the motoneurons were activated before the arrival of the corticospinal impulses. The STDP rule says that if the postsynaptic cell is consistently activated prior to the presynaptic input the connection strength will decrease, as confirmed in this experiment. This study provides the first direct demonstration that STDP can be produced in single cells using normal firing rates of cells recorded during free behavior.



Figure 2. Corticospinal connections strengthened by a BBCI. (A) Schematic showing action potentials of CM cell triggering intraspinal stimuli via neurochip (NC). (B) Cortical recording (top) and SpTA of EMG (bottom) for CM spikes followed after delay of 25 ms by spinal stimulus. SpTA shows postspike facilitation and poststimulus response in same target muscle. (C) SpTAs of EMG acquired before (day 0) and after (day 1) a 22 hr period of conditioning, showing analysis interval (pink square), baseline \pm 2 SD of SpTA (horizontal gray lines), and mean percent increase [MPI] above baseline of feature (horizontal red lines and black numbers). Conditioning increased MPI by 66% (p = 0.0003). Drawings represent monkey performing task on days 0 and 1 and behaving freely during conditioning. From (Nishimura et al 2013a).

A third application of BBCIs is to deliver activity-dependent reinforcement by contingent stimuli delivered to intracranial reward sites (Eaton & Fetz 2012). For example stimulating certain sites in nucleus accumbens can be shown to sustain performance on an operant task (like the target tracking in Fig. 1). Delivering stimuli in such a site triggered by increases in muscular EMG showed that the monkey generated more EMG triggers during "time in" periods when the stimuli were available than during alternating "time-out" periods when the stimulator was turned off. Similar results were obtained when the stimuli were triggered from activity of motor cortex neurons (Libey et al 2013). By operating during free behavior, the BBCI can provide ample time for the monkey to discover the appropriate behavior that delivers reinforcement. An early demonstration of closed-loop operant conditioning was the study of Delgado in which amygdala spindling was used to deliver contingent stimulation in a brain-stem site, using telemetry to close the loop between the brain and requisite instrumentation (Delgado et al 1970). After 2 hours of activity-dependent stimulation the amygdala spindling was reduced specifically at the recording site (not the contralateral side), indicating that the stimulation was aversive, and the control was specific.

In summary, there are innumerable applications of BBCIs, depending on the type of signal recorded, where the stimulus delivered and the transform between recorded activity and stimulation. Each pair of sites has its own functional relationships, which can be investigated by closedloop activity-dependent stimulation. Promising clinical applications of BBCIs are to bridge lost biological connections allowing the brain to regain function, and to strengthen weakened connections that have been damaged by injury. So there are innumerable promising basic research and therapeutic applications for BBCIs remaining to be explored (Potter et al 2014).

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References

Azin M, Guggenmos DJ, Barbay S, Nudo RJ, Mohseni P. 2011. A miniaturized system for spike-triggered intracortical microstimulation in an ambulatory rat. *IEEE Trans Biomed Eng* 58: 2589-97

Bensmaia SJ, Miller LE. 2014. Restoring sensorimotor function through intracortical interfaces: progress and looming challenges. *Nat Rev Neurosci* 15: 313-25

Caporale N, Dan Y. 2008. Spike timing-dependent plasticity: a Hebbian learning rule. *Annu Rev Neurosci* 31: 25-46

Carmena JM, Lebedev MA, Crist RE, O'Doherty JE, Santucci DM, et al. 2003. Learning to control a brain-machine interface for reaching and grasping by primates. *PLoS Biol* 1: E42

Dan Y, Poo MM. 2004. Spike timing-dependent plasticity of neural circuits. *Neuron* 44: 23-30

Delgado JM, Johnston VS, Wallace JD, Bradley RJ. 1970. Operant conditioning of amygdala spindling in the free chimpanzee. *Brain research* 22: 347-62

Donoghue JP. 2002. Connecting cortex to machines: recent advances in brain interfaces. *Nat Neurosci 5* Suppl: 1085-8

Eaton RW, Fetz E. 2012. Operant conditioning of cortical single-unit activity during constrained and free behavior using spike triggered stimulation of intracranial reinforcement sites. *Society for Neuroscience Abstracts*

Fetz EE. 2007. Volitional control of neural activity: implications for brain-computer interfaces. J *Physiol* 579: 571-9

Fetz EE, Baker MA. 1973. Operantly conditioned patterns on precentral unit activity and correlated responses in adjacent cells and contralateral muscles. *J Neurophysiol 36:* 179-204

Ganguly K, Carmena JM. 2009. Emergence of a stable cortical map for neuroprosthetic control. *PLoS Biol 7*: e1000153

Jackson A, Mavoori J, Fetz EE. 2006a. Long-term motor cortex plasticity induced by an electronic neural implant. *Nature* 444: 56-60

Jackson A, Moritz CT, Mavoori J, Lucas TH, Fetz EE. 2006b. The Neurochip BCI: towards a neural prosthesis for upper limb function. *IEEE Trans Neural Syst Rehabil Eng* 14: 187-90

Jackson A, Zimmermann JB. 2012. Neural interfaces for the brain and spinal cord--restoring motor function. *Nature reviews. Neurology* 8: 690-9

Jarosiewicz B, Chase SM, Fraser GW, Velliste M, Kass RE, Schwartz AB. 2008. Functional network reorganization during learning in a brain-computer interface paradigm. *Proceedings of the National Academy of Sciences of the United States of America* 105: 19486-91

Libey TG, Eaton R, Roberts Z, Fetz EE. Society for Neuroscience Abstracts2013.

Lucas TH, Fetz EE. 2013. Myo-cortical crossed feedback reorganizes primate motor cortex output. *J Neurosci* 33: 5261-74
Markram H, Gerstner W, Sjostrom PJ. 2011. A history of spike-timing-dependent plasticity. *Front Synaptic Neurosci* 3: 4

Mavoori J, Jackson A, Diorio C, Fetz E. 2005. An autonomous implantable computer for neural recording and stimulation in unrestrained primates. *J Neurosci Methods* 148: 71-7

Moritz CT, Lucas TH, Perlmutter SI, Fetz EE. 2007. Forelimb movements and muscle responses evoked by microstimulation of cervical spinal cord in sedated monkeys. *J Neurophysiol* 97: 110-20

Moritz CT, Perlmutter SI, Fetz EE. 2008. Direct control of paralysed muscles by cortical neurons. *Nature* 456: 639-42

Nicolelis MA. 2003. Brain-machine interfaces to restore motor function and probe neural circuits. *Nat Rev Neurosci* 4: 417-22

Nishimura Y, Perlmutter SI, Eaton RW, Fetz EE. 2013a. Spike-timing-dependent plasticity in primate corticospinal connections induced during free behavior. *Neuron* 80: 1301-9

Nishimura Y, Perlmutter SI, Fetz EE. 2013b. Restoration of upper limb movement via artificial corticospinal and musculospinal connections in a monkey with spinal cord injury. *Frontiers in neural circuits* 7: 57

Potter SM, El Hady A, Fetz EE. 2014. Closed-loop neuroscience and neuroengineering. *Frontiers in neural circuits* 8: 115

Radhakrishnan SM, Baker SN, Jackson A. 2008. Learning a novel myoelectric--controlled interface task. *J Neurophysiol* 100: 2397-408

Rebesco JM, Stevenson IH, Kording KP, Solla SA, Miller LE. 2010. Rewiring neural interactions by micro-stimulation. *Front Syst Neurosci* 4

Rolston JD, Gross RE, Potter SM. 2010. Closed-loop, open-source electrophysiology. *Front Neurosci* 4

Rouse AG, Stanslaski SR, Cong P, Jensen RM, Afshar P, et al. 2011. A chronic generalized bi-directional brain-machine interface. *J Neural Eng* 8: 036018

Velliste M, Perel S, Spalding MC, Whitford AS, Schwartz AB. 2008. Cortical control of a prosthetic arm for self-feeding. *Nature* 453: 1098-101

Venkatraman S, Elkabany K, Long JD, Yao Y, Carmena JM. 2009. A system for neural recording and closed-loop intracortical microstimulation in awake rodents. *IEEE Trans Biomed Eng 56:* 15-22

Zanos S, Richardson AG, Shupe L, Miles FP, Fetz EE. 2011. The Neurochip-2: an autonomous head-fixed computer for recording and stimulating in freely behaving monkeys. *IEEE Trans Neural Syst Rehabil Eng 19*: 427-35

PALESTRAS LECTURES

LEARNING ABOUT THE BRAIN BY USING BRAIN MACHINE INTERFACES

Nuno Loureiro^{*}, Vítor B. Paixão^{*}, Rui M. Costa^{*}

The brain has a remarkable ability to learn complex rules by changing its neural activity. A Brain Machine Interface (BMI) is a system that records and converts neural activity to control external devices. There are many different paradigms that could give the brain control of an external device through a BMI. We discussed approaches that are active, i.e. that require the engagement of the subject in controlling a device, and where the subject controlling the device develops a sense of agency, i.e. knowledge or awareness that it is controlling the device.

The first approach consists of decoding brain operations. This is probably the most classically used paradigm. It relies on understanding the natural transformation that the brain does to control the body, upper limbs for example, and then to use a decoder (a transformation, a read out) that relies on that transformation to control a robotic arm, in the same example. So typically this approach relies on understanding how the brain executes a natural motor plan and then build a model that relates brain activity to physical movement, and then use this model to have the brain control a device. This type of approach stemmed naturally from prominent studies trying to predict movement direction or velocity from brain activity in motor cortex (Georgopoulos et al., 1986), and has worked rather successfully in both animals and humans (Wessberg et al., 2000) (Taylor et al., 2002) (Velliste et al., 2008) (Serruya et al., 2002) (Carmena et al., 2003) (Shenoy et al., 2003) (Hochberg et al., 2006). It typically uses a rather large number of neurons or activity channels, and its most successful use has been using invasive neural recordings in both humans and non-human primates (Carmena et al., 2003; Hochberg et al., 2006). The classical implementation of this approach implies the recording of neural activity in each subject during natural movement

^{*} Champalimaud Centre for the Unknown, Lisbon, Portugal.

to obtain a model for that particular subject and then the freezing of the model and the application of this model in brain-control mode (Wessberg et al., 2000). Since the first studies were published (Chapin et al., 1999; Wessberg et al., 2000), some adaptations/additions have been done that have made this paradigm more powerful. One for example, is to give feedback to the subject about the performance of the object or actuator, so that the brain understands the transformation and adapts it (Taylor et al., 2002) (Carmena et al., 2003). Another has been to search for the best decoders possible, and even to use adaptive decoders that adapt as the subject makes mistakes, so that each subject can get maximum performance (Santhanam et al., 2006) (Orsborn et al., 2014). Yet another has been to try to get general rules of how the motor cortices encode movement, and use those rules to implement the decoder, rather than the particular fit of every subject (Velliste et al., 2008).

Another set of approaches has been to classify the brain activity or brain states when subjects are thinking of a particular movement or situation, or when they are paying selective attention to a particular stimulus. In the imagery approach the subject is asked to imagine particular movements (motor imagery) or situations (imagery in general) and then the activity of brain areas such as the motor cortex is recorded and a classifier is applied to separate for example activity when the subject is thinking of moving the left hand from activity when the subject is thinking of moving the right hand (Pfurtscheller et al., 2003b) (Pfurtscheller et al., 2003a) (Sitaram et al., 2007). This differential activity is decoded by the classifier as a binary signal (for example left versus right, up versus down) and so the classifier can be used as a decoder to control devices (for example a cursor). In practical terms the subject then thinks about moving the right hand or the left hand to control a cursor to go right or left, for example. This approach has been successful in treating patients with stroke and also in brain-machine interface control (Neuper et al., 2006) (Naeem et al., 2006) (Pfurtscheller et al., 2003b) (Pfurtscheller et al., 2003a) (Sitaram et al., 2007) (Ortner et al., 2012).

Another variation of the use of classifiers of brain states as decoders that has had some success is the use of different stimuli to evoke brain activity (even related potentials recorded from an encephalogram, for example) to evoke particular brain activity, and use a classifier to differentiate the activity evoked by different stimuli. The subject can modulate the response of the brain to a particular stimulus by paying more attention to that stimulus (Muller-Putz et al., 2005). The subject can therefore make binary choices by focusing the attention in a particular stimulus when it is presented than another (Muller-Putz et al., 2005) (Guger et al., 2012a) (Fazel-Rezai et al., 2012) (Guger et al., 2012b). For example, if a particular visual stimulus means go left and another means go right then the subject would focus on the stimulus that means go left to choose left and vice-versa for right. This has been used successfully to control BMIs, namely to do spelling in computers (Guger et al., 2012b).

In our talk we focused the discussion on operant BMI paradigms, which we have been developing in collaboration with the Carmena Lab at Berkeley. In these paradigms the brain is connected to a decoder that transforms its neural activity in control of an actuator (a cursor, a sound, a robot) through a set of arbitrary rules, and then given feedback of its control of the actuator. The brain then learns to control the actuator by a mechanism of operant conditioning. The operant learning paradigm was first successfully implemented by having the activity of single neurons in the pre-central cortex of monkeys control an actuator (Fetz, 1969). In later studies it was shown that primates could learn to control decoders that used the activity of an ensemble of neurons (not just a single neuron). These studies also showed that a monkey's brain was able to develop and consolidate a map that represented how to control the disembodied device (Ganguly and Carmena, 2009), much like we consolidate motor skills (Costa et al., 2004) (Jin and Costa, 2010) (Doyon et al., 2003) (Karni et al., 1998). Furthermore, after consolidation of the first decoder, primates are able to learn a second separate decoder to control the BMI, and were also able to switch back and forth between the two. These findings suggest that Brain-Machine control can be learned, consolidated, and resistant to interference in learning.

Operantly learning to control new Brain Machine Interfaces involves plasticity throughout the brain, much like controlling one's own arm or learning how to type in the computer. A recent study of ours found coherence between the activity of neurons controlling a BMI and activity in other structures, suggesting that not only the neurons that directly influence the BMI are responsible for the control of the actuator, but that other structures in the brain may also be involved in the process (Koralek et al., 2013). Furthermore, it was also shown that plasticity in corticostriatal circuits, which are usually involved in the operant learning of physical actions (pressing a lever, typing in a keyboard, etc.), are also involved and required for the operant learning of Brain-Machine control (Koralek et al., 2012).

This control has been shown to be sensitive to devaluation of the outcome, and to the contingency between brain activity and obtainance of the outcome, suggesting that subjects (animals so far), develop a sense of agency and understand the contingencies between brain activity, the control of the actuator, and the obtainance of the outcome (Koralek et al., 2012).

These studies show that the paradigm of operant control of BMIs can be very powerful. Studies of neurofeedback have attempted to have subjects learn what their neural activity represents (Hardman et al., 1997), and have shown success in BMI control (Hinterberger et al., 2005) (Neuper et al., 2003). However, there are no published studies as of yet using this BMI learning paradigm with a fixed decoder from day to day in humans.

We also discussed preliminary data on a novel Brain-Machine-Interface (BMI) paradigm that can be used to control devices and study learning dynamics in humans. We designed a decoder, i.e. a fixed set of rules necessary to transform the neural activity of a user (recorded using an electroencephalogram (EEG) into an output control signal. As in the mouse task, the decoder is maintained constant throughout training, so that all changes in performance can be attributed to changes in the neural activity. This operant EEG-based BMI task for humans can then be used to study the underlying learning dynamics.

The task consisted of three 10-minute engaged runs per day, throughout a training period of 10 days. This information is used to set the position of a ball on a screen. Both the decoder and selected electrodes to be used are established during the first session, and do not change throughout the training period. Preliminary results show that users reach an above-chance control and learn the decoder in just a few days, as their performance increases throughout training. Furthermore, subjects can remember this for a few weeks. This Operant-BMI approach may provide great benefits for users in a wide variety of domains. In order to test its applicability to a real-life scenario, we set to test whether this method could be used to control an airplane. We conducted a pilot experiment as a proof of principle for our hypothesis. The neural activity was converted using the same decoder and fed into the control algorithm of a DA-42 airplane simulator. We observed that after training one user was able to reach and maintain the target with an accuracy of $\pm 20^{\circ}$ during the interval.

We concluded that operant learning of BMI control can be akin to operant learning of control of our own body, using even similar circuits and molecular mechanisms, and a very powerful paradigm for BMI control.

References

Carmena, J.M., Lebedev, M.A., Crist, R.E., O'Doherty, J.E., Santucci, D.M., Dimitrov, D., Patil, P.G., Henriquez, C.S., and Nicolelis, M.A. (2003). Learning to Control a Brain-Machine Interface for Reaching and Grasping by Primates. PLoS Biol *1*, 193-208.

Chapin, J.K., Moxon, K.A., Markowitz, R.S., and Nicolelis, M.A. (1999). Realtime control of a robot arm using simultaneously recorded neurons in the motor cortex. Nat Neurosci *2*, 664-670.

Costa, R.M., Cohen, D., and Nicolelis, M.A. (2004). Differential corticostriatal plasticity during fast and slow motor skill learning in mice. Curr Biol *14*, 1124-1134.

Doyon, J., Penhune, V., and Ungerleider, L.G. (2003). Distinct contribution of the cortico-striatal and cortico-cerebellar systems to motor skill learning. Neuropsychologia *41*, 252-262.

Fazel-Rezai, R., Allison, B.Z., Guger, C., Sellers, E.W., Kleih, S.C., and Kubler, A. (2012). P300 brain computer interface: current challenges and emerging trends. Front Neuroeng 5, 14.

Fetz, E.E. (1969). Operant conditioning of cortical unit activity. Science 163, 955-958.

Ganguly, K., and Carmena, J.M. (2009). Emergence of a stable cortical map for neuroprosthetic control. PLoS Biol 7, e1000153.

Georgopoulos, A.P., Schwartz, A.B., and Kettner, R.E. (1986). Neuronal population coding of movement direction. Science *233*, 1416-1419.

Guger, C., Allison, B.Z., Grosswindhager, B., Pruckl, R., Hintermuller, C., Kapeller, C., Bruckner, M., Krausz, G., and Edlinger, G. (2012a). How Many People Could Use an SSVEP BCI? Front Neurosci *6*, 169.

Guger, C., Krausz, G., Allison, B.Z., and Edlinger, G. (2012b). Comparison of dry and gel based electrodes for p300 brain-computer interfaces. Front Neurosci 6, 60.

Hardman, E., Gruzelier, J., Cheesman, K., Jones, C., Liddiard, D., Schleichert, H., and Birbaumer, N. (1997). Frontal interhemispheric asymmetry: self regulation and individual differences in humans. Neurosci Lett *221*, 117-120.

LECTURES

Hinterberger, T., Veit, R., Wilhelm, B., Weiskopf, N., Vatine, J.J., and Birbaumer, N. (2005). Neuronal mechanisms underlying control of a brain-computer interface. Eur J Neurosci *21*, 3169-3181.

Hochberg, L.R., Serruya, M.D., Friehs, G.M., Mukand, J.A., Saleh, M., Caplan, A.H., Branner, A., Chen, D., Penn, R.D., and Donoghue, J.P. (2006). Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature *442*, 164-171.

Jin, X., and Costa, R.M. (2010). Start/stop signals emerge in nigrostriatal circuits during sequence learning. Nature *466*, 457-462.

Karni, A., Meyer, G., Rey-Hipolito, C., Jezzard, P., Adams, M.M., Turner, R., and Ungerleider, L.G. (1998). The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex. Proc Natl Acad Sci U S A *95*, 861-868.

Koralek, A.C., Costa, R.M., and Carmena, J.M. (2013). Temporally precise cellspecific coherence develops in corticostriatal networks during learning. Neuron *79*, 865-872.

Koralek, A.C., Jin, X., Long, J.D., 2nd, Costa, R.M., and Carmena, J.M. (2012). Corticostriatal plasticity is necessary for learning intentional neuroprosthetic skills. Nature 483, 331-335.

Muller-Putz, G.R., Scherer, R., Brauneis, C., and Pfurtscheller, G. (2005). Steadystate visual evoked potential (SSVEP)-based communication: impact of harmonic frequency components. J Neural Eng 2, *123*-130.

Naeem, M., Brunner, C., Leeb, R., Graimann, B., and Pfurtscheller, G. (2006). Seperability of four-class motor imagery data using independent components analysis. J Neural Eng 3, 208-216.

Neuper, C., Muller, G.R., Kubler, A., Birbaumer, N., and Pfurtscheller, G. (2003). Clinical application of an EEG-based brain-computer interface: a case study in a patient with severe motor impairment. Clin Neurophysiol 114, *399*-409.

Neuper, C., Muller-Putz, G.R., Scherer, R., and Pfurtscheller, G. (2006). Motor imagery and EEG-based control of spelling devices and neuroprostheses. Prog Brain Res *159*, 393-409.

Orsborn, A.L., Moorman, H.G., Overduin, S.A., Shanechi, M.M., Dimitrov, D.F., and Carmena, J.M. (2014). Closed-loop decoder adaptation shapes neural plasticity for skillful neuroprosthetic control. Neuron *82*, 1380-1393.

Ortner, R., Irimia, D.C., Scharinger, J., and Guger, C. (2012). A motor imagery based brain-computer interface for stroke rehabilitation. Stud Health Technol Inform *181*, 319-323.

Pfurtscheller, G., Muller, G.R., Pfurtscheller, J., Gerner, H.J., and Rupp, R. (2003a). 'Thought'-control of functional electrical stimulation to restore hand grasp in a patient with tetraplegia. Neurosci Lett *351*, 33-36.

Pfurtscheller, G., Neuper, C., Muller, G.R., Obermaier, B., Krausz, G., Schlogl,

A., Scherer, R., Graimann, B., Keinrath, C., Skliris, D., et al. (2003b). Graz-BCI: state of the art and clinical applications. IEEE Trans Neural Syst Rehabil Eng 11, 177-180.

Santhanam, G., Ryu, S.I., Yu, B.M., Afshar, A., and Shenoy, K.V. (2006). A high-performance brain-computer interface. Nature 442, 195-198.

Serruya, M.D., Hatsopoulos, N.G., Paninski, L., Fellows, M.R., and Donoghue, J.P. (2002). Instant neural control of a movement signal. Nature *416*, 141-142.

Shenoy, K.V., Meeker, D., Cao, S., Kureshi, S.A., Pesaran, B., Buneo, C.A., Batista, A.P., Mitra, P.P., Burdick, J.W., and Andersen, R.A. (2003). Neural prosthetic control signals from plan activity. Neuroreport *14*, 591-596.

Sitaram, R., Zhang, H., Guan, C., Thulasidas, M., Hoshi, Y., Ishikawa, A., Shimizu, K., and Birbaumer, N. (2007). Temporal classification of multichannel near-infrared spectroscopy signals of motor imagery for developing a brain-computer interface. Neuroimage *34*, 1416-1427.

Taylor, D.M., Tillery, S.I., and Schwartz, A.B. (2002). Direct cortical control of 3D neuroprosthetic devices. Science *296*, 1829-1832.

Velliste, M., Perel, S., Spalding, M.C., Whitford, A.S., and Schwartz, A.B. (2008). Cortical control of a prosthetic arm for self-feeding. Nature *453*, 1098-1101.

Wessberg, J., Stambaugh, C.R., Kralik, J.D., Beck, P.D., Laubach, M., Chapin, J.K., Kim, J., Biggs, S.J., Srinivasan, M.A., and Nicolelis, M.A. (2000). Real-time prediction of hand trajectory by ensembles of cortical neurons in primates. Nature 408, 361-365.

BRAIN-COMPUTER INTERFACE IMPLANTS: THE POWER AND POTENTIAL OF CORTICAL SURFACE ELECTRODES

Nick Ramsey *

Abstract

Modern tools in human neuroscience provide valuable new ideas for Brain-Computer Interface solutions for paralyzed people. Interest in brain implants is increasing, given the promise of better signals and better performance. Development of implants requires a solid understanding of brain function, topography and brain signals. Research with implants is, however, severely limited to only experimental BCI implants or patients with electrodes implanted for diagnostic purposes, hence alternative methods for research are urgently needed. Several paths are currently pursued regarding implants, with variations in types of electrodes. The most recent development involves brain surface electrodes, the topic of this paper. I here discuss the concept of implantable BCI and the research leading to research with paralyzed people.

Introduction

Brain-Computer Interface (BCI) technologies are designed to convert brain signals to command signals for software (e.g. text editors on computers) or hardware (e.g. wheelchair). They are primarily of interest to people with severe motor disabilities (e.g. due to neuromuscular disease or severe stroke), where standard assistive technologies offer no solution. Other applications of BCI include gaming with faster user-actions since nerves and muscles can be bypassed, or tracking of brain states for driving a vehicle or operating machinery (give alarm if person becomes distracted). Most BCI research uses scalp EEG electrodes to obtain brain signals, but the skull imposes a significant attenuation and blurring of brain signals.

^{*} University Medical Center of Utrecht, The Netherlands.

So far, no scalp EEG system can decode brain signals well enough for clinical application. Electrodes can also be positioned underneath the skull, on or in the cortex, yielding dramatically better brain signals. Yet, there is no implant yet for clinical application. Evidence to support the expectation that implants will work well, has to meet much higher standards than is the case for scalp-EEG solutions, while means to obtain such evidence is significantly limited since one needs to implant in people to be able to collect evidence. Nevertheless, development of implants is proceeding at an accelerating pace. Here, research performed the last 3-4 decades in non-human primates has benefitted development of BCI with needle electrodes. As I will explain, evidence for decoding of brain signals obtained from brain surface electrodes can be provided with the use of state of the art brain imaging techniques, allowing for proof of concept research in healthy volunteers, thus reducing the need for research with implants or animals.

With recent successes in decoding intracranial human brain signals for control of robot arms [1,2], the importance of understanding the source and nature of brain signals for BCI becomes important. Several issues are key to future application of BCI technology to paralyzed end users. First, which brain regions yield decodable signals will need to be explored. Second, the stability of neural signals and the false detection rates for decoding are likely to determine acceptance of BCI systems. Third, tradeoffs between signal features and long-term effects of implants on tissue and signal quality need to be evaluated. In this paper I will focus on the first issue.

The most successful recent reports are based on single and multineuron recordings from the motor cortex [1,2]. The research follows decades of non-human primate research with indwelling electrodes (needles inserted into the grey matter layers of the neocortex) and capitalizes on accumulating insight in the behaviour of motor neurons. Accordingly, BCI systems based on indwelling electrodes primarily utilizes the motor system. The signals from multiple neurons (spikes) are translated into continuous control signals for actuators like a robotic arm, providing a user with a replacement of the arm, with which actions can be generated.

With advancing understanding of the human brain obtained with non-invasive functional neuroimaging techniques, other brain regions and brain functions become of interest for BCI [3]. The human brain exhibits a highly organized topographical distribution of functions across the cortex. A very approximate topography has been uncovered with neuropsychological research (linking deficits to damaged brain regions), but only now we can localize specific functions and associated regions for each individual person, with use of fMRI [4]. Moreover, with increasing strength of the magnetic field the spatial resolution increases, revealing ever more detailed spatial organization of the human cortex [5]. Spatial patterns of neural activity associated with specific mental events, are robust enough for some degree of decoding, as evidenced by a growing body of fMRI studies [6,7].

For BCI purposes, the spatial activity patterns are of great interest. The knowledge of functions served by brain regions broadens the spectrum of intracranial BCI beyond the motor system. For instance, the visual system can be used to decode the direction of covert spatial attention (see below). Electrodes placed on the exact locations of informative brain regions could be the basis of BCI based on signals not from multiple neurons but from neuronal ensembles (tens to hundreds of thousands of neurons)[8]. Patients with epilepsy sometimes have such electrodes implanted for a week or so, to locate the source of seizures. They can also participate in BCI research, but their number (and available time for research) is severely limited. fMRI would be a logical alternative but it does not measure the same as ECoG.

fMRI measures neural activity in terms of metabolic activity in grey matter, and this is highly correlated with power in the high gamma range as measured with ECoG electrodes [9,10,11]. We have recently shown that activity patterns in the hand region of sensorimotor cortex matches quite well (accurate to 1-2 mm) between fMRI at 7 Tesla, and ECoG with a distance of 3 mm between electrodes [12], and that the magnitude of fMRI activity correlates well with that of gamma power in ECoG [10]. Hence, fMRI at 7 Tesla provides a promising means of investigating optimal regions for ECoG-based BCI. Importantly, decoding neural activity patterns is most suitable for classifying discrete events as opposed to continuous movements. Hence controlling a robot arm is not the primary goal of ECoG BCI. Instead, discrete pattern classification capitalized on the ability to control computer programs by selecting specific icons (hence routines) from multiple, or clicking trough menu's. Perhaps an appropriate analogy is writing (robot arm control) versus typing (ECoG classification).

Decoding of patterns of neural activity on the cortex with 7T fMRI has revealed that much information can be obtained from patches of cortex as small as a few square cm [5, 8]. Patterns representing specific movements and sensory events are generated by collections of neuronal ensembles. Different sensations, perceptions and actions engage different sets of ensembles, resulting in different patterns on the cortical surface. fMRI measures rather slow vascular responses to neural activity and can not resolve temporal patterns at the neuronally relevant scale of tens of ms. Hence where temporal information is important, fMRI will not (yet) be capable of revealing that. In what follows I will discuss two new target regions for electrode placement in ECoG BCI, and one more conventional region but with a different goal. Studies involved 7T fMRI and/or ECoG.

Studies

Decoding gestures from the sensorimotor hand area

We showed that 4 different hand gestures (from the sign language alphabet) can be decoded with fMRI based on signal from the sensorimotor hand region alone, with an accuracy of 63% (chance level 25%)[8]. This is an under estimation though, because we also found a strong correlation between consistency of making the gestures, and decoding performance. Hence, with more extensive training of the gestures, near 100% decoding can be expected. The same paradigm was used in several ECoG patients, with high-density ECoG grids (32 or 64 electrodes with 3 mm pitch) [13]. Here the position of the grid was not always accurate on the hand knob. In those with good position, 70-95 % decoding was achieved. With a poor position (1-2 cm away from the knob), near chance levels were observed. These findings encourage further investigation of gesture-base BCI, where we envision that the paralyzed user can spell text by trying to make one of 10-20 gestures, and move through software menu's by selecting icons.

Decoding speech from sensorimotor face area

Spoken phonemes can be decoded from electrical signals from the

face. Different phonemes require different muscles and should therefore be decodable from motor cortex. With fMRI we failed to obtain good decoding, which was due to similarity of activity patterns across 4 phonemes. Facial movements, however, could be decoded with very high accuracy (85%, chance level 25%). Here also, decoding was performed on a selected patch of cortex. In several ECoG patients high-density grids were positioned on the face area. Here decoding of phonemes was poor as it was with fMRI. However, when adding the temporal dimension in the feature selection algorithm, a significant improvement was obtained, leading to more than 70% accuracy.

Decoding from covert visual attention (COVISA)

Directing visual attention to a specific point in the visual field can be performed without moving the eyes to that point. Brain activity responds to this covert attention and can be detected with fMRI [14]. We recently showed that fMRI patterns can be decoded for detecting and discriminating attention to the left and to the right [15] and to 4 directions (adding top and bottom)[16], with accuracies of 92% and 80% respectively. With more advanced feature selection, and with inclusion of only voxels in the cortical surface (excluding deeper voxels and sulci) we still obtained 91% performance (chance 25%)[17]. Finally we performed an online experiment where volunteers could control a robot in real time in another room. Control was conducted with COVISA [18]. Participants all succeeded in moving the robot along a specific trajectory with significant accuracy. These studies provide proof of concept that COVISA BCI could be used for navigation of a tele-presence robot and perhaps a wheelchair

State of the art BCI implant

The research described above mainly focuses on decoding advanced intentions from brain activity patterns, for BCI implants. This level of complexity is, however, not a prerequisite for an implant. Devices need to be developed and approved for human use, requiring significant investment while the success of BCI implants in daily use by paralyzed people at home, is by no means a given. To move BCI into medical application and independent home use, we first need to overcome the huge challenge of improving reliability of decoding to a level close to reliability of moving one's own limbs. Low reliability will lead to user dissatisfaction and consequently will discourage commercial interest in BCI implant manufacturing and slow down development. Testing BCI systems only under laboratory circumstances is likely to lead to overly optimistic expectations regarding their performance at the users home (with no technical experts available)

To bridge the gap between experimental and practical daily use of a BCI implant for paralyzed people, we initiated a clinical study in 2014 [19], with the goal of accomplishing a very reliable (hence simple) BCI system, that can serve the needs of the most severely paralyzed, notably people with Locked-in Syndrome. The Utrecht Neuroprosthesis system (UNP) only features 2-4 channels and can thus not decode larger brain activity patterns. It will also only generate a digital click. With this, a brain-controlled button so to speak, users can operate a wide range of standard assistive technologies, such as spelling software or programs to control lights and doors. The implant was manufactured in close collaboration with a large company, and involves surgical positioning of several electrodes under the skull. Patients will, if all succeeds, be able to communicate independently from their caregivers at any time of day or night, just by clicking through menu's on a computer screen. The research leading up to the UNP trial included evidence of decodability in epilepsy patients with grids [3, 20], ways to deal with false positives [21] and predictive value of fMRI for locating optimal electrode sites [9].

In summary, neuroscience provides insights in human brain function that can guide research on intracranial BCI, extending beyond the more conventional sensorimotor cortex indwelling electrode approach. Which approach will prove to be the most successful in becoming a device that meets the needs of paralyzed people, is as of yet quite unclear. Intracranial systems will have to compete with non-invasive BCI approaches also, some of which are currently being tested in end user studies. However, the high-field fMRI studies are increasingly promising in providing proof of concept. Moreover, fMRI can be used also to evaluate effects of BCI on brain activity itself (changes following multiple BCI sessions in the scanner), and on the subjective experience of the user. Finally, since we do not know how users respond to BCI implants and what level of performance is required for their satisfaction, studies with very basic implants are necessary. These will provide the necessary insights into what is needed to make more versatile BCI systems meet the needs of paralyzed users.

References

1. L. R. Hochberg, D. Bacher, B. Jarosiewicz, N. Y. Masse, J. D. Simeral, J. Vogel, S. Haddadin, J. Liu, S. S. Cash, P. van der Smagt, J. P. Donoghue, Reach and grasp by people with tetraplegia using a neurally controlled robotic arm, Nature. 2012 May 16;485(7398):372-5.

2. J. L. Collinger, B. Wodlinger, J. E. Downey, W. Wang, E. C. Tyler-Kabara, D. J. Weber, A. J. McMorland, M. Velliste, M. L. Boninger, A. B. Schwartz, Highperformance neuroprosthetic control by an individual with tetraplegia, Lancet. 2013 Feb 16;381(9866):557-64.

3. N. F. Ramsey, M. P. van den Heuvel, K. H. Kho, F. S. Leijten, Towards human BCI applications based on cognitive brain systems: an investigation of neural signals recorded from the dorsolateral prefrontal cortex, IEEE Trans Neural Syst Rehabil Eng. 2006 Jun;14(2):214-7.

4. G. J. Rutten, N. F. Ramsey, The role of functional magnetic resonance imaging in brain surgery, Neurosurg Focus. 2010 Feb;28(2):E4.

5. R. M. Sanchez-Panchuelo, S. Francis, R. Bowtell, D. Schluppeck, Mapping human somatosensory cortex in individual subjects with 7 T functional MRI. J Neurophysiol. 2010, 103:2544–2556.

6. J. V. Haxby, Multivariate pattern analysis of fMRI: the early beginnings, Neuroimage. 2012 Aug 15;62(2):852-5.

7. Y. Miyawaki, H. Uchida, O. Yamashita, M. Sato, Y. Morito, H. C. Tanabe, N. Sadato, Y. Kamitani, Visual image reconstruction from human brain activity using a combination of multiscale local image decoders, Neuron, 60(5):915{929, 2008.

8. M. G. Bleichner, J. M. Jansma, J. Sellmeijer, M. Raemaekers, N. F. Ramsey, Give Me a Sign: Decoding Complex Coordinated Hand Movements Using High-Field fMRI, Brain Topogr. 2013 (in press)

9. D. Hermes, K. J. Miller, M. J. Vansteensel, E. J. Aarnoutse, F. S. Leijten, N. F. Ramsey, Neurophysiologic correlates of fMRI in human motor cortex, Hum Brain Mapp. 2012 Jul;33(7):1689-99

10. J. C. Siero, D. Hermes, H. Hoogduin, P. R. Luijten, N. Petridou, N. F. Ramsey, BOLD consistently matches electrophysiology in human sensorimotor cortex at increasing movement rates: a combined 7T fMRI and ECoG study on neurovascular coupling, J Cereb Blood Flow Metab. 2013 Sep;33(9):1448-56

11. J. P. Lachaux, P. P. Fonlupt, P. P. Kahane PP, L. Minotti, D. Hoffmann, O. Bertrand, M. Baciu, Relationship between task-related gamma oscillations and BOLD signal: new insights from combined fMRI and intracranial EEG. Hum Brain Mapp 2007, 28:1368–1375.

12. J. C. Siero, D. Hermes, H. Hoogduin, P. R. Luijten, N. F. Ramsey, N. Petridou. BOLD matches neuronal activity at the mm scale: a combined 7T fMRI and ECoG study in human sensorimotor cortex, Neuroimage (In Press)

13. M.G. Bleichner, Z.V. Freudenburg, J.M. Jansma, E.J. Aarnoutse, M.J. Vansteensel, N.F. Ramsey, Give me a sign: Decoding complex hand gestures using high – density electrocorticography, Brain Struct Func (In Press)

14. J. A. Brefczynski, E. A. DeYoe, A physiological correlate of the 'spotlight' of visual attention, Nat Neurosci 1999, 2(4):370–374

15. P. Andersson, J. P. Pluim, J. C. Siero, S. Klein, M. A. Viergever, N. F. Ramsey, Real-time decoding of brain responses to visuospatial attention using 7T fMRI, PLoS One. 2011;6(11):e27638.

16. P. Andersson, N. F. Ramsey, M. Raemaekers, M. A. Viergever, J. P. Pluim, Real-time decoding of the direction of covert visuospatial attention, J Neural Eng. 2012 Aug;9(4):045004

17. P. Andersson, N. F. Ramsey, M. A. Viergever, J. P. Pluim, 7T fMRI reveals feasibility of covert visual attention-based brain-computer interfacing with signals obtained solely from cortical grey matter accessible by subdural surface electrodes, Clin Neurophysiol. 2013 Nov;124(11):2191-7

18. P. Andersson, J. P. Pluim, M. A. Viergever, N. F. Ramsey, Navigation of a telepresence robot via covert visuospatial attention and real-time fMRI, Brain Topogr. 2013 Jan;26(1):177-85.

19. www.neuroprosthesis.eu

20. M.J. Vansteensel, D. Hermes, E.J. Aarnoutse, M.G. Bleichner, G. Schalk, P.C. van Rijen, F.S.S. Leijten, N.F. Ramsey. Brain-Computer Interfacing Based on Cognitive Control. Ann Neurol. 2010 67(6): 809-16

21. A. Torres Valderrama, P. Paclik, M.J. Vansteensel, E.J. Aarnoutse, N.F. Ramsey. Error probability of intracranial brain computer interfaces under non-task elicited brain states. Clin Neurophysiol 2012 123(12):2392-401

BRAIN-MACHINE INTERFACES (BMIS) IN PARALYSIS

Ander Ramos Murguialday *

Brain Machine Interfaces (BMIs) are systems that record signals from the brain and translate them into signals that can be used to control any kind of device, from a computer cursor, to a wheelchair, a robotic arm or even to music. Recently BMIs have been postulated as functional tools for several clinical conditions. During the presentation Ander Ramos-Murguialday talked about two clinical applications for BMIs: 1) Motor restoration: mainly talking about restoring motor function in paralyzed stroke patients and 2) Communication: regarding the restoration of communication of completely locked in patients due to amyotrophic lateral sclerosis (ALS).

Motor restoration (STROKE)

Initially most of the developed BMIs tended to provide visual feedback, as simple as a cursor moving, a thermometer, or as complex as a multiple degrees of freedom robotic arm movement. Later on other means of feedback were used as auditory or tactile feedback. All of these possibilities were tried before and the neurophysiology involved was studied. From a motor rehabilitation point of view (especially for stroke patients, who normally preserve their afference) there was a mean of feedback that had not been explored before: the proprioception.

This modality appeared to be the most natural way to close the loop between the intention to produce one movement and the same exact movement, i.e. motor restoration. Some first approaches were performed in a sequential manner. First the BMI user had to complete a classic BMI task (e.g. moving cursor on the screen to reach a target) imagining a movement (e.g. opening and closing the hand) and were provided with visual feedback [Barbero et al 2010, Leeb et al 2006, Blankertz et al

^{*} Institute of Medical Psychology and Behavioral Neurobiology, Eberhard Karls University of Tubingen, Germany.

2008, Abbott 2006, Hinterberger et al 2004]. If the task was successfully accomplished a robotic orthosis will reproduced the movements used for the motor imagery task (open and close the hand). Ramos-Murguialday and colleagues used a motor sensorimotor rhythm based BMI coupled with a robotic orthosis in an online manner (i.e. with a delay around 250 msec), thus closing the loop in a more "natural" fashion. They demonstrated that although using EEG technology (prone to noise), the system could be used to induce motor learning. Furthermore, proprioceptive feedback of the sensorimotor rhythm resulted in stronger activations of the networks involved in visuomotor tasks [Ramos-Murguialday et al 2012]. This effect was used in a proof of concept double blinded controlled clinical study with 30 stroke patients with complete hand paralysis.

Injuries of the corticospinal system, e.g. due to stroke, belong to the leading causes of long-term disability (Ward et al 2004). Each year approximately 20 million people suffer a stroke in the industrialized nations (MacMahon et al 2005). Of those who survive, five million remain severely handicapped and dependent on assistance in daily life. While motor function can significantly improve in the first months after stroke, further recovery is often slow or non-existent (Krakauer et al 2005, Gladstone et al 2002, Duncan et al 1992, Party 2008). The last years yielded the development and clinical assessment of various neurorehabilitation approaches, some of them have proven to be highly efficient (Langhorne et al 2011), e.g. constraint-induced movement therapy (CIMT), but these rehabilitation strategies require sufficient residual motor function often not present in chronic stroke patients. For these patients no standardized and accepted treatment strategy exists.



Figure 1. Stroke Rehabilitation BMI Experimental Setup: Left panel: patient controlling the reach and grasp movement of his paretic limb using the EEG-based BMI system. On the right Dr. Ramos-Murguialday adjusting the robotic orthosis hand to be controlled by means of an EEG-BMI by the user.

30 chronic stroke patients (20 male, mean age: 53.7±11.9 years; interval since stroke: 67.8 ± 57.6 months) without residual finger extension were randomly assigned to two different treatment groups: an experimental group receiving contingent BMI feedback during training (n=16), and a control group receiving random (sham) BMI feedback (n=14). While the experimental group (n=16) received daily ipsilesional BMI training translating ipsilesional sensorimotor-rhythm modulation into contingent paretic upper limb motions, in the control group (n=14) paretic upper limb motions occurred independent of brain activity. Both interventions were followed by one hour of behavioral physiotherapy. This regime was applied over four weeks (Ramos-Murguialday et al 2013). Twice before the first and after the last training day, a battery of tests comprising upper limb motor function was assessed using a combined hand and arm modified version of the standard impairment scale called Fugl Meyer, electromyography (EMG), transcranial magnetic stimulation (TMS), electroencephalography (EEG) placebo questionnaires and functional MRI, were performed.

Fugl Meyer (FMA) scores improved significantly more in the experimental than in the control group, presenting a significant

improvement of FMAS scores the experimental group only (3.41 ± 0.563) points difference, p=0.018) reflecting a clinically meaningful change from no activity to some in paretic muscles.

The significant reduction in motor impairment in the experimental group correlated with changes in functional MRI laterality index and with paretic hand electromyography activity increase. Placebo-expectancy scores did not show any difference between groups. Therefore, Ramos-Murguialday et al concluded that the addition of BMI training to behaviorally oriented physiotherapy can be used to induce functional improvements in motor function in chronic stroke patients without residual finger movements and may open a new door in stroke neurorehabilitation (Ramos-Murguialday et al 2013).

Communication restoration (Amyotrophic Lateral Sclerosis)

Patients with progressive motor neuron disease, particular ALS, Guillain-Barre' syndrome and subcortical brain cardiovascular accidents, as well as patients with traumatic brain injury in vegetative state (Kotchoubey et al 2005) may suffer from locked-in syndrome (LIS) or completely locked-in syndrome (CLIS). LIS is defined as complete paralysis with one or a few voluntary functions left (usually small eye or face movements). CLIS consists of complete cessation of volitional control of all voluntary somatic–motor functions. It is speculated that patients in LIS and CLIS show intact auditory and tactile perception and intact cognitive functions, usually measured with ERPs (Kotchoubey et al 2005) or fMRI (Owen et al 2006). However, visual perception is also frequently compromised through paralysis of eye muscles (no blinking and poor care-giving).

Currently there is a lack of physiological measures to define the transition from the LIS to the CLIS in a patient suffering from amyotrophic lateral sclerosis (ALS). Furthermore, no standardized assessment scale exists for the late stages of ALS. However, there is a fundamental difference between the two: communication is still possible within LIS but up to now impossible in the CLIS (Kübler and Birbaumer, 2008; Hinterberger et al., 2005a).

The only remaining possibility to retain communication in the CLIS depends on neuroprosthetic devices, particularly brain-computerinterfaces (BCIs). Successful application of visual or autonomic signals or sniffing in the CLIS was only reported once in a single case using recordings of pH from mouth saliva (Wilhelm et al., 2006). BCIs depend on differentiable neural signals (i.e. to encode a "yes" and "no" signal). Therefore, a precise characterization and prediction of the CLIS seems mandatory (Kübler and Birbaumer, 2008). Peripheral autonomic psychophysiological measures could also be used for communication analogous to the use of skin conductance responses (SCR), heart rate (HR) and respiration in lie detection. Patients may signal "yes" or "no" by changing one of those response systems activities. In the paralyzed artificially ventilated ALS patient HR-variability might be severely reduced by the paced artificial respiration and lack of muscle activity necessary for HR-increases. Voluntary operant regulation of HR-decrease is extremely difficult to learn and uses different psychophysiological mechanisms (Cuthbert et al., 1981) than control of HR-increase. Therefore, HRcontrol, sniffing or breathing control is not possible in advanced ALS.

To investigate the transition between LIS and CLIS, Ramos-Murguialday and colleagues (2011) performed six different physiological tests in an ALS patient who went through the above mentioned transition and was implanted with an electrocorticographic grid of electrodes epidurally, to gain insight into the associated physiological changes and to propose the most appropriate approach for a communication system in CLIS, supported by neurophysiological data.

At the very end of the LIS there was no facial muscle activity, nor external anal sphincter but eye control. Eye movements were slow and lasted for short periods only. During CLIS event related brain potentials (ERP) to passive limb movements and auditory stimuli were recorded, vibrotactile stimulation of different body parts resulted in no ERP response. Therefore Ramos-Murguialday and colleagues concluded that eye movements were the last communication mean in CLIS because the eye muscle was shown to be the last muscle group under voluntary control. Furthermore, since vibrotactile stimulation at several fingers and lip did not elicit any brain recorded ERP, they concluded that ALS might be considered as a multisystem disorder, even affecting afferent sensory pathways. After these first results auditory and proprioceptive brain-machineinterface (BMI) systems were recommended to establish a communication channel in CLIS.



reg. 5. Loss activity during passive interesting, on the top and and/or the cover (out-) scores comparing non-version and indectionals of section 3 (Lists) on the ent sand passive movements alone and on the right passive movements and motor imagery simultaneously AUC scores. In black the values that are statistically significant comparing hand versus foot movements. At the bottom the AUC scores in the frequency bin from 30 to 24 Hz plotted on the ALS patient X-rays (Pett, session 1 and 2 LIS and right, session 3 CLIS) comparing hand versus foot passive movements. In white the statistically significant AUC values. The hole in the center of the electrode grid is due to high impedance or lost channels.

Figure 2. From: Ramos-Murguialday et al 2011. Clin Neurophysiology

Recently other strategies were tested on CLIS patients, like Semantic classical conditioning (DeMassari et al Brain 2013, Furdea et al. J. Neuroscience Methods 2012) recording EEG and fNIRS (Gallegos-Ayala et al In Press) with promising results.

References

Abbott A (2006) Neuroprosthetics: in search of the sixth sense. Nature 442: 125-127.

Ayala, G.G., Furdea, A., Ruf, C.A., Flor, H., Birbaumer, N. Brain communication with a completely locked-in patient using bedside near-infrared spectroscopy. Neurology (in press).

Barbero A, Grosse-Wentrup M (2010) Biased feedback in brain-computer interfaces. J Neuroeng Rehabil 7: 34.

Birbaumer, N. (2013). Brain-machine-interface in chronic stroke rehabilitation: a controlled study. Annals of Neurology, 10.1002/ana.23879.

Blankertz B, Tomioka R, Lemm S, Kawanabe M, Muller KR (2008) Optimizing spatial filters for robust EEG single -trial analysis. Ieee Signal Processing Magazine 25: 41-56.

Cuthbert BN, Kristeller J, Simons R, Hodes R, Lang PJ. Strategies of arousal control: biofeedback, meditation, and motivation. J Exp Psychol Gen 1981;518–46

De Massari, D., Ruf, C.A., Furdea, A., Matuz, T., van der Heiden, L., Halder, S., Silvoni, S., Birbaumer, N. (2013). Brain communication in the locked-in state. Brain, 136, 1989-2000.

Duncan PW, Goldstein LB, Matchar D, Divine GW, Feussner J. Measurement of motor recovery after stroke. Outcome assessment and sample size requirements. Stroke; a journal of cerebral circulation. 1992; 23(8): 1084-9.

Furdea, A., Ruf, C., Halder, S., De Massari, D., Bogdan, M., Rosenstiel, W., Matuz, T., Birbaumer, N. (2012). A new (semantic) reflexive brain-computer interface: in search for a suitable classifier. Journal of Neuroscience Methods, 203, 233-240.

Gladstone DJ, Danells CJ, Black SE. The fugl-meyer assessment of motor recovery after stroke: a critical review of its measurement properties. Neurorehabilitation and neural repair. 2002; 16(3): 232-40.

Hinterberger T, Neumann N, Pham M, Kubler A, Grether A, et al. (2004) A multimodal brain-based feedback and communication system. Exp Brain Res 154: 521-526

Hinterberger T, Wilhelm B, Mellinger J, Kotchoubey B, Birbaumer N. A device for the detection of cognitive brain functions in completely paralyzed or unresponsive patients. IEEE Trans Biomed Eng 2005a; 52(2):211–20

Krakauer JW. Arm function after stroke: from physiology to recovery. Seminars in neurology. 2005; 25(4): 384-95.

Kübler A, Birbaumer N. Brain-computer interfaces and communication in paralysis: extinction of goal directed thinking in completely paralysed patients? Clin Neurophysiol 2008;119(11):2658-66

Kotchoubey B. Event-related potential measures of consciousness: two equations with three unknowns. Prog. Brain Res 2005; 150:427–444.

Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. Lancet. 2011; 377(9778): 1693-702.

Leeb R KC, Friedman D, Guger C, Scherer R, Neuper C, Garau M, Antley A, Steed A, Slater M, and Pfurtscheller G (2006) Walking by thinking: The brainwaves are crucial not the muscles. Presence-teleoperators and virtual environments 15: 500-514.

MacMahon S. Introduction: The global burden of stroke. Clinician's Manual on Blood Pressure and Stroke Prevention Ed: J Chalmers Science Press, London. 2002: 1-6.

Owen AM, Coleman MR, Boly M,et al.Detecting awareness in the vegetative state. Science 2006; 313:1402.

Party ISW. National clinical guideline for stroke. 3rd ed: London: Royal College of Physicians; 2008. p. 187.

Ramos Murguialday, A., Hill, J., Bensch, M., Martens, S., Halder, S., Nijboer, F., Schoelkopf, B., Birbaumer, N., Gharabaghi, A. (2011). Transition from the Locked in to the completely Locked-in State: a physiological analysis. Clinical Neurophysiology, 122, 925-933.

Ramos-Murguialday, A., Broetz, D., Rea, M., Läer, L., Yilmaz, Ö., Brasil, F., Liberati, G., Curado, M., Garcia-Cossio, E., Vyziotis, A., Cho, W., Agostini, M., Soares, E., Soekadar, S., Caria, A. Cohen, L.G., Birbaumer, N. Brain-machine interface in chronic stroke rehabilitation: a controlled study. Ann Neurol. 2013; doi:10.1002/ana.23879.

Ward NS, Cohen LG. Mechanisms underlying recovery of motor function after stroke. Arch Neurol. 2004; 61(12): 1844-8.

Wilhelm B, Jordan M, Birbaumer N. Communication in locked-in syndrome: effects of imagery on salivary pH. Neurology 2006; 67(3):534–5.

MIND-MATTER INTERACTION EXPERIMENTS WITH LIGHT

Dean Radin *

Introduction

The double-slit experiment shows that the deep structure of quantum reality is fundamentally different from the appearances of the everyday classical world. Thomas Young first described this experiment in 1801. Two hundred years later readers of Physics World magazine voted it "the most beautiful experiment." Nobel Laureate physicist Richard Feynman famously declared that, "[The double-slit experiment] has in it the heart of quantum mechanics. In reality, it contains the only mystery."

The experiment demonstrates that elementary particles, like photons and electrons, behave like particles when you look at them and like waves when you don't. This is not just a minor statistical effect that one can observe with a stream of particles; it is also true for each particle independently. Technically, the process of looking in the context of an optical interferometer is called gaining "which-path" information, referring to knowledge of which path a particle takes as it travels through the apparatus.

Feynman called this effect a mystery for two reasons: First, it violates the common-sense doctrine of realism, which assumes the existence of an objective world independent of observation. Second, it demonstrates that quantum objects, unlike classical objects, can simultaneously exist in different forms, in this case as both waves and particles. In general these mysteries are known as the "quantum measurement problem" (QMP).

The QMP forced the developers of quantum theory to reconsider previously held assumptions about the nature of observation, measurement, and information. In discussing how to interpret this effect, physicists including John von Neumann1 and Eugene Wigner², plus contemporary figures such as Bernard d'Espagnat³ and Henry Stapp⁴,

^{*} Institute of Noetic Sciences, Petaluma, CA, USA.

have proposed that consciousness – conceived of as the last step in any measurement, i.e., the process of becoming aware that a measurement had occurred – may be an essential reason why a particle "collapses" from unobserved wave-like to observed particle-like behavior.⁵ While the proposers of this concept were prominent, their idea was considered too radical for comfort. This was partially because terms like "consciousness," "observation" and "measurement" are open to many interpretations, and also because for many physicists it seemed anathema to introduce the slippery subjective into what is otherwise a firm objective reality. As a result, the hypothesis that consciousness collapses the wavefunction has been relegated to an uncomfortable minority status and is studiously avoided in mainstream physics. We will refer to the von Neumann hypothesis as the "consciousness collapse hypothesis" (CCH).

The taboo about asking certain uncomfortable questions is so strong in the academic world that it even extends to experimental tests of the philosophical foundations of quantum theory. For more than fifty years this topic was considered untouchable for serious scientists.^{3,14} As noted by historian Olival Freire in discussing the history of tests of Bell's theorem,

Some of the physicists who decided not to hire Clauser [the first to test quantum entanglement] were influenced by the prejudice that experiments on hidden variables were not "real physics." His former adviser, P. Thaddeus, wrote letters warning people not to hire Clauser to do experiments on hidden variables in quantum mechanics as it was "junk science," a view shared by other potential employers.

But of course this does not mean the question is impervious to empirical exploration. Indeed, as with many topics regarded as controversial, the primary resistance is sociological and not technical. To test the CCH, one could use consciousness as a detector of which-path information instead of a more conventional physical device. In a suitably designed system they could perceive the photons directly by looking,^{6,7} or they could imagine that they could see them by "extrasensory" means. We have taken the latter approach because it allows for a rigorous means of examining just the role of consciousness itself.

Previous studies

Four classes of previous experiments have studied the CCH concept as a solution to the quantum measurement problem. They involve (a) studies testing the effects of intention on the statistical behavior of random events linked to quantum sources,⁸ (b) studies involving macroscopic systems such as the use of human physiology as "targets" of intentional influence,⁹ (c) experiments involving sequential observation to see whether a second observer could consciously or unconsciously detect if a quantum event had been observed by a first observer,¹⁰ and (d) our present focus on experiments investigating conscious influence of photons in optical interferometers.¹¹⁻¹³

Together these four classes of experiments comprise nearly a thousand experiments conducted by over a hundred investigators over six decades. Collectively they strongly suggest the existence of direct mind-matter interactions.¹⁴ Of these studies, the first that most closely matched Feynman's reference to the "only mystery" in the double-slit experiment was a study reported in 1998 by physicists Stanley Jeffers of York University and Michael Ibison of Princeton University.¹⁵

Jeffers asked a team of participants at York to observe – solely with the mind's eye – light passing through a double slit. Ibison asked a team at Princeton to do a similar task, using an improved optical apparatus. In both cases the mental effort periods were thirty seconds in length, alternated with 30 second no-effort control periods. The team at Princeton reported marginally significant evidence in favor of an observational effect; the team at York reported a non-significant result (although their data did show a larger sample variance than expected by chance, suggesting the presence of a real but unstable effect).

In interpreting these outcomes it is useful to know that the Princeton test employed a small team of participants with experience in maintaining focused intention in these types of experiments, and the test was conducted in a laboratory where the staff was sympathetic to the possibility of mind-matter interactions. By contrast, the York test employed unselected participants recruited without regard to their interest or skill in the task, and conducted by an experimenter who was not sympathetic to the idea of mind-matter interactions or experienced in conducting this type of experiment.

Michelson interferometer

Based on the Jeffers/Ibison results, we decided to repeat this experiment. All optical interferometers exhibit the same basic effect, that is, wavelike interference as long as the observer does not know the path that photons took when traveling through the optical apparatus, and particle-like diffraction patterns when the observer does know. Given this, for our first experiment we used a Michelson interferometer rather than a double-slit apparatus because the former is somewhat easier to setup than the latter.

Each arm of the Michelson interferometer was several inches in length. One of those arms was defined as the target area. It was in this area that we asked people to imagine that they could see the photons, with their mind's eye alone, as they traveled through that arm. If they could achieve this task (via clairvoyance, given that this task did not involve the ordinary senses), then they would gain which-path information and cause the wavelike interference to collapse. The collapse would be in proportion to the degree of information obtained, and because in most people clairvoyance is rather weak and imprecise, the amount of collapse that we expected to see in this experiment was small, but nonzero assuming that clairvoyance existed.

We used a low power Helium Neon laser to send a one-millimeter beam into the interferometer. The beam passed through a set of neutral density filters to reduce the illumination intensity, and then through a diverging lens and a half-silvered mirror. That mirror caused half the beam to go to one fully reflective mirror and the other half to a second fully reflective mirror. The resulting beams two reflected off those mirrors, they were directed back through the half-silvered mirror, and then they combined into a single beam to create an interference pattern. The pattern was recorded by a highly sensitive, thermoelectrically cooled digital camera, which was in turn controlled by a computer to record digital images at a rate of one per second. To help isolate the interferometer from ambient vibrations, it was secured to the floor of a twenty-eight-hundredpound, double-steel-walled, electromagnetically shielded, optically sealed room, which in turn rested on a vibration isolation mat on a ground-level concrete floor. During a test session, participants sat quietly, one at a time, on a chair or on the floor, about six feet away from the outer wall of the shielded chamber. I asked each participant to imagine that he or she could mentally "see" the photons in the target arm of the interferometer. If they found that task too difficult to imagine, then they could try to mentally "block" the photons. They did this with eyes closed, sitting quietly outside the shielded room.

The computer automatically took camera shots of the interference pattern, one shot per second, and I announced each test run condition following a preset sequence of counterbalanced conditions: *concentrate* on the interferometer now, or relax and withdraw your attention from the interferometer. One experimental session consisted of a series of concentrate and relax periods, each lasting 30 seconds and alternating over the course of a half-hour. This may not sound particularly difficult, but to do this task with attentively and with high focus is not trivial. Without attention training practice, such as meditation, thoughts soon begin to wander, so even in sessions lasting just a few minutes, non-meditators tend to drift into fantasies rather than attend to the experiment under way. Thus, to check if the ability to focus was a factor in this experiment, some of the participants recruited for this study were explicitly required to have meditation experience.

For the sake of simplicity, I based the formal analysis of the data in this experiment not on a change in the precise shape of the interference pattern, but rather on a decrease in the illumination level averaged over the entire camera image during the concentration condition as compared to the relax condition. To then test the design and analytical procedures for possible problems, I also included control runs to allow the system to record interference patterns automatically without anyone being present in the laboratory or paying attention to the interferometer. Data from those control sessions were analyzed in the same way as the experimental sessions.

Five meditators with more than two years of active practice contributed nine test sessions; five others with no meditation experience, or less than two years of practice, contributed nine additional sessions. The CCH predicted an overall negative score for each experimental session, which would be related to a decrease in interference. Overall the results showed a significant decrease in interference, as predicted, with odds against chance of 500 to 1.^a The same analysis applied to the control sessions showed results close to chance expectation, indicating that the experimental results were not due to artifacts. The group of experienced meditators showed combined results of odds against chance of 107,000 to 1, and the non-meditators obtained results close to chance expectation, supporting the speculation that people with attention training would perform better than non-meditators. This experiment was published in 2008.¹³

Double-slit Experiments 2 – 7

For the next series of experiments, we decided to use a double-slit system. Our custom-made apparatus directed a low-power Helium-Neon laser beam through a neutral density filter and then through two slits etched into a metal foil slide. The slits were 10 microns (millionths of a meter) wide and separated by 200 microns. The wavelike interference pattern produced by this apparatus was recorded 20 times per second by a high-resolution digital camera (3,000 pixels in a line), and the apparatus was housed inside a light-tight, eighth-inch thick aluminum box.

To test if observation by the mind's eye affects wave interference, one approach is to focus on certain points of the interference pattern, like the height of the interference peaks or troughs. In these studies we took another approach and calculated the interference pattern's Fourier transform to determine two spectral peaks: One associated with light diffracting through each of the single slits, and a second associated with light interfering through the two slits. The measurement of interest was the ratio R between the double and single slit spectral magnitudes. The CCH predicts that this ratio should *decrease* when attention is placed on the optical system.

During a test session, a computer directed the participant's attention toward or away from the optical system, in 15- to 30-second epochs. One test session consisted of forty such epochs presented in a randomized

a For the sake of expediency in this report, study outcomes are described in terms of odds against chance instead of p-values, confidence intervals, or effect sizes. Such technical details are available in the cited references.

counterbalanced order. The participant sat quietly about two meters away from the sealed double-slit apparatus. All test sessions were conducted inside an electromagnetically shielded test chamber at the Institute of Noetic Sciences.

In analyzing the data we expected that any results observed in the interferometer data would necessarily lag behind the assigned instructions (i.e. "now please concentrate" vs. "now relax") by 3 to 5 seconds. The delay would be due to the mental processing time it takes to switch gears between two different focuses of attention. Thus the analytical results reported here were based on a 2-second lag, unless otherwise mentioned.

Experiment 2. The first double-slit pilot study presented 40 attention epochs in each single session, each epoch 15 seconds in length. After running 35 sessions, we found that the spectral ratio R declined modestly in accordance with the CCH, with odds against chance of 17 to 1. Meditators performed slightly better, with odds of 18 to 1, and non-meditators obtained results near chance. Control tests using the same equipment in the same location, but without participants present, showed a nonsignificant result.

Experiment 3. In the next experiment, we developed a way to provide real-time audio feedback of the R signal, and we increased the attention epoch lengths to thirty seconds. For feedback, during relax periods the computer played a soft droning tone, and during concentration periods it played a musical note that changed pitch to reflect the up or down movement of the R signal. Participants were told that if they were successful during the concentration periods, then the pitch of the musical note would *go down* (to indicate collapse of the wave function). After running 31 sessions, the results of the study again provided evidence in favor of the hypothesis, with modest odds against chance of 12 of 1. Again meditators showed better performance with odds against chance of 48 to 1; nonmeditators' results were close to chance.

Experiment 4. To check on a potential artifact in the previous studies, we explored if the proximity of the participants near the optical system might have influenced the results. Heat differences associated with small changes in body position six feet away from the optical system would

have amounted to temperature changes of a tiny fraction of a degree, but we still needed to see if this was sufficient to cause the optical system to systematically expand or contract due to tiny temperature fluctuations. We placed four thermocouples on and around the optical system, then we had thirteen people conduct a total of 33 test sessions, and we identified all the test sessions that showed a marked drop in R. For those sessions we investigated whether the thermocouple measurements also showed a change in temperature. The test ultimately included six meditators and seven nonmeditators. In testing for the possibility of temperature-mediated effects, we examined all of the sessions contributed by meditators that resulted in negative (meaning in the predicted direction) scores. Among those 16 sessions there were no significant temperature differences, not on the laser tube itself, or the double-slit apparatus housing, or in front of the apparatus, or within a meter in front of the participant. This meant that the decline in R observed in the 16 selected sessions was not driven by systematic variations in temperature. So proximity of the human body did not explain the results we were seeing.

Experiment 5. In our next study, we explored a "nonlocal" aspect of the consciousness collapse interpretation. The idea we tested was that the quantum wave function collapses when observation occurs, *and not when the data are generated.* That is, unlike events in the everyday world, where actions occur in particular locations and unfold in ordinary clock time, events in the quantum domain do not occur *in time* as normally experienced. This is what is meant by the spooky "nonlocal" nature of quantum mechanics—events are connected across the usual limitations of space *and time*.

To prepare for this study, we recorded fifty sessions in the laboratory in April 2009. No one was present during the data generation and recording process, and the data, while safely stored on a hard disk, remained unobserved. Two months later, participants were asked to view a strip-chart display, which unbeknownst to them was playing back the still-unobserved data that was recorded back in April. As in the previous experiments, participants were invited to mentally cause R to go as low as possible when the computer gave them the instruction to concentrate on the double-slit, and to withdraw their attention when given the instruction to relax. Twenty-two participants contributed one test session each; 10 of them indicated that they had a regular meditation practice. The remaining 12 were classified as nonmeditators. The meditator subgroup supported the hypothesis with odds against chance of 175 to 1. The nonmeditators obtained chance results. This suggests that the effects observed in these studies are not causal in the usual sense of that term. They do not "happen" in real time; indeed they work just as well forward as backward in time.

Experiment 6. Having gained some confidence that the results of these studies were not artifacts and were consistent with the predictions of the CCH, we conducted a formal, pre-planned replication. We selected 31 participants who we predicted would perform well because of their meditation or other attention-focusing practice. The results over 50 sessions were remarkable; overall that group achieved odds against chance of 268,000 to 1. Fifty matched control sessions showed chance results.

Experiment 7. In the last study of this series, we explored the role of participants' personalities and beliefs in modulating this effect. We again ran a series of 50 preplanned sessions, but this time we recruited 50 participants who, unlike in the previous study where we attempted to optimize our selection process, were chosen to represent a broad range of personality traits, meditation experience, and beliefs (about the possibility of extrasensory perception). The combined result was associated with odds against chance of a modest 9 to 1, which was expected given that we had recruited some people who were expected to *not* perform well on this task. The correlations between results on the double-slit task versus belief and capacity for absorption were both in alignment with expectations (r = -0.27, p = 0.03, and r = -0.21, p = 0.07, respectively). Fifty matched control runs produced results in accordance with chance.

Double-slit Experiments 8 – 10

After publishing the above six studies in *Physics Essays* in 2012, our offices and laboratory moved to a new location.¹¹ We decided to see if we could replicate the effect in the new location, and to see if data resulting from
that experiment could be mathematically modeled to provide clues about the underlying mechanisms. We also conducted two new experiments.

Experiment 8. This experiment used the same Helium Neon doubleslit apparatus that we used in the previous six studies. In an attempt to optimize our results, all individuals recruited for this study were selected based on three criteria: They were required to exhibit superior performance in a previous experiment of this type, or they maintained an active meditation practice, or they exercised some other form of regular mental discipline requiring focused or creative imagination, such as musician, intentional healer, or visual artist.

The experimental protocol specified that the concentration epochs would each last for 30 seconds; the relax epochs would be 30 seconds plus an additional 0 to 9 seconds, determined randomly on each successive relaxation period. Each test session consisted of 40 such epochs presented in counterbalanced order. Including pre- and post-session baseline data, on average a single session lasted about 25 minutes, during which approximately 30,000 camera frames were recorded (at about 20 frames per second). Real-time performance feedback was provided during the concentration epochs by having the volume of a droning tone controlled by the R ratio between double-slit and single-slit spectral power. As in the previous studies, when R declined the volume increased, thus reflecting the outcome of interest.

A new element introduced in the analysis portion of this experiment was to examine both spectral magnitude and phase. That is, the complex numbers resulting from a Fourier transform of a signal provide both the magnitude of the idealized frequencies that together comprise the signal, while the latter tell us (in simplified terms) where the oscillatory period of each of those frequencies begins. We also introduced a number of transforms to remove potential drifts and autocorrelations in the data. It is important to note that all of those transformations were applied uniformly to the data without regard to the assigned attentional conditions, thus the transformations could not have introduced spurious effects in the test of the CCH. Put another way, the objective and subjective aspects of this experiment were kept strictly independent of each other. Twenty-one selected participants contributed data in 50 pre-planned sessions. The results were strongly in the predicted direction, with odds against chance of 416,000 to 1. The same experimental and analytical methods were also applied to data collected in 100 control sessions, and those results were closely in alignment with chance expectation. We then applied the experimental data to a mathematical model of the double-slit setup, based on the equations of Fraunhofer diffraction, to explore various interpretations of this outcome. That analysis indicated that perturbation of two features of an idealized double-slit system would have produced the results observed in our experiment: A shift in the distribution of light between two slits, and a shift in the horizontal stability of the laser beam. If either or both of those effects occurred, the interference pattern would have changed in accordance with our observations.

Experiment 9. A remaining concern in all the previous experiments was the possibility of artifacts produced by proximity between the participant and the optical apparatus. To rigorously exclude this possibility, we conducted an experiment over the Internet using a double-slit optical system built to the same specifications as the earlier experiments. A completely automated design was employed that allowed the experiment to be accessed by anyone over the web, 24 hours a day, without intervention by the investigators.

In 21 counterbalanced epochs, participants were instructed to direct their attention toward or away from a double slit system. Attention-toward (concentrate) epochs were 30 seconds in length, and attention-away (relax) epochs were 30 seconds plus an additional 0 to 5 seconds, determined randomly on each successive relax epoch. The first epoch was a relax period; data from that epoch was used for subsequent performance feedback. That was followed by 20 alternating concentrate and relax epochs.

Participants conducted this experiment through a Flash-based client program that they accessed by visiting a web page (www.ionsresearch. com). The client received live streaming data from the double-slit system web server, and from that data it provided graphical feedback. Various security measures were put in place to ensure the integrity of the data and to track each participant's usage of the system.

Between December 2011 and August 2012, over 13,000 people from 121 countries visited the double-slit website. About half were in the United States. Approximately 1 in 10 people signed up for the test, and about half of that group completed the logon process and actually took the test.

To assist users in understanding the nature of the task, the website provided text descriptions and links to instructional videos. During a session, performance feedback was provided in the form of a simple graph, where a line went up if double-slit spectral power was decreasing, and vice versa. In addition, the pitch of a whistling wind sound would also go up to allow users to conduct the experiment without looking at the screen. The computer also provided prerecorded voice instructions to announce the attentional conditions with the phrases "now please concentrate" or "now please relax." There were 21 approximately 30-second epochs (relax epochs ranged randomly from 30 to 35 seconds), so a typical test session lasted a little over 11 minutes.

Because of Internet transmission delays, data buffering, human taskswitching costs, and other uncontrollable delays and distractions, we anticipated that there would be a lag between the time the web server sent a message to the client program to instruct the user to concentrate or relax, versus when we might see an effect in the data. Measurements of these various factors indicated that we would expect to see delays in the range of 5 to 10 seconds.

To provide control data, the web server was programmed to simulate users by automatically conducting a test session at the beginning of each hour. These sessions were conducted in exactly the same way as human trials, and in particular from the double-slit system's point of view, it was not possible to tell if data being served over the Internet was destined for a control session or a human session.

The formal portion of the test was specified to run until a minimum of 2,000 completed experimental and 2,000 completed control sessions had been recorded. Pilot tests began in November 2011 to test data integrity and network security procedures; the formal test began in January 2012. After 10 months the planned goal was achieved, at which time a total of 2,240 experimental sessions had been contributed, and of which 2,089 were completed. These sessions were contributed by 685 people from 120 countries. During the same period 2,303 completed control sessions were recorded.

Results of the experiment, using the same means of data analysis employed in the previous experiment, were in alignment with those observed in the previous studies. The maximum deviation occurred at a lag of 9 seconds, and at this lag the double-slit spectral power and phase significantly declined, with odds against chance of 384,000 to 1. The control data conformed close to chance expectation.

Experiment 10. This experiment explored the possibility that there might have been something idiosyncratic about the equipment used in the previous studies. To test this possibility, we designed a new double-slit system and used a diode-pumped solid-state laser tuned for exceptional power stability and long coherence length. The beam from this laser was passed through a clear quartz crystal, then a neutral density filter, and then through two slits with widths of 10 microns and separated by 200 microns. The quartz crystal was used to expand the beam diameter from 1 mm to approximately 3 mm. The resulting interference pattern was recorded by a 2,048 pixel CCD line camera, and camera images were recorded every 55 milliseconds.

Analysis of data from 20 test sessions contributed by 10 participants showed a significant deviation in double-slit spectral power and phase, in alignment with the results of the previous experiments. The composite result was associated with odds against chance of 166 to 1. Twenty matched control sessions conducted in the same environment and with the same equipment and analysis methods resulted in an outcome close to chance expectation. This series of three studies was published in *Physics Essays* in 2013.¹²

Single Photon Double-slit Experiments

The purpose of the next series of experiments was to more closely examine the effect of consciousness on individual quantum events. To achieve that goal, we used a single-photon double-slit optical apparatus (TeachSpin, Buffalo, New York). This 1-meter long device produces single photons by passing yellow photons^b produced by a dim incandescent bulb through a green filter. The relatively few photons that

b That is, the electromagnetic frequency associated with what we describe as the color yellow.

pass through the green filter go through a collimating slit that further reduces the number of photons in the system. The remaining photons then pass through a double slit. To detect variations in light intensity in the resulting interference pattern, the photons then pass through a single slit that can be placed at various positions along that pattern, and photons are detected using a photomultiplier tube (PMT). The output of the PMT goes through a discriminator circuit that separates background noise from photon detection signals, and that output is in turn counted by a digital circuit. In our design we set the counter to record the number of photons observed each second.

Under typical operating conditions, about a thousand photons per second may be detected at the PMT, or one photon per millisecond. When the single collimating slit and the double-slits are removed, the count rate increases to about a million per second, or one photon per microsecond. The time-in-flight of any one photon in the 1 meter channel is on the order of 3 nanoseconds or 0.003 microseconds, thus at any given time it is very likely that there is just one photon in the apparatus. That is, 99.7% of the time there are no photons in the apparatus, and only about 0.3% of the time there will be one photon in flight. Because photons are generated independently, the probability that there will be even two photons in flight at the same time is less than 0.001%. Thus for the vast majority of time the optical system operates with one photon at a time.

The single slit near the PMT is on a movable stage, so it is possible to move the final single slit and count the number of photons at different points along the interference pattern. In so doing it is easy to demonstrate that the photons are indeed distributed according to the expected interference pattern.

The CCH prediction in this experiment was that the number of photons counted in an interference trough would *increase* during the concentration periods as compared to the counts at the same location during the relax periods. Counts were expected to increase because if wave-like behavior declined due to observation, then the interferencemediated prohibition that created the interference trough in the first place would weaken, allowing more photons to arrive in that location. **Experiment 11.** Our first pilot study using the single-photon apparatus involved 19 participants who together contributed a total of 72 test sessions. Each session consisted of 10 concentrate epochs of 30 seconds each, and 10 relax epochs of 30 seconds plus 0 to 5 additional seconds, determined randomly. The conditions were instructed by the computer using a recorded voice, "now please concentrate" or "now please relax." Performance feedback was provided by displaying second by second photon counts on a graph.

The pilot test collected a total of 49,165 seconds of data, of which about half were in the concentrate condition and half in the relax condition; the remaining counts were in an inter-epoch baseline condition. The prediction was a rise in count rate during concentration; the results of a t-test for the mean difference in counts during the concentrate vs. relax epochs, at zero lag, was a nonsignificant decrease. The results were thus weakly in the direction *opposite* to the CCHI prediction. Examination of the data at different lags showed in a more interesting outcome.

Figure 1 shows the result of a lag analysis from -60 to +60 seconds, along with a similar analysis for 300 additional sessions conducted without observers as controls. For the experimental data the graph indicates the presence of a statistically significant decline (z = -2.5) in count rates at a lag of -10 seconds. As expected, this difference is reversed, becoming a significant increase 30 seconds later at lag +20 seconds.^c By contrast, none of the excursions in the control data achieved statistical significance. (These results were exploratory, unexpected, and not adjusted for multiple testing, so the modestly significant experimental outcome observed here should be regarded with caution.)

c This reversal must occur because epochs were 30 seconds in length, thus shifting the data by 30 seconds would in effect reverse the meaning of each attentional condition, thus each concentrate epoch would become a relax epoch, and vice versa.



Figure 1. Lag analysis for experimental sessions (filled black squares) and control sessions (open red circles). This indicates that 10 seconds after assignment of the attention instructions, the average count rate recorded during concentrate epochs declined as compared to the average count rates recorded during relax epochs.

Experiment 12. Following the pilot study, we conducted five additional studies. None of these have been formally published as of this report, so the designs and preliminary outcomes will just be briefly described. Experiment 12 was a replication of the pilot test using an improved photon counter and a "volitional" design, whereby rather than having the computer instruct the participant when and how to interact with the optical system, the participant was allowed to decide at will. Each session in this experiment required 30 volitional trials, and each trial consisted of a button press to start the trial (whereupon a recorded voice announced, "preparing"), a 5-second preparation period (indicated with "waiting"), and then a 30-second concentrate period (announced with, "now please concentrate"). At the end of each concentration period the voice announced, "now please relax." The volitional design was partially introduced to force participants to stay alert throughout each session; it was also useful in reducing the attention task-switching delay time. That is, each trial in a volitional design included a 5-second period to "shift mental gears" and prepare to concentrate, thus unlike in instructed protocol designs, in a volitional protocol there was no need to perform a lag analysis.

Participants wore headphones providing real-time performance feedback during the concentration epochs, in which the counts of photons per second varied the volume of a droning tone, with higher counts leading to louder tones. Participants were also allowed to view the photon count rates second by second on a graph. The study involved 20 pre-planned sessions. As in the pilot study, the results again showed a surprisingly significant *decline* in photon counts during the concentration periods (z = -5.0), contrary to what the CCH would predict.

Experiment 13. This study was a similar, volitional design as in the previous experiment. As a new feature, it also included a 32-channel EEG recording of each participant as they ran the experiment. As such, to avoid interference with the EEG recordings, the study used audio speakers rather than headphones to provide performance feedback, and the feedback (a recorded voice speaking a number from 1 to 10, where 10 indicated a large rise in photon counts during the concentration epoch and 1 indicating no rise) was provided only at the end of each trial. The experiment was conducted with eyes closed, and 20 individuals each provided one session. Each participant also filled out the Cloninger Temperament and Character Inventory. The results showed an overall modest increase in photon counts during the concentration condition (z = 2.5), and a number of significant EEG and personality correlates. Details will be reported in a formal publication.

Experiment 14. Following up on the previous study, 20 sessions were preplanned and contributed by 20 people. No EEG measurements were taken. This study also included continuous performance feedback provided over headphones and the use of a vibration isolation table, on which the single-photon double-slit apparatus was placed. The results showed no significant changes in photon counts.

Experiment 15. This experiment used a Nexus-10 neurofeedback system (Mind Media, The Netherlands) to train each of two participants over 13 repeated sessions to learn how to produce states of high attention and high relaxation. Each neurofeedback session was immediately followed by a double-slit session as described in the previous experiment. The experiment was divided into two segments. The first half was a volitional task, as described above; the second half was an instructed task. These two methods were used because participants reported as the experiment proceeded that the extremely calm state they were able to achieve through the neurofeedback training was disrupted when they had to switch into the volitional double-slit task. As a result, after session 6 we changed the interaction task to an instructed design so they did not have to initiate each trial.

This study provided clear evidence that the neurofeedback training was effective, in that the difference in magnitude of EEG alpha (8-12 Hz) power between concentrating and relaxing conditions became progressively larger. The results of the double-slit portion of the experiment showed that the volitional task showed a modestly significant rise in photon counts (z = 1.78), but the instructed task showed a nonsignificant decline (z = -0.59).

Experiment 16. The last experiment in this series explored whether a hypnotic induction before each session would improve the results. The hypnosis program was custom-designed to augment participants' belief that they would be able to do the task. This test had two participants each conduct 10 sessions with the double-slit system, using a volitional design, each time after listening to the hypnosis program. In terms of a trend, the study showed that the mean differences between counts in the concentrate vs. relax conditions became progressively larger as the number of sessions increased (r = 0.55, p = 0.007, see Figure 2). However, in terms of the absolute double-slit photon counts, overall there was a nonsignificant decrease (z = -0.634).



Figure 2. Trend in z scores comparing mean photon counts in the concentrate vs. relax conditions in Experiment 16, over 10 sessions each for two people (r = 0.55, p = 0.007).

Discussion

Sixteen experiments were conducted to explore a radical consciousness-based solution to the quantum measurement problem; we called this the consciousness collapse hypothesis (CCH). Two types of optical interference systems were used in these studies, a Michelson interferometer and a double-slit interferometer, and also two types of light sources, a continuous laser and a single-photon source. Overall, the continuous laser experiments provided evidence in alignment with the CCH, suggesting that wave-like interference declined when people were asked to direct their attention toward the optical systems. The single-photon experiments gave mixed results, sometimes providing evidence suggesting that observation decreased interference, and other times suggesting that observation sharpened interference. The reason for the ambiguous results in the single-photon experiments is not yet clear, but we speculate that it might be related to the quantum Zeno effect.

The quantum Zeno effect refers to the fact that observation of a quantum system will cause the dynamics of that systems to either "freeze," in which case the evolution of the system slows down or in extreme cases stops, or to "accelerate" and cause a faster evolution than the system would follow if unobserved.⁴ The latter phenomenon is known as the quantum anti-Zeno effect.¹⁶

Quantum Zeno and anti-Zeno might be relevant to the results we observed in the single-photon experiments because the former effect would "cool" the system, resulting in reduced noise and in turn produce sharper fringes, and the latter effect would "heat" the system and result in more noise or fuzzier fringes. The mode of observation, and whether a quantum Zeno or anti-Zeno effect might manifest, would be adjusted by the way the task is defined in each experiment. When working with a continuous laser system – producing trillions of photons per second as compared to a few dozen per second – these purely quantum effects may be smoothed out and not be as noticeable.

Not enough is known at this point to be able to specify in advance when a given experiment is more likely to display a quantum Zeno or anti-Zeno effect. This implies that a better measurement in the singlephoton studies might be shifts in photo count variance (absolute deviations from chance) rather than shifts in means (directional deviation from chance). All this is speculative, of course, but a closer consideration of quantum Zeno effects might shed more light on the results of mindlight interaction experiments.

In summary, a series of 16 experiments testing the possible role of consciousness in the behavior of quantum systems indicated that this continues to be a fruitful area of exploration. In particular, the results of such experiments may yield new clues about the relationships among quantum effects, observation, mind, and consciousness.

References

1. Neumann JV. *Mathematical Foundations of Quantum Mechanics*. Princeton, NJ: Princeton University Press; 1955.

2. Wigner EP. Symmetries and reflections: Scientific essays of Eugene Wigner. Bloomington, IN: Indiana University Press; 1967.

3. D'Espagnat B. The Quantum Theory and Reality. Scientific American. 1979:158.

4. Stapp H. *Mindful Universe:* quantum mechanics and the participating observer. New York: Springer; 2007.

5. Atmanspacher H. Quantum Approaches to Consciousness. *The Stanford Encyclopedia of Philosophy* 2011; Summer 2011 Edition: <u>http://plato.stanford.edu/</u><u>entries/qt-consciousness/</u>. Accessed May 20, 2012.

6. Merali Z. Quantum effects brought to light. Nature. 2011.

7. Pomarico E, Sanguinetti B, Sekatski P, Zbinden H, Gisin N. Experimental amplification of an entangled photon: what if the detection loophole is ignored? *arXiv*. 2011.

8. Radin D, Nelson R. Evidence for consciousness-related anomalies in random physical systems. *Found Physics*. 1989;19:1499.

9. Schmidt S, Scheider R, Utts J, Walach H. Distant intentionality and the feeling of being stared at: Two meta-analyses. *British Journal of Psychology.* 2004;95:235.

10. Bierman DJ. Does consciousness collapse the wave-packet? *Mind and Matter.* 2003;1(1):45.

11. Radin D, Michel L, Galdamez K, Wendland P, Rickenbach R, Delorme A. Consciousness and the double-slit interference pattern: Six experiments. *Physics Essays.* 2012;25(2).

12. Radin D, Michel L, Johnston J, Delorme A. Psychophysical interactions with a double-slit interference pattern. *Physics Essays.* 2013;26(4):553-566.

13. Radin D. Testing nonlocal observation as a source of intuitive knowledge. *Explore*. 2008;4(1):25.

14. Radin D. Entangled minds. New York City: Simon & Schuster; 2006.

15. Ibison M, Jeffers S. A double-slit diffraction experiment to investigate claims of consciousness-related anomalies. *Journal of Scientific Exploration*. 1998;12:543.

16. Prezhdo OV. Quantum anti-zeno acceleration of a chemical reaction. *Phys Rev Lett.* Nov 20 2000;85(21):4413-4417.

MIND-MATTER INTERACTIONS – ON THE ROLLERCOASTER FROM DATA TO THEORY AND BACK AGAIN

Harald Walacb *

Abstract

Since the foundation of the Society for Psychical Research in 1882, the question whether mind could directly interact with matter without the aid of an intermediate causal chain of action was deemed decisive. It would speak for a world-view that allows for consciousness as a unique entity, not only as derived from matter. It is therefore not surprising that this question stood in the center of theory, empirical observations and experiments in parapsychology ever since. The database of the Princeton Engineering Anomalies Research (PEAR) Lab that focused on this question has therefore been a pillar of this strand of research. It started to shake with the large, unsuccessful, multisite replication of Jahn et al (2000) and the Bösch, Steinkamp & Boller (2006) meta-analysis of those data. Theorising by Walter von Lucadou already in the 90ies and followed up by von Lucadou, Walach & Römer in 2007 actually predicted the very sequence and patterning observed in these data. This theory assumes that mind-matter-interactions are generalised types of non-local entanglement correlations between physical and mental systems. Therefore, they are not to be treated as classical causal couplings, else time-reversal paradoxes would ensue. If treated as such they either need to break down or they shift direction. Following this reasoning, Walter von Lucadou introduced a different type of experiment with a meta-experimental approach. In such an approach no direct experimental evidence is attempted but only an indirect one. Here, non-local correlations are captured via a correlation-matrix, where a purported entanglement between mental and physical system becomes obvious in a set of variables producing a

^{*} Institute of Transcultural Health Sciences, European University Viadrina, Frankfurt (Oder), Germany.

correlation matrix. The prediction, across experiments, then, is that the absolute number of significant correlations will be significantly above what is expected by chance, but that the actual cells that display significant correlations will shift unpredictably across experiments. Thereby the system maintains its general type of correlated state but the correlations cannot be used to code causal signals, observing the postulated boundary conditions. In this chapter I sketch the theoretical situation, illustrated by data from the Bösch, Steinkamp & Boller (2006) data-set, as well as von Lucadou's original data and our recent replication.

Introduction

The Historical Heritage of Parapsychology

The rise of the natural-science model in the 17th and 18th century was accompanied with a double movement: The scientific enthusiasts were sure that the analytical method of physics and chemistry, together with mathematical modeling will eventually allow science to understand and explain all natural phenomena and to reduce those phenomena that were not seen as pertaining to the domain of science ultimately to natural and scientifically explainable phenomena. Lightning, for example, long understood as of divine origin, was explainable as electric discharge. And so scientific enthusiasm was soaring high in the 19th century, extending its wings to such phenomena as consciousness and the mind. Prototypical is the famous letter that Emil du Bois Reymond (1818-1896), famous professor of physiology at the Charité in Berlin wrote to his friend (Du Bois-Reymond, 1918)¹: "Brükke and myself, we have conspired to make known the truth that in our organism there are only physicalchemical forces at work. And where those are not sufficient for explaining phenomena we will have to look for such forces, using the mathematicalchemical method, in their concrete mode of action. Or else we have to

¹ p. 108, translation mine; original quote: "Brücke und ich, wir haben uns verschworen, die Wahrheit geltend zu machen, dass im Organismus keine anderen Kräfte wirksam sind, als die gemeinen physikalisch-chemischen; dass, wo diese bislang nicht zur Erklärung ausreichen, mittels der physikalisch-mathematischen Methode entweder nach ihrer Art und Weise der Wirksamkeit im konkreten Falle gesucht werden muss, oder dass neue Kräfte angenommen werden müssen, welche, von gleicher Dignität mit den physikalisch-chemischen, der Materie inhärent, stets auf nur abstossende oder anziehende Componenten zurückzuführen sind."

assume other types of forces, which, however, are similar to the chemicalphysical ones, inherent in matter, and can always be reduced to attractive and repulsive forces." What du Bois-Reymond describes here is the first known testimony of natural science researchers to attempt to reduce mental and physiological phenomena purely to material interactions and physical-chemical forces, or similar ones. He wrote this letter in his youthful years of studies, when he distanced himself from his teacher Johannes Müller, in 1839, when he began studying medicine together with Brücke, Freud's future teacher of physiology. Only 33 years later, in 1872, when he was well known and well reputed, he gave his memorable speech in Leipzig before the Society of Natural Researchers, where he took back his bold statement of youthful times and proclaimed his famous "ignoramus et ignorabimus": we do not know the nature of the mind and we will never know.

However, this personal turn of du Bois-Reymond remained an individual retraction of an older researcher. Science as a collective movement took up not only the sentiment of the young researcher but made it a program, quietly and implicitly assuming: Mind and conscious experience will ultimately be explainable in terms of material and chemical interactions. Modern day neuroscience is predicated on such sentiments and thus, this materialist stance, expressed by du Bois-Reymond in the heydays of scientific optimism, is well and alive, perhaps more so than ever (Churchland, 1986; Dennett, 1991; Edelman & Tononi, 2001; Metzinger, 2003; Tononi, 2004). Thereby, the Cartesian program of mechanising nature has finally reached its consummation by mechanising what Descartes saw as ultimately different, the mind, which in modern theories is also seen as a very complex material system that can be understood as a series of computations produced by the chemicoelectrical activities of neurons.

Already in the early days of scientific enthusiasm in the 19th century a counter movement was formed by those researchers that were not satisfied with the common stance of implicit materialistic analysis of all natural events, even the mind and consciousness. The foundation of the Society of Psychical Research in the UK in 1882 was such a clear counter-movement

(Society for Psychical Research, 1882)². Here, researchers gathered that tried to empirically counter the materialist dominant model by providing empirical evidence for the fact that minds actually can influence matter directly, or that mental events happen outside or independent of a body. Therefore they studied mediumistic phenomena and gathered spiritualist accounts. The goal was clear: to prove scientifically that the mind can influence matter directly, and hence is an independent, irreducible entity. Thus, the long history of parapsychological research can, in a way, be seen as a tradition of research demonstrating independent influences of consciousness in our physical world, and by the same token of causal and ontological independence of consciousness. Thus, the long tradition of mind-matter-interaction research has to be seen against this background. Slowly, it matured from naturalistic case series and collections of well documented anecdotes and observations to experimental studies in the laboratory. Initiated by J.B. Rhine of Duke University, others followed suit and by the end of the last millenium most academic parapsychological research, in as much as it existed, was experimental laboratory work.

The Implicit Assumptions of the Experimental Paradigm and the Problem of Absolute Presuppositions

By adopting the experimental stance, parapsychologists also adopted the implicit presuppositions underlying it. One of the most important philosophical insights of the 1930ies and 40ies with multiple and independent sources can be summed up as follows:

Any system, whether formal or of a natural language, must, by necessity, make assumptions or stipulate presuppositions that cannot be again vindicated by the system itself.

^{2 &}quot;It has been widely felt that the present is an opportune time for making an organised and systematic attempt to investigate that large group of debatable phenomena designated by such terms as mesmeric, psychical and Spiritualistic. From the recorded testimony of many competent witnesses, past and present, including observations recently made by scientific men of eminence in various countries, there appears to be, amidst much illusion and deception, an important body of remarkable phenomena, which are primâ facie inexplicable on any generally recognised hypothesis, and which, if incontestably established, would be of the highest possible value (The SPR, 1882, S. 3)."

This structure of the necessary self-referentiality of theoretical systems has been observed and proven true by Gödel for mathematics (Gödel, 1931), by Wittgenstein for language as such - and then admitted by Carnap for all scientific theoretical models - (Wittgenstein, 1958, orig. 1953) and by Collingwood for any theoretical-philosophical system (Collingwood, 1998, orig. 1940). Collingwood coined the term absolute presuppositions for such assumptions that are necessary for a system to be operative, but rarely reflected upon, discussed or made explicit. This terminology was later adapted by Thomas Kuhn into what he termed "paradigm" (Kuhn, 1955): an implicit working model of scientific operations, including a set of accepted methods and standards, assumptions and truisms that are taken for granted, predicated on a world model that is assumed to be true until a new model is stipulated that overthrows in a paradigmatic revolution this old paradigm. Independent of the theoretical leaning one wishes to adopt, the structure is always the same: we have to make assumptions and stipulate presuppositions in order for any scientific model to work.

The presuppositions made by the "scientific" model are rarely explicitly discussed and very often taken for granted by those "doing science". Among them are the following:

• The assumption that systems can be analytically separated and studied in isolation. What we learn from those separated systems can be then put together to a mosaic of the whole: the analytical assumption.

• The assumption that the most important and the relevant section of the world is described by material and energetic interactions: the materialist assumption.

• The assumption that all causes are local and regular; they are mediated by contiguous contact and interaction of material particles that convey the energetic interaction, and by the same token that causes from a distance have to be and can be analysed in terms of local chains of particle interactions: the localist assumption.

• The assumption that the world is regular, at least those parts of the world that are relevant for us. Stretches in time and in space are uniform: the regularity assumption.

This is neither a comprehensive nor an exclusive list, but sums up what to me are the most problematic assumptions of the currently accepted model when it comes to the understanding of mind-matterinteractions. By doing experiments in the framework of science, parapsychology subscribed to these assumptions, probably unwittingly and also involuntarily. Every psychokinesis (PK) experiment that tries to document a direct influence of mental events on material events assumes that there is some sort of "influence" that is mediated by some sort of agent – a "PK force", some sort of radiation or similar regular influence –, can be enacted and replicated by others and documented by stringent experimentation.

Since conventional science is often also fraught with sources of errors and mistakes, it has become part of the standard procedure to not only do an experiment, but to repeat it, ideally by different experimenters and in different locations or under different circumstances to probe for causal stability and generalisability (Schmidt, 2009). Thus, part and parcel of the scientific protocol is a replication of experiments and the postulate of independent replicability of results. Even though this ideal is often not met, even within mainstream science, it is being raised as a standard, whenever unconventional challenges are voiced (Sheldrake, 1998a, 1998b, 2013).

Parapsychologists adopted this model and have tried to conform to it. Thus, they conceived of mind-matter-interactions in terms of fieldmodels of consciousness where consciousness fields interact with material fields in regular but as yet unknown ways (Jahn & Dunne, 1987, 2001; Radin, 1997a). World models, however, have, in general, at least two functions: They guide our attention and teach us, what to expect. More importantly, perhaps, they also tell us what to implicitly ignore. Thus they shape what we are able to perceive in a very concrete way. This is certainly useful to some extent, as it helps us reduce the complexity of the world into a set of useful and workable partitions. But when it comes to science it also hinders our activities, as we are unable to see phenomena that do not fit the expected model. This can actually be reconstructed from the way our brain and our perception works: We are, to some extent, prediction engines (Gray, 1990, 1995). We predict what is to expected and change our world model according to mismatches with this prediction. However, whatever lies completely outside of the predicted range of phenomena will not even be seen, unless it is very salient, very dissonant, or unless the observer is very astute and keen.

A classical historical example for this guiding and structuring role of a world model is the discovery of the heart-beat by William Harvey, physician to the English king, around 1618. Harvey did not believe the standard opinion that was derived from Aristotle's physiology that was slightly edited by Galenos, Celsus and some other authorities in antiquity. This model held that the heart was a convection warmer, warming the blood that was again cooled by the brain. Thus it explained circulation, and there was no place for a pumping heart. Only when Harvey discovered in vivisection experiments in dogs that the heart was actually moving and thus pumping blood he developed the concept of the heart being a pump that propelled the blood through the circulatory system, and hence producing a distinct sound, the heart-beat. When Harvey published this finding, an outcry was heard throughout Europe. One of the spokesmen of medicine and philosophy, the Venetian Emilio Parisano, wrote: "There is no one in Venice who can hear a heart beat" (Parisano, 1647, p 107).

Clearly, mothers would have heard the heart-beat of their children and lovers those of their beloved. But as a phenomenon it was not known and thus, as a scientific fact it did not exist. For a scientific fact is always a phenomenon plus the requisite theory explaining or predicting it. And in that sense the heart-beat was not a fact, nor was it a common phenomenon perceived by the majority of people as such, because there had not been a theory for it.

This example demonstrates how world-models and absolute presuppositions, shape expectations and thus experience, and thus restricts our phenomenal range. What we do not expect by theory, we normally do not perceive, unless we are astute observers that are willing and able to suspend their theories and expectations at least for a certain amount of time.

The Theoretical and Practical Failure of the Standard Paradigm

PK research is a good example of how the accomodation to an accepted paradigm actually ruins the credibility of the research if it tries to conform to the dominant world-model. This world model assumes that direct influences of mind on matter should be causal, and thus

regular and replicable. The PEAR research program and other researchers actually adopted this model and tried to prove such a causal stability and influence (Walach & Jonas, 2007). Initially, it seemed reasonably successful (Jahn & Dunne, 1987, 2001). But the largest ever done independent replication, the consortium replication program in which the labs in Freiburg and Giessen in Germany together with the PEARlab in Princeton adopted the protocol of the PEAR lab and created the largest to date database of micro-PK data, was unsuccessful and came out flat negative on the predefined outcome, mean-shift from statistical expectation value (Jahn et al., 2000). Although secondary analyses were able to show that there was some anomalous signature in the data, presenting itself in deviations of the variance (Atmanspacher, Bösch, Boller, Nelson, & Scheingraber, 1999), and in non-linearity parameters (Atmanspacher, Ehm, Scheingraber, & Wiedenmann, 2001; Pallikari, 2001), this failed replication demonstrates that whatever is going on here cannot be conceptualised as a regular, local cause. Thus, in pulling together all the available evidence, Bösch, Boller and Steinkamp concluded that the PK-Effect in those REG-experiments can only be demonstrated statistically, if this large replication study is excluded, or if one operates under the assumption that no small studies with negative outcomes exist which is not a well defensible assumption given the ease with which such experiments can be run once they are set up (Bösch, Steinkamp, & Boller, 2006). Thus, the attempt to demonstrate causal independence and local influence of mind on material systems, using the database which gathered the largest amount of data, failed. Does this mean that PK influences do not exist, or that PK is an illusion, or that there are no direct couplings between mental and physical systems without an interactive mediation?

No, obviously this cannot be concluded from the data, although this is frequently done. What can be concluded is that there is no reason to assume a causal-local model to be operative. But might there be other models? Yes, we think so.

An Entanglement Model of Generalised Non-Locality

Walter von Lucadou has long held that effects found in parapsychology are examples of non-local correlations between mental and physical systems, in case of PK or clairvoyance, or between mental and mental systems, in case of telepathy or precognition (Kornwachs & Lucadou, 1979, 1985; Lucadou, 1994, 1995, 2001; Lucadou & Kornwachs, 1980). Part and parcel of this theoretical stance is that there is no signal-transfer process between systems, but only correlative parallelisms. And because entanglement correlations are non-local, they cannot be used to transfer signals, and if they are so used, they break down (Lucadou, Römer, & Walach, 2007). And this is the reason, why experiments in parapsychology fail in the long run, and, at the same time, parapsychological effects seem to be quite ubiquitous in lived experience and the real world. This needs some explanation.

Einstein's model of Special Relativity holds that every signal in the universe can maximally travel at the speed of light, i.e. roughly at 300.000 km per second (Reichenbach, 1957). This framework also defines time. For time is laid out by the forward-traveling light cone, as it is called, i.e. light, or other types of radiation, that is radiated out from a source covers an ever wider cone as it travels, and it needs time for the travel. This is why some of the stars in a long distance are actually already gone, when we see their extinguishing light in the supernova explosion, as the light might have taken several million years to travel the distance. Whatever is connected by such light or radiation cones is called "locally connected", i.e. in direct causal relationship. All our scientific causal models presuppose such a causal structure.

Now there is a different structure of non-local relationship known from quantum mechanics (QM)³. Schrödinger discovered it in the formalism of QM already in 1935 (Schrödinger, 1935). The discovery was this: QM is formulated in a way that within a quantum system all elements are only jointly clearly defined, and individually only as probability waves. As soon as a measurement takes place, a particular variable is measured to have a certain value. It is unclear which value this will be, but QM predicts the probability to receive a value of this particular magnitude. Now, if we have a conjoint system, the system is only defined as a whole. Its elements remain undefined until measured. So we have here a complementarity between the global variable, the clear definition of the

³ Whenever I say "quantum mechanics" I mean the physical theory proper. When I refer to a theoretical group of models I say "quantum theory" to delineate it from the physical application.

system and its state, and the local variables, the maximally undefined state of its local variables. It is called complementary, because there is maximal incompatibility between these states of full definition and probability description. Because this is so, the single elements of the system remain undefined, but highly correlated. If one of these elements is measured, the potential of all probabilities collapses instantly into a defined value. Which one this will be is unclear. However, once it does, it is immediately clear from the theoretical structure, which value a corresponding variable will be measured at. There is clear theoretical predictability, but no localcausal interaction between those parts of the system. This structure has been called "entanglement" by Schrödinger. Einstein opposed it. Because he saw clearly that it undermines the deterministic and local structure of the physical world (Einstein, Podolsky, & Rosen, 1935).

As a thought experiment one could conceive of a quantum system that is spread out over the universe, say one light-year across space. If one part of the system was measured on earth, then the other part measured on Alpha Centauri would immediately collapse into a corresponding state, known to the measuring scientist on Alpha Centauri. It is as if the particles had communicated in a mysterious way and bridged the one light-year gap in no time, contradicting locality, being non-locally correlated.

The debate was only solved, when, following a joint-probability argument developed by John Bell (1987), and a concretisation of the thought experiment by Bohm, an experimental set-up was realised that allowed for testing the prediction of QM experimentally. It was realised by a beam-splitting crystal that splitted one photon into an entangled system of two twin-photons. These twin photons are individually undefined in one of their properties, for instance the polarisation angle of each photon. The polarisation angle is the angle at which a photon vibrates as it travels. But they are conjointly defined regarding the sum of these angles. If polarisation measurements are conducted, typically the analyzers are oriented at certain angles, known from theory to produce many or very few measurements. Now, QM predicts that the jointly measured polarisation angle has to be highly correlated, i.e. if we adjust the polarisation angle to be measured at one photon to a value highly unlikely then the angle measured at the other photon will be one corresponding to the first one and more photons with correspondingly

more probable angles will be measured, and vice versa. That is to say the polarisation angles measured will be correlated. Exactly which angle will be exhibited by an individual photon cannot be predicted. But if a certain angle is measured in one analyser, then a corresponding angle will be measured in the other analyser (This is a short exposition; a more precise and elaborate description can be found in Nikolaus von Stillfried's PhD thesis, which is available online (N. v. Stillfried, 2010).

Classical physics would predict that the two measurements should be uncorrelated. QM predicts that the photons are entangled, if they are produced by the same source and hence have to be treated as belonging to one quantum system. Experimental data vindicated QM in a series of tests starting with the famous experiments by Aspect and colleagues (Aspect, Dalibard, & G., 1982; Aspect, Grangier, & Roger, 1982), and could be demonstrated even over macroscopic distances several kilometers apart, if the system is appropriately isolated against interactions (Salart, Baas, Branciard, Gisin, & Zbinden, 2008). It has been shown in comparatively macroscopic systems (Lee et al., 2011), and it could also be demonstrated that entanglement can also work "backwards in time" (Ma et al., 2012).

Thus from a physical point of view it is quite clear that non-locality and entanglement is a physical fact at the level of true quantum systems. Although other interpretations are possible, this seems to be the majority view in the physics community. A lot of technological applications that are being developed depend on this phenonemon: quantum computing and quantum encryption being just two prominent examples. What is impossible from a physical and theoretical point of view is to transmit "causal" signals non-locally, i.e. against the arrow of time. If this were possible, we would run into time-reversal paradoxes that have been analysed in the 70ies: We then could telegraph into the past and hire a killer who could kill our grandmother which would make it impossible for us to be around and telegraph in the first place (Fitzgerald, 1971). The emphasis is here on "causal". While it is perfectly possible to have non-local correlations that reach into the past and into the future, from a theoretical point of view, it is not possible to use those correlations as if they were causal.

What does "causal" and "signal" precisely mean? "Causal" means, in our current physical view, that we can measure an interaction between

two systems that is based on interaction particles, such as photons or the like. A "signal" means that we can encode a message of at least one byte, say "1" or "0", or "yes" or "no". A causal, local signal would be one that is always and repeatedly available to transmit an information using physical interaction vectors, such as particles. Thus, ideally, a causal, local signal can be used at will. A non-local, causal signal would be one that could be used to transmit a signal across the time barrier, as it would be faster than light. So far, no interaction particles have been measured to my knowledge that can do this. And if it were possible, we would indeed run into time-reversal paradoxes. Thus, "non-local" and "causal", or "nonlocal" and "signal" are contradictions in terms. Non-local signals can only be theoretically construed under certain conditions, for instance complex field models, and would therefore require a profound rewriting of our physical textbook knowledge. It is not impossible, but difficult, and the mainstream community has some aversions against such proposals, as science aims to be parsimonious and is conservative in principle (Walach, 2010; Walach & Schmidt, 2005).

Now it is very important to understand that parapsychological research within an experimental paradigm is actually the attempt to nail a non-local signal as a causal one. This is so, because direct experimentation is always, by definition, an attempt to isolate a cause. If parapsychological effects were due to such non-local causes, it would create all the problems described above. One could envisage to set up a series of experiments that are direct replications. One uses the outcome of the first experiment to define a signal, for instance "measurement above mean" as "1" or "below mean" as "0". As soon as in the second experiment a measurement below the mean is found, the signal code "0" is registered. This could then, at least in principle be used to code a signal and a message which is based on a non-local system. And this constitutes a violation of special relativity. This seems to be prohibited by nature (Lucadou, Römer, & Walach, 2007). And this is obviously the reason why the problem of experimental validation of PSI effects mainly becomes visible as a problem of replication. It is not the case that experiments fail for the first time, on the contrary. The deviations are often very large in first-time experiments (Bem, 2011; Schmidt, Schneider, Binder, Bürkle, & Walach, 2001). And very gifted researchers such as Dean Radin have practically made a principle out of it to never repeat an experiment in exactly the same way. Apparently, the replications often "fail" in the sense that the original effects are difficult to reproduce, often reverse themselves into negative directions opposite to the deviation predicted (Ritchie, Wiseman, & French, 2012). And this is what makes critics skeptical (Alcock, 2003). Understandably so, as long as parapsychologists insist that their effects are of a subtle causal nature.

The fact that long series of experiments approach a null-effect has to date only be verified with the micro-PK meta-analyis of Bösch, Boller & Steinkamp (2006). Other meta-analyses have been able to verify effects over an ensemble of studies (Mossbridge et al., 2014; Schmidt, 2012; Schmidt, Schneider, Utts, & Walach, 2004; Storm, Tressoldi, & Di Riso, 2012; Tressoldi, 2011). But if it is true that PSI-effects are non-causal and non-local in nature then no amount of direct experimentation will be able to distil an effect out of systems in the long run. We would expect the effect to decline over time, which is a signature that can be found in the Bösch, Boller & Steinkamp (2006) data. Figure 1 displays a correlation analysis between effect sizes and time when the study was conducted or published (data courtesy Holger Bösch-Hartmann). Although the correlation is small, it is clearly visible and negative. Over time the regression line touches the zero-point, and we would expect that the same will be the case for other experimental paradigms.



Figure 1. Scatterplot of correlations between micro-PK study-effect sizes and time. The vertical axis displays effect-size where 0.5 is the mean chance expectation, i.e. an effect-size of zero. The horizontal axis gives the time when the study was conducted/published. Data according to and by courtesy of Bösch, Boller & Steinkamp (2006). The size of the bubbles represent the size of the experiments.

This is, why we think that a non-local model, conceptualising PSIeffects as non-local correlations is both easier to join with mainstream theoretical models, fits the experimental findings better and is true to the phenomenology. Such a model would see PSI-effects as the expression of non-local correlations within systems and between systems. They can be very real, they can also have an effect in people's lives or generate meaning. They can even be used in defined frameworks that are not controlled and not causal. Some healing practices, such as homeopathy or shamanic healing, would be examples in our view (Walach, 2003, 2005). And some gifted people can possibly more often than others use such correlations for meaningful interactions, such as diagnosing disease, or sensing future dangers, as has been testified phenomenologically multiple times in the ethnographic literature (Kale, 1995; Müller, 1987; Rose, 1956; Sax, Quack, & Weinhold, 2010). But as soon as one would use these effects to generate technology from it that is meant to operate reliably on a quasicausal principle the effects would dwindle away or break down.

To use an example: One might be able to use PSI in individual cases to warn of dangers. Anticipatory responses to threatening stimuli have been demonstrated experimentally (Hinterberger, Studer, Jäger, Haverty-Stacke, & Walach, 2007; Mossbridge, Tressoldi, & Utts, 2012; Radin, 1997b) and make a lot of sense in an evolutionary frameworke (Sheldrake, 2013). However, constructing a technical device out of it that would use, say, the autonomic response as measured by the electrodermal activity to warn a soldier of danger, as in (Mossbridge et al., 2014), will be doomed to failure in the long run, although certainly initially spectacular effects are to be expected.

So the difference between a causal non-local model of PSI and a nonlocal entanglement model of PSI is not that the one works and the other does only sometimes. The difference is constituted in the theoretical structure presupposed. While a causal model of PSI presupposes a signal that is unkonwn to our standard physics and has to travel faster than light, contradicting special relativity, an entanglement model is more parsimonious and presupposes "only" that a generalised form of non-locality exists that is, however, not causal in structure. Thus, phenomenologically such correlations will be observable, but technologically they won't be of use reliably. They can be used comparatively reliably, as long as their presumed causal structure is not probed. That is, why we prefer telephones over telepathy.

A Model of Generalised Entanglement

Now what would such an entanglement model look like? It actually follows from a very simple assumption. If we assume that the general structure of QT is relevant not only for the physical realm, as in QM proper, but also potentially in other types of systems, then we will have to use a generalised form of QT which, by its very structure, predicts a generalised form of entanglement. What does that mean, and why would one want to do that?

We have asked ourselves: What is the minimal definition of any system or description to need a quantum theoretical description rather than a classical one? And it turns out: the one and only one requirement is that a theory can handle incompatible or complementary operations or variables (Atmanspacher, Römer, & Walach, 2002). And the stipulation is: Incompatible operations or variables are relevant also in other areas than in the quantum mechanical realm proper. In QM they are well known and well defined: measuring position and measuring momentum are such incompatible operations. You cannot measure position with a high precision and momentum at the same time with a similarly high precision. If you do that, you lose your knowledge about momentum, and vice versa. This is what the Heisenberg uncertainty relationship in essence is about.

The formal expression for that is that in QM, in fact in every QT that is dealing with such incompatible variables or operations, you have to use a non-Abelian algebra. An Abelian algebra is the one that is used to model classical theories. In it we have a law of commuting operations: whether you take first 2 and multiply by 3 or the other way round is irrelevant. The result is always 6. The formal expression for that is $a^*b - b^*a = 0$. If you insert "2" and "3" for "a" and "b" you can immediately see that this is true. This is the formal expression for the fact that in a classical situation the sequence of operations is irrelevant, or that measuring one variable does not influence the measurement of the other. You can use laser optics to measure the momentum of a cannon ball and then its position or vice versa. The measurement will neither disturb the cannon ball, nor will the sequence of the measurements make a difference, exactly because the measurement has not disturbed the ball in its trajectory.

Now in any quantum type situation this is different. The measurement disturbs what is measured, and hence the sequence of measurements is not irrelevant. The formal expression is given by a non-Abelian type of algebra: $p^*q - q^*p > 0$. Inserting "2" and "3" makes immediately clear that this is a strange situation. It is in fact the formal representation of a Heisenberg-type uncertainty relationship. It arises because in QM it is important what we measure first, since a measurement of a particle's location will blur our knowledge about its momentum, and vice versa. Another way of putting this is saying that complementarity is at the heart of every quantum type theory. Complementarity means incompatibility of variables or operations. More precisely, we call complementary those observations and operations that are incompatible – in QM even maximally incompatible – yet need to be applied conjointly to describe a fact – for instance light – or a measurement situation. As we have seen in the description of physical entanglement above, complementarity is also at the root of entanglement. More precisely, entanglement is a certain type of complementarity, namely the complementarity between a global observable of a system, for instance the global polarisation angle of a two photon system which is defined, and a local observable, for instance the concrete values of its elements that are undefined until measured.

Thus, from generalising QT it follows that also entanglement should have a generalised counterpart:

Whenever global descriptions of a system and local descriptions of parts of that system are complementary, we would expect non-local correlations between those systemic elements.

We could thus use generalised entanglement as a theoretical concept to understand phenomena like PSI, which are clearly non-local, but not causal. But is there a scope for such a postulate? Does complementarity or incompatibility also play a role in the world of us mortals? We think it does. Agreed: it is well defined as a concept only in the physical realm proper. But phenomenologically it is also important in our lived experience. Here are a few candidates for complementary pairs, which we need to describe things or situations (Stillfried & Walach, 2006; Walach & Stillfried, 2011; Walach & von Stillfried, 2011):

The human being is always conjointly separated and in communion or community, socially speaking. He or she is also himself or herself a systemic assembly or conjunction of separate elements, psychologically and physiologically. Complementarity exists between the description "community" and "individuality" or "union" and "separability". Other potential candidates for such pairs of complementary descriptions might be

- actuality and potentiality
- freedom and structure
- confirmation and novelty
- knowledge and uncertainty
- love and hatred
- good and evil

to name but a few.

To be sure, there needs to be a thorough philosophical analysis to clarify these concepts and answer the question whether they are truly incompatible or complementary. What is important here is that complementary pairs are not just nominal opposites but incompatible descriptors. While an opposite of a term can be expressed as the logical negation of that term, a complementary notion cannot. For instance, the opposite of love is indifference, not hatred. The opposite of actuality is non-existence, and the opposite of confirmation is denial, and so forth.

So whenever we have a system that can meaningfully be separated from its environment and this system contains single separable elements, our model predicts non-local correlations between those systemic elements. This model can be used to reconceptualise PSI (Lucadou, Römer, & Walach, 2007), and this will be more concretely done in a separate publication.

If this is true, what does this mean for experimental research?

Nailing Jelly: The Experimental Quest for PSI and a Potential Solution

If our stipulation is correct that PSI is real, but not a causal signal, then classical experimentation will fail in the long run, and has failed PSI already, as we have seen. But is there a chance for a novel type of experiment to capture the effect? After all, physics has experimentally demonstrated entanglement. In order to answer the question, we need to understand how the physical entanglement experiments are different from what has been done in PSI research so far.

Physical experiments test a correlation of two seemingly independent data streams of, say, polarisation measurements of twin photons in two analysers, against a theoretical expectation. The expectation is derived from two competing theoretical assumptions, expressed by Bell's inequality. Details are not important at this point. Entanglement is experimentally proven, if Bell's inequality is violated, because it describes the boundaries which correlations need to conform to, if the two data streams are classical and thus uncorrelated. PSI experiments do not have such a theoretical backbone. Hence they need a direct experimental set-up, whereby the standard against which to test is generated by the experimental procedure itself, the control condition. But this set-up automatically constitutes the potential for coding a signal, as described above: A replication experiment could use the outcome of the previous experiment for such coding. This is impossible in classsical physical entanglement experiments, and there is a formal proof that physical entanglement correlations cannot be used for causal signal transfer, provided by Hartmann Römer as an appendix to our von Lucadou, Römer & Walach (2007) paper⁴.

This is the reason, why Walter von Lucadou has devised an indirect experimental micro-PK procedure in analogy to the physical situation. The analogy consist of the following elements:

- There is no direct experimental control condition to gauge a deviation of the mean shift against, and mean-shift of hits a classically conceived PSI-PK effect is not the target of the experiment.
- This avoids even the potential coding of a signal.
- The target outcome is a matrix of correlations between physical variables of the system and psychological variables of the operator.
- Since the matrix is large the system has many degrees of freedoms to exhibit the effect.
- The outcome measured is the number of significant correlations in the whole matrix. As there is no precise prediction about the positions of significant cells of correlations within the matrix, no signal can be derived. And replication experiments do not force the system into a causal framework.
- In any experiment and replication experiment we would expect that roughly the same number of significant correlations will be visible, but the correlations will appear in unpredictable cells. Thereby the experiment will demonstrate the entanglement between the operator and the physical system, but since there is no chance of encoding the signal, the experimental condition will be able to preserve the correlations. Should new variables be added to the system, the effect might even benefit from this and become stronger.

⁴ Specialists might argue that quantum teleportation is just such a usage. But here it is important to realise that it always relies on the existence of a second, classical channel that defines the meaning of the data stream.

Walter von Lucadou has conducted altogether five studies with that set-up, and all but one produced a significant number of correlations (von Lucadou, 1986, 1995; 2006; see Table 1).

Study	N sig corr	N subj	Psych Var	Phys Var	Numb corr	Z	Е
Lucadou 1986	75	299	24	23	552	5,1325603	0,218
Lucadou 1991	28	307	16	8	128	3,1035636	0,274
Radin 1993	32	1	16	23	368	2,6340387	0,137
Dataset 2	39	386	27	18	216	6,2253021	0,423
Dataset 3	11	386	27	18	216	0,0441511	0,003
Innov Set 3	21	220	27	18	216	2,2517051	0,0153

Table 1. Previous Studies with the Correlation-Matrix Approach; number of significant correlations, number of subjects in the experiment, number of psychological and physical variables, number of correlations and according z-score and effect-size.

The Replication of the von Lucadou Matrix-Experiment

Hence we set out to replicate this design. We started from scratch, implementing the whole experiment anew, by reprogramming the display and the experimental procedures. The REG-devices were newly built by the workshop of the University Hospital in Freiburg according to von Lucadou's specifications. The sampling of the REG-devices was smoothed by a Markov-window with lag one. A Markov-chain with lag one is a time series with one degree of auto-correlation or memory, i.e. each value is correlated with the preceding one. This creates a time series with a small memory effect, and this is how many natural processes, for instance the weather, behave. Thus, although the process is purely random, the appearance is more natural to the observer. The sampled process was used to steer the growth or shrinkage of a fractal spiral (see Figure 2) that was displayed on a computer screen to the subjects.



Figure 2. Display of the Fractal on a Computer Screen. On top of the screen an arrow would point to the left, or to the right, or to the center to indicate the direction toward which the operator should try and "influence" the growth ("arrow right") or shrinkage ("arrow left") of the fractal, or the instruction to leave it stable ("arrow center").

On top of the screen an arrow would point to the left, or to the right, of to the center to indicate the direction toward which the operator should try and "influence" the growth ("arrow right") or shrinkage ("arrow left") of the fractal, or the instruction to leave it stable ("arrow center"). This was the experimental instruction to operators. Each of these subruns ("left", "right", "center") consisted of 80 trials, and three such subruns of 80 trials completed one run. Three repeated runs constituted one experiment. An operator was requested in an information sheet and in an ensuing oral instruction to "influence the display mentally, by the power of their will or imagination" to achieve the desired direction of the fractal. They were told that they could use the left and right shift keys to move the experiment forward and potentially "influence" the behavior of the machine. In fact what happened was that the shift keys only moved the sampling process forward one step but was otherwise unconnected to the behaviour of the system.

The physical variables derived from this experiment were, for each sub-run:

- 1. deviation from randomness (the classical "mean shift" of REG experiments")
- 2. largest deviation from ideal outcome (difference between largest deviation and ideal target, i.e. a variance measure)
- 3. deviation of the data stream from Markov-chain behaviour
- 4. mean-voltage at REG output
- 5. standard-deviation of mean-voltage at REG output

The psychological variables derived from this experiment were, for each sub-run:

- 1. number of left key presses
- 2. number of right key presses
- 3. number of double key presses
- 4. time to run the whole sub-run (mean time between button presses)
- 5. standard-deviation of the time to run the sub-run

Thus, each sub-run created 5 physical and 5 psychological variables, and since 9 such subruns constituted one experiment we have, for every experiment, a matrix of 45 physical by 45 psychological variables, yielding a correlation matrix of 2025 cells.

Operators were recruited at conferences, meetings and seminars. We recruited 243 participants who competed 503 experiments. 103 experiments were provided by Walter von Lucadou in Freiburg, 400 by Majella Horan and Harald Walach in Frankfurt (Oder). Optional stopping was excluded by the rule that the experiment would stop when 300 participants are included or the 30th of December 2013 is reached, whichever occurred first. Data were not analysed until all data were in, the database was logged, and the evaluation protocol was deposited.

Immediately after each experiment, the system produced a set of empty runs to simulate the behaviour of the system at the experiment. The actual psychological variables of the operator were used to construct, together with the empty run, an according control run. Thus, each true experimental run was mirrored by a control run that consisted of automatically produced physical variables together with psychological variables of an actual subject that had not, however, produced the according physical data. By that procedure we were able to produce two kinds of controls: the ideal statistical situation, i.e. the number of correlations expected by statistical theory, following the theorem of big numbers, and an active control that simulates an experiment.

The analysis of the experiment is still ongoing and a publication is in preparation, hence we can here only describe preliminary data and results.

We calculated non-parametric correlations, used a two-tailed p-value of p < 0.05 (or one-sided p-value of p <0.1), as in previous experiments, and, as sensitivity analysis we adjusted the p-value to p < 0.01, and p < 0.001. We used the standard formula for the difference of significance of two correlation matrices (Figure 3) that yiels a z-score.

$Z=(CE-CD)/\sqrt{(2^*CD^*(1-CD/NC))}$

with CE= number of significant correlations in experimental condition CD= number of significant correlation in control condition NC= number of correlations in correlation matrix

Figure 3. Statistical formula that allows to estimate whether two correlation matrices are statistically different

We first analysed those variables that are also part of the previous experiments and found a significant difference between the correlation matrices for all significances tested. We then analysed the full matrix and in a first preliminary analysis we found a clear statistically significant result.

p <	Significant Experiment	Correlations Control	Expected	Difference	z-Score
0.05 (two-sided)	476	415	205	61	2,38
0.025 (")	278	199	101	79	4,17
0.005 (")	94	44	20	50	5,39
0.0005 (")	16	4	2	12	4,24

Table 2. Preliminary Results from Matrix-Experiment Replication using
What is interesting about these results is a two-fold structure: First, the effect-size, i.e. the z-score, is not reduced, as the criterion of how many significant correlations are counted in the the experimental and control matrix is increased. The second interesting observation is that increasing the significance criterion weeds out spurious correlations that affect the control matrix and likely also the experimental matrix. This can be seen in the fact that the number of significant correlations in the control matrix is gradually approaching the number of those correlations expected by theory. Since we test the difference score of correlations between control and experimental matrix this inflation of correlations does not affect our statistics. But it is to be expected, since some of the variables are highly correlated (e.g. the number of left and right key presses).

Thus, our replication seems to have borne out von Ludacou's prediction that the matrix approach will in fact allow for a reproduction of the effect, but at the same time not press it into a causal-local framework. Since our analysis is not finished yet, some caveat's need to be borne in mind:

Our experiment was one with an active zero-control, as demanded by Walleczek and as implemented by Yount and colleagues as one of the few experiments in the unconventional sector (Taft, Moore, & Yount, 2005; Yount et al., 2004). We achieved this by using an actual psychological set of variables and combining it with an empty run of the system. However, critics might still stipulate that the correlations observed might have been driven by some third event that happened at the time, and only if a robot with no intentions and no consciousness, driven by another random process would have conducted the control experiment would have there been a true control condition. While this is right from a purist point of view, it is obviously not realistic, and we hold that our control is the closest one can get to an active zero-control condition. Since our metric and statistics was build on the difference between the active and the control matrix, and since control data were engendered right at the same time, whatever might have affected the system – variances in power supply, field-effects, cosmic radiation, time effects, variances in the earth magnetic field and whatever else - has affected both data-streams in a similar way and will have been accounted for by our difference approach.

However, we will still want to calculate Monte-Carlo simulations to make sure that our data are not biased.

Also, some of our variables are highly correlated, such as the keypresses. We will want to make sure that this does not affect our data. But again the difference approach should have taken care of this.

Thus, as a preliminary conclusion we summarise that our replication of the matrix-experiment was successful and could demonstrate more significant correlations between a human operator and the behaviour of a REG-device than expected by chance. We interpret this to demonstrate two things:

First, PSI effects, in that case PK effects, can indeed experimentally be verified. Second, these effects seem indeed to be purely correlational in nature and have to be interpreted and conceptualised in analogy to quantum entanglement correlations. This is why we assume them to be generalised non-local correlations derived from a generalised type of nonlocality or entanglement as predicted by our generalised quantum theory model. We would predict that any attempt to replicate our results will be successful, if the system is left free to move the effect around within the matrix, and it will fail if replication experiments try to predict the precise location of the correlations. This is so, because the latter would constitute the coding of a signal, which is prohibited by the No-Signal-Transfer theorem of our model. At the same time, this might also be an experimental way to distinguish between the two theoretical concepts.

Another way to elaborate on our model would be to probe to what extent the consciousness and intention of the experimenter is part of the experimental system. In a way, it is quite arbitrary to delineate the experiment as the coupling between the operator and the physical machine. Why would not the experimenter setting up the experiment, or the larger environment, within which it is conducted, also play a role? One could test that by having the same experiment run by different experimenters.

In conclusion, we seem to have indeed found an experimental set-up that allows us to capture PSI effects and their non-local nature by providing enough freedom for the system through a correlational approach. Thus, our results support the idea that PSI effects are indeed non-local and non-causal entanglement correlations between systems, as predicted by generalised quantum theory.

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References

Alcock, J. E. (2003). Give the null hypothesis a chance: Reasons to remain doubtful about the existence of PSI. *Journal of Consciousness Studies*, 10(6-7), 29-50.

Aspect, A., Dalibard, J., & G., R. (1982). Experimental test of Bell's inequalities using time varying analyzers. *Physics Review Letter*, 49, 1804-1807.

Aspect, A., Grangier, P., & Roger, G. (1982). Experimental realization of Einstein-Podolsky-Rosen-Bohm-Gedankenexperiment: A new violation of Bell's inequalities. *Physics Review Letter*, 49, 91-94.

Atmanspacher, H., Bösch, H., Boller, E., Nelson, R. D., & Scheingraber, H. (1999). Deviations from physical randomness due to human agent intention? *Chaos, Solitons and Fractals,* 10, 935-952.

Atmanspacher, H., Ehm, W., Scheingraber, H., & Wiedenmann, G. (2001). Statistical analysis of time series with scaling indices. *Discrete Dynamics in Nature and Society*, *5*, 297-309.

Atmanspacher, H., Römer, H., & Walach, H. (2002). Weak quantum theory: Complementarity and entanglement in physics and beyond. *Foundations of Physics*, 32, 379-406.

Bell, J. S. (1987). *Speakable and Unspeakable in Quantum Mechanics*. Cambridge: Cambridge University Press.

Bem, D. J. (2011). Feeling the future: Experimental evidence for anomalous retroactive influences on cognition and affect. *Journal of Personality and Social Psychology*, 100, 407-425.

Bösch, H., Steinkamp, F., & Boller, E. (2006). Examining psychokinesis: the interaction of human intention with random number generators - a meta-analysis. *Psychological Bulletin*, 132, 497-523.

Churchland, P. S. (1986). Neurophilosophy. Toward a Unified Science of the Mind-Brain. Cambridge, Mass.: MIT Press.

Collingwood, R. G. (1998, orig. 1940). An Essay on Metaphysics (revised ed.). Oxford: Clarendon Press.

Dennett, D. C. (1991). Consciousess Explained. Boston: Little, Brown & Co.

Du Bois-Reymond, E. (1918). *Jugendbriefe von Emile DuBois-Reymond an Eduard Hallmann.* Berlin: Dietrich Reiner.

Edelman, G. M., & Tononi, G. (2001). *Consciousness: How Matter Becomes Imagination* London: Penguin Books.

Einstein, A., Podolsky, B., & Rosen, N. (1935). Can quantum-mechanical description of reality be considered complete? *Physical Review*, 47, 777-780.

Fitzgerald, P. (1971). Tachyons, backwards causation and freedom. *Boston Studies in the Philosophy of Science*, 8, 415-436.

Gödel, K. (1931). Ueber formal unentscheidbare Sätze der Principia Mathematica und verwandter Systeme I. *Monatshefte für Mathematik und Physik*, 38, 173-198.

Gray, J. A. (1990). Brain systems that mediate both emotion and cognition. *Cognition and Emotion*, 4, 269-288.

Gray, J. A. (1995). The contents of consciousness: A neuropsychological conjecture. *Behavioral and Brain Sciences*, 18, 659-722.

Hinterberger, T., Studer, P., Jäger, M., Haverty-Stacke, C., & Walach, H. (2007). The slide-show presentiment effect discovered in brain electrical activity. *Journal of the Society of Psychical Research*, 71, 148-166.

Jahn, R. G., & Dunne, B. J. (1987). *Margins of Reality. The Role of Consciousness in the Physical World*. San Diego: Harcourt Brace Jovanovich.

Jahn, R. G., & Dunne, B. J. (2001). A Modular Model of Mind/Matter Manifestations (M5). *Journal of Scientific Exploration*, 15, 299-329.

Jahn, R. G., Dunne, B. J., Bradish, G. J., Dobyns, Y. H., Lettieri, A., Nelson, R. D., et al. (2000). Mind/machine interaction consortium: PortREG replication experiments. *Journal of Scientific Exploration*, 14, 499-555.

Kale, R. (1995). Traditional healers in South Africa: a parallel health care system. *British Medical Journal*, 310, 1182-1185.

Kornwachs, K., & Lucadou, W. v. (1979). Psychokinesis and the concept of complexity. *Psychoenergetic Systems*, 3, 327-342.

Kornwachs, K., & Lucadou, W. v. (1985). Pragmatic information as a nonclassical concept to describe cognitive processes. *Cognitive Systems*, 1, 79-94.

Kuhn, T. (1955). *The Structure of Scientific Revolutions*. Chicago: University of Chicago Press.

Lee, K. C., Sprague, M. R., Sussman, B. J., Nunn, J., Langford, N. K., Jin, X.-M., et al. (2011). Entangling macroscopic diamonds at room temperature. *Science*, 334, 1253-1256.

Lucadou, W. v. (1986). Experimentelle Untersuchungen zur Beeinflußbarkeit von stochastischen quantenphysikalischen Systemen durch den Beobachter. Frankfurt: Haag + Herchen.

Lucadou, W. v. (1994). Wigner's friend revitalized? In H. Atmanspacher & G. J. Dalenoort (Eds.), *Inside versus Outside* (pp. 369-388). Berlin: Springer.

Lucadou, W. v. (1995). The model of pragmatic information (MPI). *European Journal of Parapsychology*, 11, 58-75.

Lucadou, W. v. (2001). Hans in Luck: The currency of evidence in parapsychology. *Journal of Parapsychology*, 65, 3-16.

Lucadou, W. v. (2006). Self-Organization of temporal structures-A possible solution for the intervention problem. In D. P. Sheehan (Ed.), *Frontiers of Time. Retrocausation - Experiment and Theory* (pp. 293-315). Melville, NY: American Institute of Parapsychology.

Lucadou, W. v., & Kornwachs, K. (1980). Development of the System Theoretic Approach to psychokinesis. *European Journal of Parapsychology*, 3, 297-314.

Lucadou, W. v., Römer, H., & Walach, H. (2007). Synchronistic Phenomena as Entanglement Correlations in Generalized Quantum Theory. *Journal of Consciousness Studies*, 14(4), 50-74.

Ma, X.-S., Zotter, S., Kofler, J., Ursin, R., Jennewein, T., Brukner, C., et al. (2012). Experimental delayed-choice entanglement swapping. *Nature Physics, online.*

Metzinger, T. (2003). *Being no one : the self-model theory of subjectivity*. Cambridge, Mass.: MIT Press.

Mossbridge, J., Tressoldi, P. E., & Utts, J. (2012). Predictive physiological anticipation preceding seemingly unpredictable stimuli: a meta-analysis. Frontiers in Psychology, 3(Artc. 390).

Mossbridge, J. A., Tressoldi, P., Utts, J., Ives, J. A., Radin, D., & Jonas, W. B. (2014). Predicting the unpredictable: critical analysis and practical implications of predictive anticipatory activity. *Frontiers in Human Neuroscience*, 8(Articl. 146), doi: 10.3389/fnhum.2014.00146.

Müller, K. E. (1987). Das magische Universum der Identität. Elementarformen sozialen Verhaltens. Ein ethnologischer Grundriß. Frankfurt: Campus.

Pallikari, F. (2001). A study of the fractal character in electronic noise process. Chaos, Solitons and Fractals, 12, 1499-1507.

Parisano, E. (1647). *Recentiorum disceptationes de motu cordis, sanguinis et chyli.* Leiden: Ioannis Maire.

Radin, D. (1997a). *The Conscious Universe. The Scientific Truth of Psychic Phenomena.* San Francisco: Harper Collins.

Radin, D. (1997b). Unconscious perception of future emotions: An experiment in presentiment. *Journal of Scientific Exploration*, 11, 163-180.

Reichenbach, H. (1957). The Philosophy of Space and Time. New York: Dover.

Ritchie, S. J., Wiseman, R., & French, C. C. (2012). Failing the future: three unsuccessful attempts to replicate Bem's 'retroactive facilitation of recall' effect. *PLoS One*, 7(3), e33423.

Rose, R. (1956). Living Magic: *The Realities Underlying the Psychical Practices and Beliefs of Australian Aborigines.* New York: Rand McNally.

Salart, D., Baas, A., Branciard, C., Gisin, N., & Zbinden, H. (2008). Testing spooky actions at a distance. *Nature*, 454, 861-864.

Sax, W. S., Quack, J., & Weinhold, J. (Eds.). (2010). *The Problem of Ritual Efficacy*. Oxford: Oxford University Press.

Schmidt, S. (2009). Shall we really do it again? The powerful concept of replication is neglected in the Social Sciences. *Review of General Psychology*, 13, 90-100.

Schmidt, S. (2012). Can we help just by good intentions? A meta-anaylsis of experiments on distant intention effects. *Journal of Alternative & Complementary Medicine*, 18, 529-533.

Schmidt, S., Schneider, R., Binder, M., Bürkle, D., & Walach, H. (2001). Investigating methodological issues in EDA-DMILS: Results from a pilot study. *Journal of Parapsychology, 65, 59-82.*

Schmidt, S., Schneider, R., Utts, J., & Walach, H. (2004). Remote intention on electrodermal activity - Two meta-analyses. *British Journal of Psychology*, 95, 235-247.

Schrödinger, E. (1935). Discussion of probability relations between separated systems. *Proceedings of the Cambridge Philosophical Society*, 31, 555-563.

Sheldrake, R. (1998a). Could experimenter effects occur in the physical and biological sciences? *Skeptical Inquirer*, 22(May/June), 57-58.

Sheldrake, R. (1998b). Experimenter effects in scientific research: How widely are they neglected? *Journal of Scientific Exploration*, 12, 73-78.

Sheldrake, R. (2013). *The Science Delusion: Freeing the Spirit of Inquiry.* London: Hodder & Stouton.

Society for Psychical Research. (1882). Objects of The Society. *Proceedings of the Society for Psychical Research*, 1, 3-6.

Stillfried, N. v. (2010). *Generalized Entanglement: Theoretical and Experimental* Explorations. Europa Universität Viadrina, Frankfurt (Oder). <u>http://opus.kobv.de/euv/volltexte/2010/33/</u>

Stillfried, N. v., & Walach, H. (2006). The whole and its parts: Are complementariy and non-locality intrinsic to closed systems? *International Journal of Computing Anticipatory Systems*, 17, 137-146.

Storm, L., Tressoldi, P. E., & Di Riso, L. (2012). Meta-analysis of ESP studies, 1987-2010: Assessing the success of the forced choice design in parapsychology. *Journal of Parapsychology, online*.

Taft, R., Moore, D., & Yount, G. (2005). Time-lapse analysis of potential cellular responsiveness to Johrei, a Japanese healing technique. BMC *Complementary and Alternative Medicine*, 5(1), 2.

Tononi, G. (2004). An information integration theory of consciousness. BMC *Neuroscience*, 5, 42.

Tressoldi, P. E. (2011). Extraordinary claims require extraordinary evidence: the case of non-local perception, a classical and Bayesian review of evidence. *Frontiers in Psychology*, 2(2), Art 117.

Walach, H. (2003). Entanglement model of homeopathy as an example of generalizsed entanglement predicted by Weak Quantum Theory. *Forschende Komplementärmedizin und Klassische Naturheilkunde*, 10, 192-200.

LECTURES

Walach, H. (2005). Generalized Entanglement: A new theoretical model for understanding the effects of Complementary and Alternative Medicine. *Journal of Alternative and Complementary Medicine*, 11, 549-559.

Walach, H. (2010). Ockham's Razor. In N. J. Salkind (Ed.), *Encyclopedia of Measurement and Statistics* (Vol. 2, pp. 707-710). Thousand Oaks, CA: Sage.

Walach, H., & Jonas, W. B. (2007). From parapsychology to spirituality: The legacy of the PEAR database. *Explore. The Journal of Science and Healing*, 3, 197-199.

Walach, H., & Schmidt, S. (2005). Repairing Plato's life boat with Ockham's razor: The Important Function of Research in Anomalies for Mainstream Science. *Journal of Consciousness Studies*, 12(2), 52-70.

Walach, H., & Stillfried, N. v. (2011). Generalised Quantum Theory—Basic idea and general intuition: A background story and overview. *Axiomathes, DOI 10.1007/* s10516-010-9145-5.

Walach, H., & von Stillfried, N. (2011). Generalizing Quantum Theory - Approaches and Applications. *Axiomathes 21 (2)*(Special Issue), 185-371.

Wittgenstein, L. (1958, orig. 1953). *Philosophical Investigations*. Oxford: Blackwell. Yount, G., Smith, S., Avanozian, V., West, J., Moore, D., & Freinkel, A. (2004).

Biofield perception: A series of pilot studies with cultured human cells. *Journal of Alternative and Complementary Medicine*, 10, 463-467.

AN ANALYSIS OF THE GLOBAL CONSCIOUSNESS PROJECT

Peter Bancel *

Introduction

The Global Consciousness Project (GCP) is a long-term experimental project that investigates the possibility of a subtle connection between the collective mental activity of humans and the physical behavior of systems in the surrounding environment. The Project formulates this proposition as a broad hypothesis that relates the output of true random number generators (RNGs) to times of intense, collective mental attention in the world:

Periods of collective attention or emotion in widely distributed populations will correlate with deviations from expectation in a global network of physical RNGs.

The GCP network consists of approximately 60 hardware RNGs installed on computers at local nodes throughout the world. The RNGs use quantum fluctuations in electronic circuits to generate bit-streams which are highly stable and therefore, within conventional interpretations of quantum mechanics, truly random. Once per second, at each local node, 200 consecutive bits are collected, summed and time-stamped. The trial sums, which nominally follow a binomial distribution with N=200 and $p=\frac{1}{2}$, are uploaded at regular intervals to a data archive in Princeton, NJ, USA. The network has been in continuous operation since August 1998 and the 15-year data archive currently holds more than 23 billion data trials.

The Project runs a formal replication experiment to test its hypothesis. Each replication begins by identifying a short time-period corresponding to an important event in the world that has drawn the attention of large

^{*} Global Consciousness Project, Princeton, NJ, USA.

numbers of people. The time-periods are typically several hours in length. The events vary in character and may entail, for example, major disasters, global celebrations, or important political events. Some instances are the 2004 Asian tsunami, New Years Eve, and the election of Barack Obama in 2008. For each replication, the event and its time-period are first specified before the prescribed data are unpacked from the archive. A previously determined statistic is then calculated and its deviation from null expectation is converted to a standard normal Z-score. With each replication, an updated cumulative result of the on-going experiment is calculated as the mean value of all replication Z-scores. As of mid-2013, the formal result stood at 0.334, on 439 events, which exceeds the null expectation of zero by 7 standard deviations. Details of the experimental procedures and methods have been documented in a series of papers (Nelson, Radin, Shoup & Bancel, 2003), (Bancel & Nelson, 2008), (Nelson & Bancel, 2011).

The experiment's highly significant result is often presented as a validation of the Project hypothesis and, by extension, as evidence for a global consciousness. However, that conclusion is not as self-evident as it might appear and a careful assessment is needed before interpreting the result. In this paper I take a critical look at the GCP and attempt to sort out some of the simpler interpretations that might account for the experiment's result. To begin, some general comments are in order.

Beyond its proposal of a global consciousness, the Project is interesting on several counts. The first noteworthy aspect of the Project, which it shares with any direct investigation into mind-matter interactions, is a possible connection to physics. While opinions differ on how or to what degree a theory of psychic phenomena needs to accommodate physics (and vice-versa) it is clear that the question is an important one and it requires experiments which demonstrate effects on well-characterized physical systems, such as is the case for the GCP network of RNGs.

Also of note are issues pertaining to experimental replicability. A common criticism of psi research is that effects remain difficult to replicate. In the eyes of many, the wide variability in psi performance, both within and across subjects, vitiates the weight of the assembled evidence. One factor that potentially contributes to the elusive character of psi is the difficulty in producing psi-conducive mental states by the mere application of an experimental protocol. Moreover, the difficulty can be aggravated when subjects are challenged to strive intentionally for a positive result in a psi task. A considerable amount of processoriented research focuses directly on this issue. The GCP, in effect, poses an alternative way around the problem by hypothesizing that global consciousness is sourced in populations blind to the experiment, thereby removing the complications that can arise from subject expectations, while at the same time effectively averaging over large numbers of people. In a sense, the GCP is a psi experiment taken in the thermodynamic limit of large N (in the jargon of physics), where N is the number of subjects simultaneously attending to an event. This underlying design consideration adds a certain appeal to the experiment since it holds the promise of an effect immune to some sources of variability normally encountered in psi research.

That populations are blind to the experiment and thus hold no intention or expectation towards the experimental outcome indicates another aspect of potential interest. A common thread in the taxonomy of psi effects is the application of conscious intention towards, or awareness of, the phenomenon in question (or at a least subconscious intention or awareness, as may apply to spontaneous cases and most presentiment experiments). This is evident in the standard definitions of telepathy, clairvoyance and psychokinesis (PK) and is closely related to the fact that the outcome of psi experiments is, generally speaking, meaningful for humans. We might adopt the term engagement, for lack of a better one, to indicate the myriad ways in which a person may be concerned about or engaged with a psi experiment (including in subconscious ways) such that it has some meaning for that person. Taken in this sense, engagement may or may not include expectation, determination, willful intention and the like. At a minimum, it signifies the intentionality of the subject towards the phenomenon at hand. Engagement also points to the deeply subjective nature of psi and the linkage between intentional states and experimental results. Subjectivity, and the self-referential loops it implies, imposes difficult and subtle problems on the framing and description of psi experiments. An interesting presentation of these issues and some of their implications has been developed by Atmanspacher and Jahn (Atmanspacher & Jahn, 2003).

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If we take engagement as a hallmark of standard psi effects, we can nevertheless ask if it is a necessary factor. Can there be psi effects when engagement is absent? Presumably psi without engagement would have different characteristics from standard psi since experimental outcomes would not be coupled to the subjects' awareness of the experiment. In a sense, engagement can be taken as a boundary condition that partly determines or constrains results. With the boundary condition removed, psi might be less "constrained" and perhaps more pervasive than instances of standard psi. At the same time, because effects would be devoid of meaning for the subjects, they could be more rudimentary and fundamental, displaying less of the diversity and richness of standard psi. We can employ the term proto-psi to distinguish between psi without engagement and psi in which engagement plays an essential role in the design and interpretation of experiments. A way to approach this experimentally is with protocols for which subjects are completely blind to the experiment's existence, and thus have no engagement with the experiment or its outcomes. Since this is consistent with the design of the GCP under a straightforward reading of the global consciousness hypothesis, it is reasonable to assert that the experiment aims to measure not standard psi, but a form of proto-psi.

The notion of proto-psi is not meant to be a theoretical proposal. I introduce it merely as an aid to thinking about how analyses to test different interpretations of the formal GCP result can be constructed. The chief distinction between psi and proto-psi is that the former links meaning and experimental outcomes and the latter excludes this linkage. Whether the linkage is best considered as correlational, teleological or even causal need not be addressed for our purposes. But it will be helpful to state the proposition more clearly.

The key point about engagement is that it references the entire experiment, including the result that the experiment yields. Imagine for a moment that we can make an approximate description of the experiment in terms of two sets of variables, μ and ε , where μ refers to the mental domain and ε to everything else such that:

 $\Psi(\mu, \epsilon)$

can provide the result of an experiment. Let us assume that, without engagement, the variable sets are separable. This allows the description to be written as:

$$\Psi \longrightarrow \Psi_{\mu}(\mu) \Psi_{\epsilon}(\epsilon).$$

If there is a psi linkage that couples the two domains, an experimental result can be represented as:

$$R: \longrightarrow L \cdot \Psi_{\mu}(\mu) \Psi_{\epsilon}(\epsilon) = \Psi_{\mu L} \Psi_{\epsilon}.$$

This representation implies that different manifestations of Ψ_{ϵ} can produce different results and that the results which obtain for Ψ_{ϵ} , as long as they are linked to $\Psi\mu$ L, need not be part of the experiment proper. There are two conclusions that can be drawn about this formulation of proto-psi. One is that results can depend on the details of Ψ_{ϵ} ; for example, different devices used for a measurement. The other is that the effects will be, in general, observed for any circumstance in which $\Psi\mu$ L is non-zero.

A different scenario occurs if engagement is present. In this case, the engagement imposes a boundary condition on the result so that μ and ε can no longer be considered separable. Furthermore, they are constrained to refer explicitly to the disposition of the experiment:

$$R(E) \longrightarrow L \cdot \Psi_{\mu}(\mu, \epsilon; E)$$

The inclusion of engagement thus implies that results are confined to the experimental configuration, so that effects will not be seen outside of this context. Additionally, different realizations of μ and ϵ can lead to the same result as long as the boundary condition is met. As an example, this picture is consistent with modern psychokinesis experimentation which finds similar types of results across a wide range of physical devices and conditions.

Proto-psi, then, proposes a segregation of the mental domain, while allowing for a source of psi linkage. The linkage is considered as a phenomenological given (in the scientific sense of the term, and not the philosophical one; a phenomenological model or theory is consistent LECTURES

with the basic tenets of physics, but is not derived from first principles) and apart from this the effect can be treated in a more or less conventional manner, as might be the case for a field acting on a physical entity. A proto-psi description of an experiment excludes all internal reference to the experimental result. Psi results that correlate with engaged intention or volition, and thus retain a self-referential character, cannot be examples of proto-psi.

While engagement is integral to the description of standard psi effects, it is also true that engagement seriously complicates the design and interpretation of psi research. To see this by degrees, consider a chemistry experiment which measures a reaction rate as a function of the temperature. The ions and molecules undergoing reaction do not possess engagement (according to the paradigm of experimental chemistry) and the experimenter's engagement need not be considered when interpreting results (again, under that paradigm). In the behavioral and clinical sciences, the subject's engagement clearly plays a central role, but that of the experimenter does not, at least from a conventional point of view. But here, engagement is not so easily circumscribed as one might imagine. For instance, the placebo and Rosenthal effects are examples of the unexpected impact that subject and experimenter engagement, respectively, can have on experimental results. So within the paradigms of psychology, sociology or medicine the reach of engagement can be problematic and difficult to control for.

It should be clear that within the paradigm of psi research, one cannot assume any functional distinction, a priori, between subject and experimenter engagement. Both can affect experimental outcomes and be responsible for psi effects. This is the problem of the experimenter effect in psi research; it is much knottier than Rosenthal-type effects since it is not possible to design experimental protocols which control for it. Although the relative engagement of subject and experimenter may be adjusted by a given protocol design, the experimenter's engagement nevertheless needs to be considered in analyses and interpretations. Moreover, the possibility of an experimenter effect is by definition at odds with any hypothesis of proto-psi. Therefore, the interpretation of the GCP hinges critically on whether the result should be considered as psi, or as a proto-psi effect: if the GCP result is consistent with proto-psi, then global consciousness

becomes a viable explanatory option; if analyses can effectively exclude proto-psi, the most parsimonious explanation of the experiment is likely to be some type of experimenter effect.

A detail of the experimental design crucial to resolving this quandary is that the raw bit-streams produced by the RNGs are XOR'd before being summed into data trials. Ideally, the RNGs produce bits that are independent and identically distributed with p=0.5. However, due to factors such as device aging and temperature variation, this is not assured for real devices which process analog noise to generate bits. An XOR (the logical "exclusive or" operation) therefore is included in the bit processing to remove first order biases that can arise in the RNGs and to insure equal frequencies of 1's and 0's in the output bit-streams. This is achieved by sequentially XORing bits from a fixed bit sequence (a bit-mask) against the RNG output¹. The mask loops as the continuous string of bits emerges from the RNG. For example, suppose that on average the RNG outputs 105 ones and only 95 zeroes each time it generates 200 bits. The XOR procedure might flip the value of every second bit, thus offsetting the bias.

An important observation is that persistent post-XOR biases, which are an implicit assumption of the GCP hypothesis, cannot be produced by a systematic change of the raw bit-stream before the XORing. For this to occur, the altered bit-stream would need to correlate with the state of the XOR mask in such a way as to yield the desired bias after passing through the XOR. Such an arrangement requires a designation of the result as well as knowing the instantaneous state of the mask. As we have seen, experimental descriptions which require referencing the outcome cannot be achieved in the context of proto-psi. Therefore, the XOR procedure is incompatible with a global consciousness effect based on proto-psi.

The most direct interpretation of this xor problem is that the GCP is unlikely to be measuring the effect it proposes, and is instead most likely measuring something more transcendental, as would be associated with engagement, rather than a physical effect associated with perturbations of

¹ At the bit level, the XOR operation performs an "exclusive or" between an input bit from the RNG and a bit taken from a mask that has an equal number of 1's and 0's. The operation results in 0 if the bits are identical and 1 otherwise. As a simple example, if the input bits are 1001 and the XOR mask is 1010, the procedure is: 1001 XOR 1010 \rightarrow 0011.

the RNG bit-streams. The xor problem effectively severs the experimental result from any simple physical effect on the analog noise generators underlying the RNGs in the network and necessitates a referencing of the result in the experimental description. This constitutes a no-go for any straightforward interpretation of the global consciousness hypothesis. However, the no-go might be circumvented if there exist sufficient loopholes to the xor problem. Thus, it will be important to examine the XOR operations in detail to determine whether there are loopholes that allow perturbations of the raw RNG bit-streams to pass the XOR. As will be elaborated below, two different XOR procedures are used in the GCP network and these will have to be studied separately.

The xor problem aside, it has been noted that, although the formal experiment returns a highly significant result, it cannot be directly interpreted as support for the GCP hypothesis (Bancel & Nelson, 2008). The reason for this ambiguity is that experimenter effects and other hypotheses can account for the effect. Prominent among these are selection hypotheses, which posit that, for each replication, the experimenter's choice of events and subsequent designation of event time-periods might lead to small biases in the event Z-scores. In these scenarios, the fortunate selection of naturally occurring random deviations is responsible for the measured effect, rather than a physical influence which alters the RNGs' behavior. The ambiguity is aggravated somewhat by the conception of the GCP experiment. The formal experiment tests only the event Z-scores and does not propose or test for any underlying mechanism or signature of the effect. Furthermore, the latitude allowed in event choices is consistent with selection bias, as this freedom is necessary to generate biased Z-scores. Interpretations based on selection are, of course, entirely consistent with the XOR design.

One can distinguish between conventional and psi models of selection. In the former case, the selection of events and their time-periods is guided by direct information about the data before the replication specifications are determined. Conventional selection can arise from either poor methodology or data-peeking which allows the experimenter to gain prior information about the replication outcome. Psi selection implies that similar information is obtained through some form of generalized ESP or precognition, and thus falls into the broader class of possible experimenter effects. Clearly, these two selection classes are difficult to distinguish by an examination of the data alone, and require an assessment of the experimental procedures in order to judge if the experimental result should be attributed to one or the other.

Selection models can, however, be distinguished from models in which a PK effect alters the output of the RNGs, either due to an experimenter effect or in a manner compatible with the GCP hypothesis (and contingent on loopholes to the xor problem). This is most evident when selection models are restricted to simple selection. In simple selection, only information of the replication Z-score is available, which implies that the data can be modeled as being selected from the unaltered, null probability distribution. A model along these lines has been described by May et al., in which they propose a psi-mediated selection with a constant effect size, ε , (May, Utts, & Spottiswoode, 1995). On its surface, the GCP experiment bears an empirical resemblance to simple selection since its effect size is constant to within experimental error.

May et al. emphasize that the constancy of ε requires that results will be independent of the amount of data collected in each experimental trial. Thus, signal-to-noise averaging, which is generally assumed for measurements of physical effects, does not apply. This offers a means to test against real physical effects in RNG PK-type experiments, in general, and for the GCP, in particular, where the amount of data contained in different events varies substantially. More generally, simple selection (with a constant ε) implies that any measure of structure in the data internal to events, and any dependencies not dictated by the requirement of a constant ε , must conform to the null hypothesis, modulo ε . In contrast, PK models predict that signal averaging should obtain. Furthermore, should XOR loopholes permit a proto-psi global consciousness, any structure associated with the proto-psi field should have a signature in the data internal to events. Thus, both PK experimenter effects and proto-psi models consistent with the GCP hypothesis and its formal result can, in principle, be tested against selection.

The rest of the paper is organized as follows. I begin by recalling some basic conclusions of the experiment which will be used to guide the analyses. Next, a primary statistic responsible for the effect is identified. From this, a phenomenological field model is constructed which provides predictions of internal data structure. The xor problem is then examined to determine if there are loopholes to the XOR no-go. Next, several examples of statistical analyses are presented which test for PK and data structure internal to events. Finally, I assess the analyses in the light of the xor problem and draw some conclusions.

Developing a model

The GCP formal experiment

The analyses presented here include 426 registered events up to the end of December 2012. The formal result yields an average event Z-score (ϵ) of 0.342 which yields a combined Stouffer Z of 7.1. The effect is small, stable and well-distributed across the events. The small effect size indicates that many events are needed in order to reach significance and that no single event is likely to yield evidence for the effect. A summary graphic of the overall experimental result is shown in Figure 1. Despite the stable effect size, it is important to emphasize that the event specifications vary widely and that the formal events should be considered as conceptual replications, rather than as exact replications. The disparate and heterogeneous set of event durations and test statistics needs to be taken into account in testing models, as well as the fact that the number of RNGs deployed in the GCP network has evolved over the course of the experiment.

Figure 2 shows that the event durations have an asymmetric, bimodal distribution, with most events lasting 1 to 12 hours, and a sizable fraction having a duration of 24 hours. Many events tend to have fairly obvious and constrained time-periods, such as sporting matches and scheduled meditations. A certain number of events, on the other hand, are diffuse and resist a precise time designation. Examples are worldwide celebrations and demonstrations, such as Earth Day or the mass demonstrations preceding the start of the Iraq-US war in 2003. The project typically assigns a default 24-hour time-period to these events, often with a start and end time fixed at midnight Greenwich Mean Time.



Figure 1. Two representations of the formal experimental results. The scatter plot shows the chronological Z-scores for all events. The reader with a good eye will discern the effect size of 0.34 in a slight upwards shift of the points away from the horizontal axis at zero. The scatter width can be seen to be about ± 2 , which is the ~ 95%CI for standard normal scores. The bold curve is the integration of the scatter plot and shows clearly the accumulating deviation from the null expectation of zero. (The vertical scale of the integration has been reduced by a factor of 10x and is not to scale with the scatter plot.) The integration demonstrates that the effect is relatively constant over time and shows no indication of a decline effect. The straight line is a guide to the eye; its slope is equivalent to the event effect size, $\varepsilon = 0.34$.

The trial-level statistic: RNG-RNG pair correlations

Before constructing the models, it is necessary to identify an appropriate test statistic. What is required is a statistic which 1) can account for the deviations of the event Z-scores in the formal experiment, and 2) be expressed in terms of the individual data trials so that data structure internal to events can be examined and tested. It has been shown that the RNG-RNG correlations, taken as the products of pairs of synchronous RNG data trials, satisfy these criteria. To discuss this, some data preparation and nomenclature needs to be introduced.



Figure 2. Numbers of events sorted by duration, and collected into bins 1-hour in width. Most events have designated durations of 12 hours or less, and these time-periods are considered to correspond fairly well to the actual unfolding of population engagement. Extended, diffuse events, for which it is difficult to estimate a time-period, are assigned a duration of 24 hours. The 81 events with 24-hour durations comprise over 50% of the event data. Six events with durations much greater than 1 day are not shown in the figure.

It will be convenient to express the binomial data trials, $B[200, \frac{1}{2}]$, as normal scores. Using all the data collected from each RNG, the trials from each RNG are individually standardized to a mean of zero and variance of 1. The normalized data trials are written:

$$B \rightarrow z(i,t),$$

where i labels the RNG and t labels the time, in seconds. The correlation statistic ξ (the lower-case letter Xi) is then,

$$\xi(\mathbf{i},\mathbf{j},\mathbf{t}) = \mathbf{z}(\mathbf{i},\mathbf{t}) \ \mathbf{z}(\mathbf{j},\mathbf{t}) \ ,$$

where the t's on the right-hand side are taken for synchronous trials (identical seconds). A derivation of this result is given in (Bancel & Nelson, 2008). The formal event Z-scores are calculated using a variety of statistics chosen according to the character of the event. Nevertheless, 84% of the events are calculated with the same statistic, which is a measure of the network variance and is referred to as the "standard analysis." A little algebra shows that the standard analysis can be re-written, to first order,

as the average of RNG Pearson correlations. To within statistical error, the correlations account for all of the effect found in the formal result.

It is worth pausing at this point to consider two advantages to reformulating the experiment in terms of trial-level correlations. First, it suggests that the effect is due to correlations between RNGs separated on average by thousands of kilometers. Inter-device correlations on this scale have not been previously measured in psi research, and a device level description of the effect will be an essential input to any attempt at theoretical modeling. Second, since the correlation pairs can be indexed by complete information of the experiment (the event, time, RNG type and location), analyses and statistical tests can study any structure associated with these experimental parameters.

The correlation statistic has several useful properties, the most notable being that its variance is 1, so that the standard deviation of the correlation average approaches $1/\sqrt{N}$, when N, the number of correlation products in the average, is large enough to invoke the central limit theorem. This is the case for all of the analyses considered below. Lastly, note that in a single second of data with k online RNGs, there will be k(k-1)/2 distinct correlation products. Further details are found in (Bancel & Nelson, 2008). Table 1 shows the effect sizes in the two formulations, event Z-scores and average correlation products, using the majority subset of 356 standard analysis events.

	3	Ztotal	σ	N
ZEvent	0.34	6.38	0.058	356
٤	0.000042	6.09	0.000007	2.10E-10

Table 1. Effect sizes and total Z-scores for the standard analysis events only, using two statistical formulations. The differences in ZTotal are due to the different weightings used. The standard analysis gives equal weight to each event Z-score when calculating ZTotal with Stouffer's method. The trial-level, correlation product method weights the correlations equally, averaging them over all events.

Field and selection models

The specific models of field and selection effects we will use need to predict testable differences in the event data, and yet be general enough to represent the broad range of possible models that might be considered within each approach. What is needed, then, are simple first-order models that capture the most salient aspects of the model classes. To achieve this, begin by considering linear models for the field and selection effects, MF and MS, such that the event Z-scores and correlations are given as:

$$M_{s} \cdot Z = \{ Z_{i} \} = \{ Z_{1}, Z_{2}, ..., Z_{n} \},$$

for events 1 through n, and similarly for the field model,

$$\mathbf{M}_{F} \cdot \boldsymbol{\xi} = \{ \, \xi_{i} \, \} = \{ \, \xi_{1}, \, \xi_{2}, \, ..., \, \xi_{n} \, \}.$$

Expand the linear models in successive orders as:

$$M = M + O2[M] + ...$$

such that:

 $M_{s} \cdot Z = Z0 + O2[Z] + ...$, where Z0 is the mean selection model effect size. Similarly, the field model becomes

$$M_{F} \xi = \xi_{0} + O^{2}[\xi] + ...,$$

where ξ_0 is the mean correlation. Keeping only the first order, the models are

$$M_{\rm S} = Z_0 + \eta,$$

$$M_{\rm F} = \xi_0 + \eta,$$

where η is a noise term representing statistical fluctuations. Finally, both models are cast in terms of the pair correlations to give event Z-scores,

$$M_s: Z0 = \xi N^{1/2}$$

and

$$M_{F}: Z = \xi_{0} N^{1/2},$$

where N is the number of unique correlations, N = T k(k-1)/2, with k the number of RNGs in the network, T the number of seconds in an event (and

the noise term is implicit). Because the models are phenomenological, the values of Z_0 and ξ_0 need to be determined empirically from experiment. For the event data, $Z_0 = 0.334$, and $\xi_0 = 0.000043$. The first order models developed here stipulate constant selection and field effect sizes, recovering simple selection from MS and yielding a mirror formulation for the field model. More sophisticated models would include higher order terms with parameters describing, in the case of selection, details of the experimenter's psychological and mental disposition, and for the field model, parameters relevant to the network and the RNGs, as well as descriptive variables of mass consciousness and the events.

To complete the discussion, the field model needs to be fleshed out and a motivation for introducing the notion of a field should be given. In the context of a proto-psi type of global consciousness effect (and assuming for the moment a no-go loophole), the field model implies that a PK effect on the RNGs arises from some aspect of coherent mental activity in the populations attending to an event. A convenient way to treat this mathematically at a phenomenological level is to introduce a coupling field that acts locally on the RNGs and is sourced in the populations concerned by the event. This step brings to light two assumptions required by the model.

The first is that the model must assume that a field acts on the RNGs, via an unspecified mechanism, in such a way that the observed correlations are produced. The second assumption is that the field depends in some way on the character and quality of mental coherence among people. This assumption allows the field to vanish locally under certain conditions, or globally, if the requirement of an effective mental coherence is not met. Further specification of what the field might be, or how it arises, is not needed or required to implement the model. But the model does explain that correlations will increase and diminish with the extent of global mental coherence, and that the correlations may exhibit spatial and temporal structure dependent on the field dynamics, which derive in turn from the coherent mental disposition of the human sources. Although this description is rather vague, it is enough to permit the field model to be expressed in more detail and to put some constraints on the mathematical form of the field. To save the reader from too much technical discussion, the details are not presented here. The interested LECTURES

reader can refer to a more extensive version of this paper which is currently in press (Bancel 2014).

In brief, under the selection model, the RNG network is unperturbed and the Z-scores calculated for events have an average value of Z0, irrespective of the experimenter's choice of test statistic, or event type or time-period.

Under the proto-psi field model, a coherence of consciousness arises when many people attend to an effective focus of attention such as the shared emotion experienced during a major global event. This can induce deviations in RNG bit-streams, and these deviations can be described phenomenologically by a field which couples the RNGs to consciousness. The field's amplitude and coherence track the unfolding event, diminishing as attention to the event dissipates. Since coupling is sourced in the globally distributed and very large number of people attending to the event, the fluctuations associated with the variability of individual people tend to average out, and the coupling is accurately described by smooth spatial variations of the field. Deviations in the RNG trial-sums lead to an excess variance of correlation pair-products among the trials. If the field coherence is sufficiently strong, as might occur during major events, the correlation mean will deviate positively. This is what is observed by the GCP experiment. For the model to describe global consciousness, it must also assume that there exists a no-go loophole that allows the correlations to pass the XOR procedure. We now turn to that problem.

The xor problem

There are two criteria for opening an XOR loophole. The first requires that a simple alteration of the raw RNG bitstream can reliably pass the XOR to produce output bit deviations as,

$$z \rightarrow z \pm \delta$$
.

The second criterion is that the output deviations must be able to correlate among RNGs across the network. To study this eventuality, the details of the XOR procedure have to be examined. Recall that a zero-bias XOR mask consists of an equal number of 0 and 1 bits that are sequentially xor'd against an input bit-stream such that an input bit passes or flips when xor'd against a mask 0 or 1, respectively. The output of an input stream of 1111 against a 0101 mask is thus 1010. There are two commercial models (Orion, Ltd. and Mindsong, Inc.) of RNG deployed in the GCP network, in roughly equal numbers, each of which uses a different XOR. We treat these in turn.

Orion RNG The Orion device outputs roughly 7800 bits/sec. The device consists of two internal RNGs dynamically xor'd against each other and then passed to the output. Upon data acquisition, the bitstream is further xor'd against a static 01 mask in software. A loophole to this procedure can be demonstrated by an example. Consider a 3-bit perturbation which acts similarly on both of the internal RNGs to produce identical twin sequences. The 3-bit sequences are next xor'd against each other yielding 000 for any given twin sequence (a bit xor'd against itself yields only 0). After encountering the software mask, the contribution of the perturbed sequence to the total trial bit-sum will then be either 1 or 2, depending on the phase of the software XOR (either 010 or 101). This satisfies the first loophole criterion since it is different from the expected bit-sum distribution of random 3-bit sequences. Any such 3-bit perturbation occurring simultaneously at a distant RNG will also result in a 000 sequence output to the software mask. Because the phase of the software masks are synchronized to the local computer clocks, which in turn are synchronized to the network, it is possible in principle to satisfy the second loophole criterion.

However, the loophole requires the GCP network to be synchronized at sub-millisecond accuracy with clock drift rates far below 1PPM (so that clocks remain synchronized over the course of hours-long events). While this is technically attainable with current time synchronization protocols, the GCP network synchronization is generally quite poor, with many nodes having time offsets of seconds or more, relative to reference clocks. The possibility that a subset of nodes is nevertheless sufficiently synchronized to maintain the loophole is highly unlikely, but this eventuality cannot be directly excluded since no record of local node clock synchronization is kept by the GCP.

Mindsong RNG The Mindsong bit rate is approximately 2600 bits/ sec. The device has an internal mask which is xor'd against a single RNG before being passed to the output port. There is no software mask applied at data acquisition. The Mindsong mask is 560 bits long and is constructed by concatenating the unique permutations of the balanced 8-bit sequence 11110000 (the exact concatenation order is specified in the Mindsong's US patent 5830064). The mask continually loops as it xor's the hardware RNG output. The devices have free-running clocks that are not synchronized to the local computer. It is easy to see that no loophole exists for the Mindsong XOR: inter-network correlations would require that the internal mask phases be synchronized at distant nodes. Since there is no synchronization, the loophole is closed for Mindsong RNGs.

Model tests

We now turn to analyses of data structure internal to the events which can help to distinguish between selection and PK models. The analyses are based on the field and selection models developed above and that nomenclature is retained in what follows. Bear in mind that the xor problem has seriously compromised a global consciousness interpretation.

As a first step, it is necessary to define an appropriate set of events. Of 426 formal events, 7 which occur before December 1998 are excluded since the GCP network showed considerable instability during its first months of operation resulting in unreliable estimates of event Z-scores. 14 New Years Eve celebrations are subject to two statistical tests, each over identical time-periods and should be included only once in the analyses done here. Potential problems with the event registration protocol have been identified in 17 early events and these are removed from the analysis to avoid a risk of confounding the selection hypothesis. Finally, 6 events that specify long time-periods of many days are excluded. These represent extreme outliers in the distribution of event time-periods and risk compromising the field hypothesis since they do not conform well to the field model's requirement of sustained focus of attention. The reduced event set contains 381 events.

The selection and field models require empirical values of the event and correlation effect sizes. The values of these parameters are $Z_0 = 0.33$ and $\xi_0 = 4.26 \times 10^{-5}$, respectively. The value of ξ_0 exceeds the null expectation by 6.15 standard deviations, which represents the significance of the formal experiment from the point of view of the field model. A check on the database as a whole, to verify that there are no spurious, persistent correlations that could bias the event data, finds an insignificant negative correlation of $\xi_{database} = -4.4 \times 10^{-7}$; CI90% (-2.5x10⁻⁶, 1.7x10⁻⁶); Z= -0.33. The non-significant average correlation measured over the entire database is thus two orders of magnitude smaller than the correlations present during events and well within the range of expected statistical noise.

The following presents three analyses that can distinguish PK from selection models. A full treatment is found in (Bancel, 2014).

Signal-to-noise test. The field model prediction for event Z-scores is $Z = \xi_0 N^{\frac{1}{2}}$, and the selection model predicts $Z = Z_0$. An estimated slope of event Z-scores (calculated from the measured correlation strength), against $N^{\frac{1}{2}}$, should therefore be positive if the field model obtains, and zero in the case of a selection effect.

However, the bimodal distribution of event-periods (Figure 2) confounds the test, since both models predict a reduced ξ for events that are longer than 12 hours. The selection model, in order to maintain a constant event Z, requires that ξ decrease as N^{-1/2}, and events with long durations in general have larger N. A reduced ξ for long events is also expected under the field model because these events use extended time periods to compensate for the difficulty in estimating precise beginning and end times of the field effect. As a consequence, long events are expected to contain considerable null data which effectively depresses the average correlation strength and reduces the event Z-score. This mimics the selection model and greatly reduces the power of regression tests.

The confound is largely removed if the analysis is restricted to events with 12-hour durations or less. In these cases, the estimation of ξ is not compromised by considerations of excess null data and the field model can be tested directly. The selection model is of course applicable for this data subset.

The data split gives 286 events with durations ≤ 12 hours and 95 with >12 hours. The average correlation strength for these subsets are 6.6 and 3.0 x 10-5, respectively, which is a significant difference (Z = 2.48). This indicates that the data split is justified in order to assure a sufficient power for the signal-to-noise test.

To set up the test, distributions of fitted slopes are calculated for each model by Monte Carlo simulation. Slope estimations for the data as well as the simulated distributions are established using the nonparametric Theil-Sen method. A auxiliary test uses linear regression to compare the two models. The field model calculation is straightforward and uses the formula above for the Z-score. Some care is required for the selection model: for each event, values of ξ are determined by $Z_0 N^{-1/2}$, except for events that were assigned a non-standard analysis in the formal experiment, in which case ξ is set to zero. By chance, the distribution of non-standard events is strongly biased towards small N, which gives a slightly positive expectation to the selection model regression slope. This underscores the importance of devising a test against the model distribution of slopes, rather than simply testing for the significance of a non-zero regression slope parameter. The powers of the two methods are similar and are calculated to be about 60% at a 95% confidence level.

Effect size variation with local time. The field model suggests that the correlation strength will be lower at night when the local populations are asleep and thus do not consciously attend to an event. The variation of the effect with local time can be tested by excluding data for which one or both RNGs fall outside of a local time window. A useful window width is 12 hours since it will fully span the human duration of sleep, and includes enough data to maintain a reasonable statistical power. The window is initially set with a start time at local midnight and an end time at noon. A Z-score is successively calculated for the data window as the start time is stepped in 1-hour increments. The result is a profile of correlation strength over the course of a 24-hour local-time day.

To do the calculation, each correlation pair-product is indexed by the two RNG's local times (accounting properly for daylight savings time), and rounded to the hour. The ξ_{ij} is excluded if one or both RNGs fall outside the local time window. The calculation is CPU intensive since there are more than 2x1010 correlation elements in the data set. The test compares windows with the start time positioned at local midnight (covering night and morning hours) and a start time at local noon (day and evening hours).

Major versus minor events. The last analysis looks at whether bigger events give a stronger effect. A binary classification into major and minor events is made and the total Z-scores for each set are calculated. The

selection model predicts a null difference, while the field model predicts that major events will produce a larger Z. The analysis is subjective since the classification requires a judgment of the historical nature of each event and its potential impact or importance for human populations. While some events are difficult to classify, many present little ambiguity. To give some examples, the New Year's Eve events, the September 11, Madrid and London terror attacks, and the 2004 and Fukushima tsunamis all fall clearly into the major event class. The deaths of Astrid Lindgren, Bob Morris and Frank Ogden, many minor organized meditations, Oprah Winfrey's visit to Africa and a James Tywman event in Iraq are reasonably classified as minor "global" events (the reader can peruse the GCP online event registry to get a sense of the range of formal events). The check is also relevant to the problem of how to include social variables in event predictions.

Results

Signal-to-noise test. The signal-to-noise test finds a of Z=2.68 against the data selection hypothesis. The test used a subset of events with durations of 12 hours or less. For completeness, I state the results when all events are included in the regression. For the field and selection models, respectively, the Monte Carlo Z-scores for regression slopes are Z=1.23 and Z=1.39. As expected, the ambiguous result for a regression on all events is resolved by the data splitting according to event durations.

Effect size variation with local time. The local time windows, midnightto-noon and noon-to-midnight, have ξ values of 2.23 and 6.23 x10⁻⁵, respectively. The difference Z-score is Z=2.06, indicating that the correlations among the RNGs are stronger during daytime hours and weaker at night. This can't be quantified as a significance probability since data exploration was necessary to develop the analysis. Still, there is a clear diurnal variation that peaks in the early evening and falls sharply after midnight, and this is consistent with the GCP hypothesis (Figure 3). A local time analysis for the full database shows that the database does not contain residual localtime diurnal variations in the correlation statistic. This latter point is quite important since it shows that local environmental variations such as day/ night temperature differences do not influence the RNG network.



Figure 3. The figure plots the evolution of the local-time correlation strength over 24 hours. Curves are repeated to allow for a better visualization of diurnal variations. Each point is the correlation strength, ξ , of the data contained in a window of 12 consecutive hours of local time. That is, both RNGs for each correlation product lie inside a local-time window 12 hours wide and centered at the point's time coordinate. The first point in the plot is centered at 00:00 hours and its window extends from 18:00 the previous evening to 06:00 the next morning. The points used for the night/day test are at 06:00 and 18:00 for the night and day periods, respectively. The upper trace shows the calculation for the event data and the lower curve is for the entire database. The lower curve shows that there are no systematic diurnal variations in database as a whole. The error bars are 1- σ deviations. Because the time windows are averaged across the globe (although time-shifted to align local times), each data point comprises equal amounts of data from the entire network. This produces identical error bars for each local time point.

Major versus minor events. The event split on 245 major and 144 minor events has a one-tailed difference Z-score of Z=2.08. The cumulating deviation of correlations for the major/minor event split is shown in Figure 4. Clearly this cannot be considered as a valid hypothesis test since the split is subjective and not blind to the event Z-scores. However, as a check on its validity, difference Z-scores can be calculated using an independent analysis such as the Day/Night variation as shown in Figures 5 and 6. The Day/Night variation is seen to be associated with the major event set and is absent for the minor events. This suggests that the major/minor split does indeed correspond to a real difference in the data related to the character of events and that it is not purely an artifact of data mining.

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Figure 4. Cumulative correlations for the data split of major and minor events.



Figure 5. Local Day/Night variation for major events.



Minor Events over Contiguous Timezones

Figure 6. Local Day/Night variations for minor events.

Discussion

The analyses presented above address two distinct, yet related questions: 1) is the formal GCP result due to PK or simple selection? and, 2) is there evidence favoring proto-psi global consciousness over an experimenter effect?

The first question is easier to treat since all of the analyses distinguish between PK and selection. The analyses and the consistency check on the major/minor event split are derived from straightforward physical assumptions under the field model which predict structure in the data that should be absent for simple selection. All return results in the direction expected by the field model. Four other tests not presented here (see Bancel, 2014) also favor the field model and are consistent with the major/minor split.

The most important analysis is the signal-to-noise test since it does not involve any secondary assumptions about the data structure. Accordingly, considerable effort has gone into assessing its validity. The Theil-Sen method was chosen because it is robust against outliers and influence points. It estimates the fitted slope as the median of point-to-point slopes taken for all pairs of points in a plot of Z versus N^{1/2} (more than 40,000 slopes for the 286 events in the data set). The Theil-Sen Monte Carlo simulation yields a probability value of 0.005 against the selection model. As a check, a Monte Carlo simulation of the models using standard linear regression finds a P-value of 0.02. Diagnostics of this regression find that 7 points have large Cook distances, indicating a substantial influence on the regression slope. When the influential points are removed, the P-value falls to 0.0053, in close agreement with the Theil-Sen estimation. An alternate method used to test for signal-to-noise was a regression on a direct linear combination of the models. This method has been developed by Dobyns to test PK against selection in RNG experiments done at the Princeton Engineering Anomalies Research laboratory (Dobyns, 2000; Jahn et al. 1997). The regression produces Z-scores for each model hypothesis individually. The result of this test finds a Z-score of 2.68 (P-value 0.0037) against selection and a Z-score of 0.11 which accepts the PK model. The three approaches thus provide consistent evidence against selection with a P-value of approximately 0.004.

While there is reasonable evidence to reject simple selection and choose PK as the favored interpretation of the GCP experiment, it is not clear that analyses can decide between experimenter PK and the global consciousness hypothesis. On the one hand, with minor conceptual adjustments all of the tests of data structure can be accommodated by either PK hypothesis. A straightforward example is simply to take the field model as a description of experimenter PK in which case the hypotheses become indistinguishable. On the other hand, the analysis of the xor problem severely weakens the case for proto-psi and by extension, the global consciousness hypothesis. However, the asymmetry of the loophole analysis provides some additional leverage for addressing the issue.

It was found that the no-go loophole is closed for the Mindsong RNGs, but remains weakly open for the Orion devices. Under the protopsi hypothesis then, the correlation statistic should show deviations among the Orion RNGs only, while Mindsong-Mindsong correlations should be at null expectation. Furthermore, because there is a significant signal-to-noise in the overall event data, a signal-to-noise regression slope should be positive for Orion RNGs, but not for the Mindsong data.

To set up the XOR loophole tests the data are split by sorting the correlation pair-products by RNG type. The split yields three subsets containing the Orion-Orion and Mindsong-Mindsong correlations, as

well as cross correlations of Orion-Mindsong RNG pairs. Table 2 shows the test results including the strengths and Z-scores for Orion, Mindsong and mixed correlations as well as the Theil-Sen and model regression tests of signal-to-noise. The homogeneous correlations of Orion and Mindsong RNGs are in agreement with the proto-psi hypothesis, with deviations from the null of approximately 3.3 and 1.2 standard deviations respectively. This is the expected result for a viable Orion loophole and a closed loophole for Mindsong RNGs. However, while the Z for Orion correlations is significant against the null hypothesis and the Mindsong Z is not, the calculated difference Z-score of these values is only Z=1.12, so that it is not possible to assert with confidence that correlations are restricted to the Orion RNGs alone. The tests of signal-to-noise also appear to favor proto-psi since they are significantly positive for the Orion correlations and accord with the null hypothesis for Mindsong RNGs, but here again the power of a difference test limits the significance of the observation.

The loophole argument is substantially weakened if cross correlations of the Orion-Mindsong RNG pairs are considered. The cross correlations are highly significant and comparable in strength to the homogeneous Orion correlations. Given that the Mindsong loophole is closed and that there is no synchronization between Orion and Mindsong outputs, cross correlations are not expected under the proto-psi model. Retaining the proto-psi hypothesis would thus require invoking an additional effect of a different kind. Although this cannot be entirely excluded, it is considerably less parsimonious than proposing a PK-type experimenter effect. Alternately, a rejection of the proto-psi proposal requires assuming that the differences in the Orion-Orion and Mindsong-Mindsong correlations are accidents of the data split and this possibility is consistent with the relatively weak powers of the loophole tests. A caveat to this conclusion is that the loophole analysis is based on a single example of how a loophole might arise. A more thorough analysis of the xor problem is thus needed before a definitive conclusion can be drawn.

Returning to the questions posed at the beginning of this section, we see that simple selection can be rejected as a model of the GCP based on the convergence of evidence for structure in the event data. The signalto-noise analysis provides a particularly strong argument. More elaborate selection models which allow for data structure can be considered, but these are difficult to distinguish from experimenter PK effects which perhaps relegates that distinction to a position of secondary importance. Theoretical frameworks which address the problem generally fall into the class of so-called observational theories (OTs) (see for example, Millar, 1978; Schmidt, 1984; Houtkooper, J.M., 2002; von Lucadou, W., Römer, H. & Walach, H., 2007). While worth pursuing, OTs are difficult to adapt quantitatively to the GCP and probably untestable for the current experiment.

Like simple selection, the analyses also render the proposal of protopsi global consciousness unconvincing. It will be interesting to undertake a more complete analysis of the xor problem, but the bar is set high for finding an adequate loophole that can explain the data in a consistent fashion. Consequently, any models which retain the notion of global consciousness will need to include engagement at some level. This requires modifying the GCP hypothesis so that the experiment can be referenced by global consciousness in some way. An indirect approach is to treat global consciousness as a proto-psi effect and allow an intermediary agent, whose behavior is modulated when global consciousness is sufficiently established, to provide the engagement that is necessary to circumvent the xor problem. An example of how this might be formulated can be drawn from the field model presented in the appendix. The model describes two steps to producing data correlations, one which generates uncorrelated bit deviations in the RNG outputs and a second which provides for the inter-RNG correlation of these deviations. The model can accommodate a modified GCP hypothesis by associating proto-psi global consciousness with the bit deviations and their correlation with the intermediary agent. A natural choice is to identify the intermediary agent with the experimenter.

The model thus separates global consciousness from the agent's engagement in a way that is amenable to analysis. Under the model, the proto-psi global consciousness provides a degree of lability to the network by inducing bit deviations in the RNGs. Subsequent correlations which arise from the network lability are associated with the experimenter's engagement, either through a selection process or PK. In analyses, the proto-psi effect is examined by measuring the second moment of the correlation statistic, while the correlations appear in measures of the first moment. An advantage of the model is that structure in the proto-psi field will be present in both measures. This provides a degree of testability to the model, as does the prediction that the proto-psi effect can occur even when correlations are absent. Under the model, both proto-psi and engaged psi effects are present, and they can be studied independently. Because proto-psi is included in the model, those effects should be measurable outside the context of the experiment itself.

An alternate to the intermediary model is to attribute engagement directly to global consciousness itself, which essentially proposes an aware entity arising at the time of events. This radical approach is not easily treated since it is confounded with simple proposals of an experimenter effect.

Correlation strength by RNG type	Z	ک
Orion correlations	3.28	0.000041
Mindsong correlations	1.17	0.000018
Orion-Mindsong correlations	5.36	0.000053

Table 2. Tests of proto-psi conjecture and XOR loophole for Orion RNGs.

Conclusions

This paper has presented analyses of the GCP which can distinguish among different interpretations of the experiment. The focus has been on two simple models, that of a global consciousness blind to the experiment which arises at the time of major world events, and simple selection of event data by the experimenter. The models provide testable predictions for the event data, and a field model for global consciousness was developed to design tests for predicted or plausible structure that should be present for global consciousness, but absent under the selection hypothesis.

The heuristic notions proto-psi and engagement were introduced to help set up the analyses. The main conclusion of that reasoning is that psi effects under genuinely blind conditions are fundamentally different from more familiar effects involving persons engaged with psi phenomena. In the case of the GCP, this leads the identification of the xor problem as a no-go for global consciousness.

The analysis of data structure rejects the simple selection hypothesis at a reasonably high level of confidence. The signal-to-noise analysis provides the most clearcut support for this conclusion. It is buttressed by the other independent tests and a number of consistency checks. While some caution should be voiced in light of the post-hoc nature of the tests and the use of data splits, the coherent picture that emerges is a reasonable argument that there is structure in the data that can be explained by a field model, but not by selection.

Tests for a loophole to circumvent the XOR no-go suggest that a straightforward conception of proto-psi global consciousness is also not tenable. While additional work should be done to establish the full scope of possible loopholes, it is hard to see how one can account for the cross correlations seen in the data.

The analyses, then, provide good arguments for rejecting both simple models and we are forced to look elsewhere for an explanation. The xor problem implies that the GCP presents us with an experimenter effect, and experimenter PK is a good avenue to explore given the extent of the data structure revealed by the analyses. Nevertheless, as mentioned in the Discussion section, more elaborate selection scenarios remain a possibility and these can be confounded with PK. The experiment may ultimately need to invoke observational theories to find a consistent explanation. This is a difficult undertaking which would require new hypotheses and experimentation. A strong criticism of the GCP is its reliance on an openended protocol for deciding event parameters and this should be replaced with an algorithmic procedure in any future version of the experiment.

A hybrid model which retains global consciousness also remains a possibility. This should be examined to determine whether further work in this direction is viable. In practical terms, perhaps the most important consequence of the analyses is that the GCP effect may indeed be subject to signal-to-noise averaging. If this is so, the effect can be studied with far greater statistical power by increasing the number of nodes in the network. A ten-fold increase in the number of RNGs would allow a full replication within 2 to 4 years. Augmenting the network 100-fold
would allow for the detection of single events in real time. The detail and power provided by vastly increased data rates would also permit the development of analyses to test models of experimenter PK effects against true global consciousness, and begin the challenging task of modeling the link between mind and matter, whatever the source of the effect may be.

References

- Atmanspacher, H. and Jahn, R. G. (2003). Problems of Reproducibility in Complex Mind-Matter Systems. Journal of Scientific Exploration, 17, 243-270.
- Bancel, P. (2014). An Analysis of the Global Consciousness Project. In Evidence for Psi, Broderick and Goertzel, eds. McFarland Press.
- Bancel, P., & Nelson, R. (2008). The GCP Event Experiment: Design, Analytical Methods, Results. Journal of Scientific Exploration, 22(3), 309-333.
- Dobyns, Y.H., (2000). Models on PEAR Data. Journal of Scientific Exploration, 14(2), 163-194.
- Global Consciousness Project, http://teilhard.global-mind.org/results.html May 1, 2013.
- Houtkooper J.M., (2002). Arguing for a n Observational Theory of Paranormal Phenomena. Journal of Scientific Exploration, 16, 171-185.
- Jahn, R.G., Dunne B., Nelson, R.D., Dobyns, Y.H., & Bradish, G.J., (1997). Correlations of random binary sequences with pre-stated operator intention: A review of a 12-year program. Journal of Scientific Exploration, 11(3), 345-367.
- May, E., & Spottiswoode, J., (2011). The Global Consciousness Project: Identifying the Source of Psi. Journal of Scientific Exploration, 25(4), 663–682.
- May, E., Utts, J., & Spottiswoode, J. (1995). Decision Augmentation Theory: Towards a Model of Anomalous Mental Phenomena. Journal of Parapsychology, 57, 195–220.
- Millar, B., (1978). The observational theories: A primer. European Journal of Parapsychology, 2, 304-332.
- Nelson, R., Radin, D., Shoup, D., & Bancel, P., (2003). Correlations of Continuous Random Data with Major World Events. Foundations of Physics Letters, 15, 537-550.
- Nelson, R. & Bancel, P., (2011). Effects of Mass Consciousness: Changes in Random Data during Global Events. Explore, 7, 373-383.
- Schmidt, H., (1984). Comparison of a teleological model with a quantum collapse model of psi. Journal of Parapsychology, 48, 261-276.
- von Lucadou, W., Römer, H. & Walach, H., (2007). Synchronistic Phenomena as Entanglement Correlations in Generalized Quantum Theory. Journal of Consciousness Studies, 14, 50-74.

CONSCIOUSNESS, FREE WILL AND QUANTUM BRAIN BIOLOGY – THE 'ORCH OR' THEORY¹

Stuart Hameroff*

1. Introduction – Consciousness and its place in the universe

We know what it is like to be conscious – to have awareness, phenomenal experience (composed of what philosophers term 'qualia'), a sense of 'self', feelings, sensations, emotions, apparent choice and control of actions, memory, a model of the world and one's body, thought, language, and, e.g. when we close our eyes, or meditate, internallygenerated images and geometric patterns. But what consciousness actually is, how it comes about and its place in the universe remain unknown.

Science generally portrays consciousness as an emergent property of complex computation among brain neurons. In this view, consciousness first appeared during evolution of biological nervous systems. On the other hand, some philosophical, spiritual and quantum physical approaches suggest consciousness depends on a fundamental property intrinsic to the universe, and that consciousness has, in some sense, been in the universe all along. Could both views be true?

The very existence of consciousness seems highly unlikely. Cosmologists tell us that if specific values for the twenty or so fundamental numbers which characterize the universe (precise charge and mass of particles, values for gravitational and other constants, etc.) were just slightly different, life and consciousness—at least as we know them would be impossible. The universe is seemingly 'fine-tuned' for life and

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^{*} Center for Consciousness Studies, The University of Arizona, Tucson, Arizona, USA.

consciousness. Why this may be so is approached by several versions of the 'anthropic principle'. In the 'strong' version (Barrow, and Tipler 1986), the universe is somehow compelled to harbor and enable consciousness, as if consciousness were engaged in its development, organizing the universe. The 'weak anthropic principle' (Carter, 1974) suggests that only our particular universe is capable of consciousness, and only this one universe, a privileged version of a multitude of universes, can be observed and wondered about. The question again boils down to whether consciousness is intrinsic to the universe, or an emergent property of brain computation.

The conventional wisdom in neuroscience and philosophy tells us consciousness emerges from brain computation, specifically complex synaptic computation among 'integrate-and-fire' ('Hodgkin-Huxley') brain neurons. The foundation for attempts to understand consciousness is that the brain is a computer. Consciousness is a computation. Some proponents further believe that when the brain's computational wiring diagram—the 'connectome'—is unraveled, mapped and replicated in silicon, brain functions including consciousness will be downloaded and recreated (Kurzweil, 2013). Consciousness would become a commodity. Huge resources are aimed at 'mapping the brain'.

But consciousness isn't necessarily computation. Physicist Sir Roger Penrose (1989) points out that while computers surpass humans in many information capacities, they don't really 'understand' anything. And as philosopher David Chalmers' (1996) 'hard problem' illustrates, phenomenal 'qualia' like redness, joy, the taste of mustard and the smell of lilac may involve some added feature, some 'funda-mental' entity or process intrinsic to the fine scale structure of the universe, akin to mass, spin or charge, perhaps embedded with fundamental values which work to anthropically optimize the universe for consciousness.

Unable to account for consciousness through strictly neuronal computational approaches, prominent neuroscientist Christof Koch (2012) has appealed to panpsychism, the notion that material particles are endowed with subjectivity, or experiential 'qualia', intrinsic to the universe as a property of matter. But matter itself, at tiny scales, is continuously 'materializing', i.e. reducing, or collapsing to definite states from multiple quantum possibilities. At the scale at which biomolecules

govern neuronal activity, the strange laws of quantum mechanics come into play, and materialism is a mirage. Consciousness seems related to the boundary between quantum and material worlds.

Physical reality is ruled by two sets of seemingly incompatible laws. In our everyday material ('classical') world, Newton's laws of motion, Maxwell's equations, the gas laws and others accurately predict behavior of particles and energy. However at tiny scales, and the size cutoff, or boundary between the two worlds is variable and unknown, the laws of quantum mechanics rule. Particles can exist in multiple locations or states simultaneously ('quantum superposition'), become spatially separated from one another, but remain connected ('entanglement'), and condense into unitary objects ('quantum coherence').

This strangeness isn't observed in our material world. Attempts to measure quantum superpositions cause them to collapse to definite states. The mystery of why this happens, why there exists some boundary, or edge between quantum and classical worlds is known as the 'measurement problem' in quantum mechanics.

Several interesting solutions to the measurement problem have been put forth. Decoherence is the notion that quantum systems which interact with the classical environment are disrupted by thermal interactions. What about isolated quantum systems?

One proposal from the early days of quantum mechanics is that the very act of conscious observation causes quantum possibilities to materialize, or reduce to definite states - consciousness 'collapses the wave function' (e.g. Wigner, von Neumann, Stapp). This view is also known as the 'Copenhagen interpretation' due to the Danish origin of Niels Bohr, one of its early proponents. But this view led to a major dilemma about unobserved, isolated quantum systems, as illustrated by Schrödinger's famous thought experiment in which the fate of an isolated cat is tied to a quantum superposition. According to Copenhagen, the cat is both dead and alive until observed by a conscious human. Absurd it was, but the question persists. Why aren't quantum superpositions seen in our material world?

The 'multiple worlds' hypothesis suggests that with each superposition, the universe separates at a fundamental level, each possibility evolving into its own universe (Everett, 1957). Thus there exists an infinite number

of co-existing, 'parallel universes'. This view has been linked to the weak anthropic principle, in which we live in the one universe, of a multitude of universes, most conducive to life and consciousness.

These approaches are flawed. But each may each hold part of an answer. The Copenhagen/conscious observer approach has its Schrödinger's cat problem, and places consciousness outside science as the external cause of collapse/reduction. But it does directly link consciousness to quantum state reduction.

'Multiple worlds' is untestable, non-falsifiable, energetically unfavorable, and doesn't deal with consciousness. But it does deal with the nature of superposition. It implies that a particle in two places at the same time is equivalent to separation, bifurcation, in the fine scale structure of the universe—spacetime geometry (irrespective of whether the separated spacetimes evolve to their own universes). Each particle location has its own spacetime geometry.

Another proposed solution to the measurement problem with concepts similar to these two features is Penrose 'objective reduction' (OR) in which quantum superpositions evolve by the Schrödinger equation until reaching an 'objective' threshold for reduction, or collapse. Similar to 'multiple worlds', Penrose OR portrays quantum superpositions as spacetime separations (due to alternate curvatures), but are unstable due to properties inherent in spacetime geometry. Before each spacetime branch evolves its own new universe, the separation reaches OR threshold by the uncertainty principle $E_{c} = h/t$ (EG is the magnitude of separation, h is the Planck-Dirac constant, and t the time at which OR occurs). At that instant, spacetime geometry reconfigures, quantum possibilities choose particular material states, and, according to Penrose, a moment of conscious experience occurs. Penrose OR turns the Copenhagen/ conscious observer approach around. Rather than consciousness *causing* collapse/reduction, consciousness is collapse/reduction, a process on the edge between quantum and classical worlds.

Generally, OR can be taken as equivalent to decoherence, the process by which a quantum system is said to be disrupted by its random environment. Superposition/separations EG arising continuously will entangle other such random superpositions and quickly reach OR threshold by $E_G = h/t$. In such cases, the conscious experience would be

primitive qualia without cognitive meaning, described as 'proto-conscious', intrinsic to the universe, accompanying OR events ubiquitously shaping material reality. This approach is similar to the 'Ground of Being' concept in Eastern philosophical terms.

OR 'protoconscious moments' are also similar to Buddhist concepts of discrete conscious moments, and to an approach to consciousness as 'occasions of experience' by philosopher Alfred North Whitehead (1929, 1933) who saw consciousness, and the universe, as a process, as sequences of events. Leibniz (1768) had 'quantized' reality, describing fundamental 'monads' as ultimate entities, but Whitehead transformed monads into 'actual occasions' occurring in a "basic field of proto-conscious experience". Whitehead occasions of experience are intrinsic to the universe, spatiotemporal quanta, each endowed, usually, with only low level, "dull, monotonous, and repetitious [...] mentalistic characteristics". Abner Shimony (1993) observed how Whitehead 'occasions' resemble quantum state reductions.

How do we get from simple proto-conscious moments, or occasions, to full, rich meaningful consciousness? In panpsychism, simple particles with simple experience must be somehow organized, or combined into a cognitive, meaningful arrangement—the 'combination problem'. Whitehead considered this problem for his 'occasions', or events, rather than particles, and described how 'highly organized societies of occasions permit primitive mentality to become intense, coherent and fully conscious'.

How can Penrose OR events be so organized, and occur in the context of brain function? The Penrose-Hameroff 'Orch OR' theory suggests OR events are 'orchestrated' into full, rich conscious moments. This paper describes how Orch OR can occur in structures called microtubules inside brain neurons, how it addresses the particular issue of free will, and discusses 'brain tuning', the possibility of addressing mental states and disorders through microtubule quantum vibrations. Consciousness is seen as intrinsic to the universe.



2. Where in the brain does consciousness occur?

Figure 1. Three waves in sensory processing. Sensory inputs from spinal cord and cranial nerves to thalamus result in primary projections (1) to primary sensory cortex, e.g. visual area 1 (V1) in occipital cortex in the back of the brain. From these areas, feed-forward projections (2) go to secondary associative and 'executive' areas cortex, e.g. pre-frontal cortex (PFC) from which tertiary projections (3) go to other brain regions whose content then becomes conscious.

The general architecture for conscious sensory processing in the brain is shown in Figure 1. Sensory inputs to thalamus result in (1) projections to primary sensory cortex, e.g. visual area 1 (V1) in occipital cortex in the back of the brain. From primary sensory areas, (2) secondary feed-forward projections go to associative and 'executive' e.g. pre-frontal cortex (PFC). From there, (3) tertiary projections go to other cortical regions whose content then becomes conscious.

The notion that this 'third wave' feedback is conscious, and first and second waves are not conscious, is consistent with philosophical approaches called 'higher order thought' ('HOT'), and neuroscientific cortical feedback models for conscious vision Lamme & Roelfsma, 2000). Experimental evidence for the association of the 'third wave' with consciousness is provided through studies of anesthesia. Despite the fact that neurotransmitters, receptors and other neurophysiology appears identical among the three waves, all three types of anesthetic molecules (volatile gas anesthetics, propofol and ketamine) selectively inhibit third wave activity while sparing primary and secondary projections (Lee et al, 2013).

There are two clarifications with this anatomical scheme. First, although the brain's medial surface is shown in Figure 3, sensory-based

cortical projections may occur more toward outer dorsal surfaces. Second, internally-generated conscious states, e.g. mindwandering, meditation and dreams, possibly mediated through default mode networks, will have different pathways, though their end targets (layer V cortical pyramidal neurons, see below) may be identical.

Third wave activity within cortex seems to also be composed of three waves, successively, and maximally, integrating information. Cortex is arranged in 6 horizontal layers, and sensory inputs from thalamus go (1) to layer 4, and thence (2) from layer 4 to layers 1, 2, 3 and 6. (3) Projections from these layers converge on layer 5 giant pyramidal neurons, the most likely site for consciousness in the brain. Apical dendrites from pyramidal neurons ascend vertically to the cortical surface, and are most directly responsible for measurable electro-encephalography (EEG), e.g. '40 Hz' gamma synchrony, the best neural correlate of consciousness. Axonal firing outputs from layer V pyramidal neurons descend, e.g. to implement behavior, exerting causal efficacy in the world. Third wave integration in cortical layer V pyramidal neurons is the most likely site for consciousness in the brain.



Figure 2. Three waves of sensory processing in cerebral cortex, a thin mantle on the very top of the brain composed of 6 hierarchical cellular layers. Primary sensory projections from thalamus (1) arrive in layer IV which projects secondary activity (2) to layers I, II, III and VI. These areas then project tertiary (3) activity to giant pyramidal neurons in layer V, where consciousness is most likely to occur. Outputs from layer V pyramidal neurons project sub-cortically, e.g. to manifest 'conscious' behavioral actions. Activity in apical dendrites from pyramidal neurons which ascend to cortical surface are most directly responsible for measurable electro-encephalography (EEG).



Figure 3. Layer V pyramidal neuron with internal networks of microtubules connected by microtubule-associated proteins ('MAPs'). Inputs from apical and basilar dendrites are integrated in pyramidal neuronal membranes and cytoskeletal microtubules. On left, a single microtubule is shown comprised of individual tubulin proteins, each in 3 possible states.

'Integrate-and-fire' layer V pyramidal neurons are the final, and maximal, integrator for sensory processing, providing a neurobiological basis for 'Integrated information theory' (Tononi, 2012). Their firing outputs control behavior, but neuroscience considers pyramidal neurons (indeed all neurons) according to the Hodgkin-Huxley (HH) standard model. In HH, each neuron is a threshold logic device in which dendrites and cell body (soma) receive and integrate synaptic inputs via excitatory and inhibitory membrane potentials to a threshold at the proximal axon (axon hillock, or axon initiation segment— 'AIS'). When AIS membrane potential reaches a critical threshold, the axon 'fires' to convey signals to the next synapse and layer of neurons.

Integration implies merging and consolidation of multiple disparate information sources. At the level of an individual neuron, integration is approximated as linear summation of synaptic membrane potentials. However integration in branching dendrites and soma requires logic, amplification of distal inputs, branch point effects, and signaling in dendritic spines and local dendritic regions. Nonetheless, according to HH, all such factors are reflected in membrane potentials, and thus the HH neuron is completely algorithmic and deterministic. For a given set of inputs, synaptic strengths and firing threshold, a fixed output in the form of axonal firings, or spikes will occur. Networks of integrateand-fire neurons regulated by synaptic strengths and firing thresholds can integrate at various anatomical scales, providing highly nonlinear functional processing. But in the end, such processes are algorithmic and deterministic, leaving no apparent room for consciousness or free will.



Figure 4. Integrate-and-fire neuronal behaviors. a. The Hodgkin-Huxley model predicts integration by membrane potential in dendrites and soma reach a specific, narrow threshold potential at the proximal axon (AIS) and fire with very low temporal variability (small tb-ta) for given inputs. b. Recordings from cortical neurons in awake animals (Naundorf et al. 2006) show a large variability in effective firing threshold and timing. Some additional factor, perhaps related to consciousness ('C') exerts causal influence on firing and behavior.

However, real neurons differ from idealized HH neurons. For example Naundorf et al. (2006) showed that firing threshold in cortical neurons in brains of awake animals vary spike-to-spike. Some factor other than inputs, synaptic strengths and the integrated membrane potential at the AIS contributes to firing, or not firing. Firings control behavior. This integration 'x-factor' deviation from HH behavior, modulating integration and adjusting firing threshold e.g. in layer V pyramidal neurons, is perfectly positioned for consciousness, causal action and free will, yet is in some way divorced from membrane potentials. What might it be?

3. A finer scale?

Interiors of neurons and other cells are organized and shaped by the cytoskeleton, a scaffolding-like protein network of microtubules, microtubule-associated proteins (MAPs), actin and intermediate filaments. Microtubules (MTs) are cylindrical polymers 25 nanometers (nm = 10^{-9} meter) in diameter, comprised usually of 13 longitudinal protofilaments, each chains of the protein tubulin. MTs self-assemble from the peanut-shaped tubulin, a ferroelectric dipole arranged within microtubules in two types of hexagonal lattices (A-lattice and B-lattice), each slightly twisted, resulting in differing neighbor relationships among each subunit and its six nearest neighbors. Pathways along contiguous tubulins in the A-lattice form helical pathways which repeat every 3, 5 and 8 rows on any protofilament (the Fibonacci series).

Each tubulin may differ from among its neighbors by genetic variability, post-translational modifications, phosphorylation states, binding of ligands and MAPs, and dipole orientation. MTs are particularly prevalent in neurons (109 tubulins/neuron), and uniquely suitable, especially in dendrites and cell bodies, for information processing, encoding and memory. In cell division, MTs dis-assemble, and then re-assemble as mitotic spindles, which separate chromosomes, establish daughter cell polarity and then re-assemble for cellular structure and function. However neurons are unlike other cells; once formed, they don't divide, and so neuronal MTs may remain assembled indefinitely, providing a stable potential medium for memory encoding.

MTs in neuronal soma and dendrites are unique in other ways as well. Each tubulin dimer (composed of slightly different alpha and beta monomers) has a dipole, a net positive charge at the beta monomer, and a net negative charge at the alpha monomer. So MTs assembled from parallel arrayed tubulin dipoles also have a net dipole, positive toward its beta monomer end, and negative toward the alpha end. In axons, and in all non-neuronal cells throughout biology, MTs are arrayed radially, like spokes in a wheel, extending continuously from the centrosome near the nucleus, outward toward the cell membrane. These radially arrayed MTs all have the same polarity, the beta plus end outward toward the cell membrane, and alpha negative end inward at the hub, anchored to the centrosome/centriole near the nucleus.

However unlike axons and all other cells, MTs in dendrites and cell bodies/soma are short, interrupted and of mixed polarity, some with their beta plus ends outward, and the rest inward, all interconnected by MAPs into local networks. Dendritic-somatic MTs are also stabilized against depolymerization by special MAP capping proteins, and are thus particularly suitable for memory encoding.

The mechanism by which memory is encoded, stored and processed in the brain remains largely unknown. The standard explanation is through synaptic plasticity, i.e. sensitivities at particular synapses guide activity and create patterns through neuronal networks. However synaptic membrane proteins which determine sensitivity are transient and continuously recycled, lasting only hours to days, and yet memories can last lifetimes. Some other factor, or factors, must be involved.

Synaptic proteins are synthesized in neuronal cell bodies/soma, and transported to synapses by 'dynein' and 'kinesin' motor proteins traveling along MTs, which appear to act as passive guides, like railroad tracks. In dendrites and soma where MTs are short, interrupted and of mixed polarity, the motor proteins must jump from MT to MT, and, at dendritic branch points, choose particular pathways to deliver their cargo to the proper synapses. How they do so seems to depend on tau, the microtubule-associated protein (MAP) thought to stabilize MTs, that also seems to serve as traffic signals, instructing motor proteins precisely where to disembark and deliver their cargo. Thus specific placement patterns of tau on MT lattices subserves synaptic function related to memory, and implies specific tau binding locations are encoded in MTs. Tau displacement from MTs results in neurofibrillary tangles, microtubule instability and cognitive dysfunction in Alzheimer's disease.

Thus memory-related synaptic function depends on information encoded in MT lattices, e.g. tau placement. As the origins of memory must reach MTs from the outside world, the question then becomes how synaptic-based inputs may encode information in MTs.

The prevalent synaptic model for memory is long term potentiation (LTP) in which brief, high frequency pre-synaptic stimulation results in long-term post-synaptic potentiation (increased synaptic sensitivity), able to influence neuronal network patterns. At the intra-neuronal level in LTP, synaptic excitation causes influx of calcium ions which convert the hexagonal enzyme calcium-calmodulin to an insect-like calcium-calmodulin kinase II holoenzyme ('CaMKII'). Each of six extended kinase domains on either side of CaMKII are able to phosphorylate (or not phosphorylate) suitable protein substrates, thus providing up

to 6 'bits' of information per CaMKII, with hundreds to thousands of CaMKII activation per synaptic excitation. Protein substrates for CaMKII phosphorylations are likely sites for memory encoding, storage and processing. What might they be?

Craddock et al (2012) showed the hexagonal CaMKII kinase array precisely matches hexagonal tubulin lattice spatial geometry in microtubules, and that each kinase domain can reach intra-tubulin amino acids suitable for phosphorylation (Figure 5). CaMKII tubulin phosphorylation may alter dynamical properties, and lead to posttranslational modifications resulting in memory 'hardwiring'. Dendriticsomatic microtubules are likely sites for memory encoding.



Figure 5. Memory trace - Calcium-calmodulin kinase II ('CaMKII'), a hexagonal holoenzyme activated by synaptic calcium influx extends 6 leg-like kinase domains above and below an association domain. The 6 kinase domains precisely match hexagonal size and geometry in both A-lattice and B-lattice microtubules.

Due to their lattice structure and organizational roles, MTs have long been suggested to function as information processing devices. Observing and wondering at the intelligent behavior of single cell organisms (lacking synapses), famed biologist Charles Sherrington said (1957): "of nerve there is no trace, but the cytoskeleton might serve". Early descriptions of MTs as computer-like devices (Hameroff, and Watt 1982; Hameroff 1997; Rasmussen et al. 1990) suggested that (1) individual tubulins act as binary bit-like information units (e.g. flexing between two conformations, or dipole states), and that (2) the microtubule lattice acted as a computational matrix or cellular ('molecular') automata. In the latter case, tubulin states interact with hexagonal lattice neighbor tubulin states by dipole couplings, synchronized by biomolecular coherence as proposed by Fröhlich (1968, 1970, 1975; Smith et al. 1984, Rasmussen et al. 1990). Simulations of microtubule automata based on tubulin states show rapid information integration and learning. If the MT memory proposal is correct, information processing relevant to cognition



and consciousness would be occurring precisely in the medium in which memory is embedded, a highly efficient and logical proposition.

Figure 6. Three time-steps (e.g. at 10 megahertz) of two types of microtubule automata. (a) Dipole paths or spin currents interact and compute along spiral lattice pathways, for example generating a new vertical spinwave (a 'glider gun' in cellular automata). (b) A general microtubule automata process.

Models of MT information processing developed in the 1980s and 1990s considered fundamental information units to be a bit-like binary state of an individual tubulin, interacting/computing with states of its six surrounding tubulin lattice neighbors. However, subsequent models have considered, instead, topological pathways of like tubulin states through two types of MT lattice geometry. In the A lattice with Fibonacci geometry (Figure 7), pathways through adjacent tubulins follow pathways which (1) travel upward/rightward, repeating every 5 tubulins on any single protofilament, and another upward/leftward, repeating every 8 tubulins. Dipole orientations along these pathways may also represent information, interact and compute, perhaps coupled to MT vibrations along these pathways.

In any case, MT-based information processing implies enormous capacity and speed. Based on tubulin binary switching and 10 megahertz processing (see below), MT-based information capacity is roughly 10⁹ tubulins per neuron oscillating at e.g. 10 megahertz (10⁷ Hz) for 1016 operations per second per neuron.



Figure 7. (a) Molecular modeling of tubulin dimer shows aromatic amino acids tryptophan, phenylalanine and tyrosine in non-polar, hydrophobic regions. Spheres are anesthetic binding sites. Curved lines enclose rings in particular aligned orientation along 5- and 8-start helical channels, containing anesthetic binding sites (with permission from Craddock et al. 2012). (b) Schematic of 5-start helical pathway of aromatic ring dipoles as suggested in Figure 7a. Top 2 pathways show alternate dipole orientations, and 3rd shows quantum superposition of both orientations. Bottom shows how anesthetics disperse dipoles, acting to erase consciousness.



Figure 8. Dipole qubit in microtubule, with classical and quantum dipole information states for the '5-start' helical pathway in tubulin and microtubules. Left: The '5-start' helix in microtubule A-lattice aligned with dipoles in intra-tubulin aromatic rings (Figure 7). Top: 'upward' dipole, bottom: 'downward' dipole. Right: Quantum superposition of both upward and downward helical paths coupled to dipole orientations, i.e. 'qubits'. Dipoles may be electric dipoles due to charge separation, or magnetic dipoles, e.g. related to electronic (and/or nuclear) spin. Similar qubit pathways may occur along 8-start pathways, or other pathways.

Dendritic-somatic MTs regulate synapses in several ways. They serve as tracks and guides for motor proteins (dynein and kinesin) which transport synaptic precursors from cell body to distal synapses, encountering, and choosing among several dendritic branch points and many MTs to find the right location. The navigational guidance seems to involve the MAP tau as a 'traffic signal' (specific placement of tau on microtubules being the critical feature). In Alzheimer's disease, tau is hyperphosphorylated and dislodged from destabilized microtubules, forming neurofibrillary tangles associated with memory loss (Matsuyama & Jarvik, 1989; Craddock et al., 2012a). In Downs syndrome dementia, post-operative cognitive dysfunction (POCD) and other cognitive disorders, MTs are also destabilized and partially disrupted.

Information integration in dendritic-somatic MTs, influenced by encoded memory, may cause deviation from Hodgkin-Huxley neuronal behavior, exerting causal agency. A deeper order, high capacity, finer scale process, e.g. at end-integration in cortical layer V pyramidal neuron dendritic-somatic MTs is a likely site for consciousness. But such a process would still be algorithmic, deterministic, and fail to address phenomenal experience—the 'hard problem'. Something is still missing. Penrose OR provides non-algorithmic (non-computable) processing, causality and addresses the hard problem. In the mid-1990s, Penrose and Hameroff teamed up to apply OR to biology, specifically OR-terminated quantum computations in brain neuronal MTs 'orchestrated' by synaptic inputs, memory and intrinsic MT resonances.

4. Penrose 'Objective Reduction' ('OR') and the 'Orch OR' qubit

Penrose OR is one proposed solution to the 'measurement problem' in quantum mechanics, the problem of why quantum superpositions particles existing in multiple states or locations at the same time, and described by a quantum wave function—are restricted to microscopic scales, not seen in the 'classical' world we experience. Other suggestions include (1) proposals by Bohr, Wigner, von Neumann, Stapp and others (the 'Copenhagen interpretation', after Niels Bohr's Danish origin) in which conscious observation causes the wave function to collapse (e.g. Schrödinger's cat), but putting consciousness outside science, and (2) decoherence, which suggests that interaction with the random, classical environment disrupts quantum states. (3) 'Multiple worlds' (Everett, 1957) proposes that each possibility evolves its own spacetime geometry, resulting in an infinite number of co-existing universes. And (4), objective reduction (OR) models specify thresholds for quantum state reduction. Among these is Penrose OR.



Figure 9. Spacetime geometry schematized as one spatial and one temporal dimension in which particle location is equivalent to spacetime curvature. Left: Top and bottom show spacetime histories of two alternative particle locations. Right: Quantum superposition of both particle locations as bifurcating space–time depicted as the union ('glued together version') of the two alternative histories (adapted from Penrose 1989, 338).

To approach superposition, Roger Penrose first equated particle states to particular curvatures in spacetime geometry, and superposition to simultaneous, alternate curvatures. Superposition may then be seen as a Planck scale separation, or bubble in the fine scale structure of the universe (Figure 1). In the 'multiple worlds' proposal, each such possible curvature would evolve its own universe. However Penrose suggested spacetime separations were unstable, and would reduce (collapse) due to an objective threshold given by a form of the uncertainty principle $E_G=h/t$. EG is the gravitational self-energy of the superposition, h is the Planck-Dirac constant, and t the time at which OR occurs, accompanied by a conscious moment, and selecting particular states of reality (Figure 2).



Figure 10. As superposition curvature EG reaches threshold (by $E_G = h/t$), OR occurs. One particle location/curvature is selected and becomes classical. The other ceases to exist.

Generally, such OR events occur in a random environment (identical to decoherence), the accompanying subjective experience lacking cognitive

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function or meaning. The Penrose-Hameroff 'Orch OR' theory proposes that biology evolved specific mechanisms to isolate and 'orchestrate' OR events ('orchestrated objective reduction' - 'Orch OR'), giving full, rich conscious experience with cognitive meaning and volitional choice. Specific Orch OR mechanisms involve a form of quantum computing in the brain, specifically via structures called microtubules found in all animal and plant cells.

In quantum computers, information is represented not just as, e.g., binary bits of 1 or 0, but also as quantum superposition (quantum bits, or 'qubits') of both 1 *and* 0. Qubits can entangle, interact and compute with other qubits non-locally, and highly efficiently, according to the Schrödinger equation. (In topological quantum computing, qubits are states of particular pathways through lattices, rather than states of individual subunits comprising those pathways.)

Two basic issues limit implementation of quantum computers. First, interaction with the classical environment disrupts the quantum superposition ('decoherence'), and must be avoided long enough for useful computation to occur. Laboratory quantum computers are hampered by decoherence due to the 'random' thermal environment, and thus constructed at extremely cold temperatures. (Topological qubits are more resistant to decoherence.)

Conceptually, Penrose OR by E = h/t replaces decoherence. Without isolation, in a random environment, OR occurs rapidly, with random outcomes. The combined EG of the system and its environment quickly reach threshold at h/t, and OR occurs with a non-cognitive, random moment of subjective experience. Presumably, this is occurring continuously, ubiquitously, throughout the universe.

If, however, superposition EG is isolated from the random environment, 'orchestrated' in a computational register (e.g. a microtubule) by inputs, memory and resonances, and follows the Schrödinger equation to perform cognitive quantum computing, then the orchestrated process will reach OR threshold by $E_G = h/t$, with EG being composed entirely of orchestrated states. Orch OR then occurs with meaningful cognition and full, rich conscious experience. Sequences of such Orch OR conscious moments provide our familiar 'stream of consciousness'. Tubulin states selected in each Orch OR event (e.g. in layer V pyramidal neuron soma and dendrites) can exert influence on triggering, or not triggering, axonal firing. Orch OR can be the source of 'conscious' deviation from Hodgkin-Huxley behavior.

Orch OR also directly addresses the second issue hampering technological quantum computing, akin to the 'halting problem' in classical computing. If E_G is isolated, premature OR/decoherence is avoided, and the quantum computation proceeds, what then stops it to cause reduction, or collapse to a set of classical values as the solution? In technological quantum computers, the isolated quantum process must, at some point, be 'measured', i.e. the system is observed, causing environmental decoherence, collapse or premature OR. This introduces randomness, and some quantum computers are intended to run the same process repeatedly to average out randomness in measurement/ decoherence.

Orch OR offers a direct solution, the quantum computation 'halting' by an objective threshold E = h/t. Moreover the specific states (conscious perceptions, actions, tubulin dipoles) selected in each Orch OR event are not randomly chosen, but a product of the quantum computation influenced at the instant of Orch OR by 'non-computable' Platonic factors inherent in spacetime geometry.

Orch OR thus proposes a conscious connection between brain biology and behavior, and the fine scale structure of spacetime geometry through the gravitational self-energy EG of the superposition separation of tubulin in $E_c = h/t$.

According to Orch OR, tubulin states are governed by electronic (and perhaps magnetic) dipoles in non-polar electron clouds, such as aromatic resonance rings of tryptophan, tyrosine and phenylalanine. 32 such rings occur in tubulin, aligned in 'quantum channels', which may align with those in neighboring tubulins, and pathways, in the MT lattice (Figures 7 & 8). These same quantum channels are where anesthetic gas molecules bind by weak, quantum-level London forces to selectively erase consciousness, sparing non-conscious processes. Superposition of tubulin dipole orientations may enable tubulins to act as qubits, and helical pathways through microtubules to act as topological qubits. But electrons have extremely low mass, and E_G for their superposition separation would be very small, requiring extremely long values of t.

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However, electron movements of one nanometer shift nearby atomic nuclei by femtometers (Mossbauer recoil and charge attraction), so superposition of electron cloud dipole orientations should result in femtometer superposition separation in tubulin atomic nuclei, sufficient for significant E_c and brief t.

 E_G for tubulin superposition separation in Orch OR was calculated in three ways: (1) as separation of 10% of the protein dimer length (~1 nanometer), (2) as separation at the level of the atomic nuclei within each atom of tubulin (femtometer, 10^{-15} meter for carbon), and (3) as separation at the level of nucleons, i.e. protons and neutrons within nuclei (10^{-16} m). The dominant effect was determined to occur at (2) femtometer separation at the level of atomic nuclei. This implies electronic (or magnetic) dipole movements and superpositions in intratubulin 'quantum channel' electron cloud resonance rings correspond with femtometer movements and superpositions of nearby atomic nuclei.

Gravitational self-energy E_G of a superpositioned tubulin is then given by $E_G = Gm^2/ac$ where G is the gravitational constant, and ac is the superposition separation distance, a carbon nucleus sphere radius equal to 2.5 fermi distances (2.5 femtometers, 2.5 x 10⁻¹⁵ meter). If t is assumed to correspond with a neurophysiological event, say 40 Hz gamma synchrony EEG (the best neural correlate of consciousness), then EG is calculated to be roughly 1010 tubulins. With 109 tubulins per neuron, estimating 0.1% tubulins as quantum coherent (the percent of quantum active molecules in superconductors), requiring 10,000 neurons for t = 25 msec gamma synchrony. But premature OR/decoherence would need to be avoided for 25 msec, a long time in the seemingly 'warm wet and noisy' intra-neuronal environment. Indeed, quantum approaches to brain biology and consciousness have seemed unlikely because of environmental decoherence.

Physicist Max Tegmark (2000) published a critique of Orch OR based on a formula he developed which calculated microtubule decoherence at brain temperature to occur at time tau of 10⁻¹³ seconds, far from 25 msec. But something was rotten in Tegmark's formula for tau, specifically a term in the denominator for superposition separation. In Orch OR, this is the femtometer diameter of atomic nuclei, however Tegmark described a superpositioned soliton separated from itself by 24 nanometers (3 tubulin lengths) along the microtubule. This gave a decoherence time tau 7 orders of magnitude smaller than it should have been, i.e. from 10^{-13} sec to 10^{-6} sec. Hagan et al. (2001) used Tegmark's same formula, correcting for Orch OR stipulations (superposition separation distance, permittivity etc.) and recalculated microtubule decoherence times to be 10^{-4} sec, suggesting topological resonances would sustain quantum coherence in microtubules for 10^{-1} to 10^{-2} sec. Tegmark's critique, and Hagan et al.'s reply, pitted theory versus theory.

In 2006, experimental research began to show that photosynthesis, the mechanism in plants by which sunlight is converted to chemical energy for food, and without which life could not exist, utilizes quantum coherence at ambient temperatures, i.e. in sunlight. Energy from each photon absorbed in one region of a plant cellular complex is transported as electronic excitations ('excitons') to another region of the complex through a series of 'chromophores', light-absorbing molecules composed of electron resonance clouds. What was surprising—stunning, really was that the excitons propagated through the chromophores by all possible pathways, essentially a quantum superposition of excitonic pathways. Further work suggested the quantum coherent superposition was aided by coupling to mechanical vibrations in the protein complex. But because the propagation distance was so short, i.e. a few nanometers within the cellular complex, the coherence persisted only for very brief periods of time, e.g. femtoseconds.

What about microtubules? Using nanotechnology, the group of Anirban Bandyopadhyay at the National Institute of Material Science in Tsukuba, Japan was able to apply 4 electrodes to a single MT at room temperature. Two electrodes were used to apply very low levels of alternating current (AC) at varying frequencies, and the other two electrodes used to record conductance through the MT. Without AC stimulation, MTs were non-conductive, their resistance extremely high. However at a number of applied AC frequencies across a wide spectrum (gigahertz, megahertz, and as low as 10 kilohertz), MT resistance dropped, and the MT became significantly conductive (Sahu et al. 2013a, 2013b). More recent studies using nanoprobes inside active neurons also show megahertz and kilohertz coherent vibrations. Particular resonant frequencies may correlate with conductance and vibrations along specific helical pathways through MT lattices. Quantum resonances as low as 10 kilohertz indicate MT coherence times as long as 10^{-4} seconds, the same MT coherence time calculated by Hagan et al. (2001) using Orch OR stipulations. If t in EG = h/t is set to 10^{-4} secs, EG of tubulins in 10 million neurons would be required. For 10^{-7} secs, 10 MHz (also proven) EG of tubulins in 10 billion neurons (or higher involvement per neuron) would be required. Indeed, Orch OR may be seen to occur at different frequency ranges, e.g. akin to different scales in music. But t = 10^{-4} secs is still too brief for physiological effects, such as gamma synchrony EEG at 25 msec.

In Hameroff and Penrose (2014) it was proposed that EEG rhythms are 'beat frequencies' of faster oscillations in microtubules. For example MT megahertz vibrations of slightly different frequencies, or energies, would interfere to give much slower 'beats', e.g. in the 1 to 100 Hz range seen in EEG. Indeed, consciousness may be more like music than computation, sequences of events, at different frequencies, in some cases harmonically related. Quantum vibrations in brain MTs punctuated by Orch OR events are also ripples, or rearrangements in fundamental spacetime geometry. Orch OR connects conscious brain activities to processes in the fine scale structure of the universe.

Each Orch OR conscious moment, e.g. occurring in dendritic-somatic MTs in layer V cortical pyramidal neurons, also selects tubulin states which govern neuronal activities including axonal firing, thus exerting causal action and conscious control of behavior. Can Orch OR account for free will?

5. Free will - Is consciousness too late?

Free will implies conscious agency – that 'we' have conscious causal control and choice of our actions. Indeed, 'we' do seem to have conscious control, but do we really? First, who, or what exactly is 'we', or 'I'? There is no agreed-upon mechanism for consciousness nor conscious agency in neuroscience and philosophy. However Orch OR does offer a mechanism for conscious causal action – tubulin states selected in each Orch OR event may trigger, or not trigger, axonal firings to implement behavior (deviation from Hodgkin-Huxley).

A second issue involves determinism, the notion that all processes in the world, and in our minds, are algorithmic and our choices inevitable and predetermined, with perhaps a dash of randomness. Determinism implies that conscious perceptions and actions follow a complex script written by the laws of nature and history of the universe. Penrose OR avoids determinism by 'non-computable', non-algorithmic influence on selection of particular states at the instant of reduction. According to OR, the quantum wave function of superposition E_G evolves algorithmically according to the Schrödinger equation up until the moment of OR at time t ($E_G = h/t$). At that instant, according to Penrose OR, non-random, 'non-computable Platonic values' embedded in the fine scale structure of spacetime geometry influence choices selected in the OR process. Whether such Platonic values are themselves algorithmic and deterministic are unknown. But to some extent at least, Orch OR dodges determinism.

A third issue with free will pertains to the timing of conscious action, in that consciousness, in some cases, appears to come too late. Neural correlates of conscious perception occur 150 to 500 milliseconds (msec) after impingement on our sense organ, yet we often consciously respond to those perceptions within 100 msec after sensory impingement. For example (Velmans 1991) analysis of sensory inputs and emotional content, phonological and semantic analysis of heard speech, preparation of spoken words and sentences, forming memories, and performing voluntary acts all occur, seemingly consciously, before the stimuli to which the responses were aimed are processed. The conclusion among neuroscientists and philosophers (Dennett & Kinsbourne 1992; Wegner 2002) has been that we act non-consciously, and have belated, false impressions of conscious causal action. This implies that free will does not exist, that consciousness is epiphenomenal, and that we are, as T.H. Huxley bleakly summarized, "merely helpless spectators".



Figure 11. The "readiness potential (RP)" (Libet et al. 1983). (A) Cortical potentials recorded from a subject instructed to move his/her hand whenever he/she feels ready, and to note when the decision was made (Conscious intent), followed quickly by the finger actually moving. (Time between Conscious intent, and finger moving is fixed.) Readiness potential, RP, preceding Conscious intent is generally interpreted as representing the Non-conscious choice to move the finger, with Conscious intent being illusion. (B) Assuming RP is necessary preparation for conscious finger movement, Actual conscious intent could initiate the earlier RP by (quantum) temporal non-locality and backward time referral, enabling preparation while preserving real time conscious intent and control.

Some evidence appears to support the epiphenomenal contention. Kornhuber and Deecke (1965) recorded electrical activity over pre-motor cortex in subjects who were asked to move their finger randomly, at no prescribed time. Gradually-increasing brain electrical activity preceded finger movement by ~800 msec, termed the readiness potential ('RP'). Benjamin Libet and colleagues (1983) repeated the RP experiment, except they also asked subjects to note precisely when they consciously decided to move their finger. (To do so, and to avoid delays caused by verbal report, Libet et al. used a rapidly moving clock and asked subjects to note when on the clock they consciously decided to move their finger). The 'conscious decision' came ~200ms before actual finger movement, hundreds of milliseconds after onset of the RP. Kornhuber, Deeke, Libet and others concluded the RP represented a non-conscious causal action of the finger movement, that many seemingly conscious actions are initiated non-consciously, and that conscious intent is an illusion. Consciousness apparently comes too late.

But does it? Strangely, apparent backward time effects are observed in brain biology related to consciousness, and theoretically allowable in quantum physics. Could quantum backward time effects rescue conscious free will? In physics, the 'arrow of time' implies a flow of time in one direction, toward increasing entropy according to the second law of thermodynamics. However, other laws of physics are generally 'time reversible', working quite well in both directions. In principle, there's no reason for an exclusively unidirectional arrow of time. In the Wheeler-Dewitt equation, which attempts to mathematically reconcile quantum mechanics and general relativity, time plays no role from an external viewpoint. However in the Wheeler-Dewitt equation, conscious observers within the universe do perceive a flow of time and events, the unidirectional flow of time being exclusively related to consciousness (c.f. Hameroff, 2003). However consciousness may utilize backward time effects.

A principal hallmark of quantum physics is quantum entanglement which implies complementary quantum particles (e.g. electrons in coupled spin-up and spin-down pairs) remain entangled when separated spatially (or temporally). Einstein initially objected, as it would require signaling faster than light, and thus violate special relativity. He famously termed it 'spooky action at a distance', and (with colleagues Podolsky and Rosen - 'EPR') described a thought experiment in which an entangled pair of superpositioned electrons (EPR pairs) would be sent in different directions, each remaining in superposition (Einstein et al, 1935). When one electron was measured at its destination and, say, spinup was observed, its entangled twin miles away would, according to the prediction, correspondingly reduce instantaneously to spin-down which would be confirmed by measurement. The issue was unresolved at the time of Einstein's death, but since the early 1980s (Aspect et al. 1982, Tittel et al. 1998) this type of experiment has been repeatedly confirmed through wires, fiber optic cables and via microwave beams in the atmosphere. Entanglement is an essential feature of quantum information technologies such as quantum cryptography, quantum teleportation and quantum computers. How does it occur?

Penrose (2004; cf. Bennett, and Wiesner 1992) proposed that measurement and reduction of one twin of the EPR pair sends quantum information backward in time to when the particles were spatially together, then onward to the second twin. According to this scheme, apparent backward time effects are necessary for entanglement, and thus ubiquitous. Aharonov has proposed that quantum state reductions send LECTURES

quantum information both forward and backward in time. In his 1989 book *The emperor's new mind*, Penrose (1989) suggested quantum effects could mediate the brain's backward time referral of subjective information reported by Benjamin Libet.

In the late 1970s and 1980s, Libet and colleagues (in addition to their RP 'move your finger' research, described above) studied the timing of conscious sensory experience in awake, cooperative patients undergoing brain surgery with local anesthesia. This allowed stimulation and recording of somatosensory cortex (e.g. of the hand), periphery (e.g. hand) and direct report of the timing of conscious experience. (To avoid delays due to reporting, subjects observed a fast moving clock, and noted precisely when a sensory perception occurred.) Two types of sensory stimulation were used, one type involving direct stimulation of the skin of the hand, recording the sensory activity from somato-sensory 'hand area' of cortex, and obtaining the subject's report of the precise time of the conscious experience (via the fast-moving clock). Generally, stimulation of the hand resulted in (1) a cortical sensory-evoked potential (EP) at 30 msec after stimulation, and (2) conscious sensory experience also occurring at 30 msec, 30 msec being roughly the time required for neural signals to reach the brain from the hand. In these same subjects, Libet and colleagues also directly stimulated the 'hand area' of somato-sensory cortex. They found no EP, and discovered that 500 msec of continuously-induced cortical activity was required for conscious sensation of the hand to occur at 500 msec. Libet concluded that 500 msec of cortical activity was required to reach threshold for conscious 'neuronal adequacy'. This requirement for several hundreds of msec of direct cortical stimulation to produce conscious experience ('Libet's half second') was subsequently confirmed by Amassian et al. (1991), Ray et al. (1999), Pollen (2004) and others. It was also consistent with the subsequent work of Velmans (1991), Dennett, Kinsbourne and others who maintained that consciousness occurred several hundred msec after sensory impingement, and after seemingly conscious responses. But then, how can conscious experience occur at 30 msec with hand stimulation and the EP?



Figure 12. Cortical potentials in Libet's sensory experiments. (A) Peripheral stimulation, e.g., at the hand, results in near-immediate conscious experience of the stimulation, an evoked potential EP at ~30msec in the "hand area" of somatosensory cortex, and several 100 msec of ongoing cortical electricalactivity. (B) Direct cortical activity of the somatosensory cortical hand area for several 100msec results in no EP, ongoing cortical activity, and conscious sensory experience of the hand, but only after ~500msec. Libet termed the 500msec of cortical activity resulting in conscious experience.



Figure 13. Libet's sensory experiments, continued.(A) Libet et al. stimulated medial lemniscus of thalamus in the sensory pathway to produce an EP (~30ms) in somatosensory cortex, but only brief post-EP stimulation, resulting in only brief cortical activity. There was no apparent "neuronal adequacy," and no conscious experience. An EP and several100 msec of post-EP cortical activity (neuronal adequacy) were required for conscious experience at the time of EP. (B) To account for his findings, Libet concluded that subjective information was referred backward in time from neuronal adequacy (~500msec) to the EP.

To address this issue, Libet and colleagues did further studies in human subjects stimulating medial lemniscus of thalamus, the primary relay station between, e.g. hand and sensory cortex. Stimulating thalamus, they observed a cortical EP at 30 msec, and ongoing cortical activity for as long as they stimulated thalamus. If the stimulation and ongoing cortical activity persisted for ~500 msec, the subjects reported conscious experience at 30 msec, the time of the EP. If, however, stimulation and cortical activity were stopped after the EP, but prior to ~500 msec, no conscious experience occurred. Somehow, the brain 'knew' whether or not cortical activity would continue for hundreds of msec after the EP for consciousness to occur at the time of the EP. Libet concluded that subjective information was referred 'backward in time' from neuronal adequacy at ~500 msec to the time of the EP at 30 msec. Libet's backward time assertion was disbelieved and ridiculed (e.g. Churchland, 1981; Dennett & Kinsbourne 1992) but never refuted. Indeed, several types of experiments have continued to show backward time effects in the brain.

Electrodermal activity measures skin impedance, usually with a probe wrapped around a finger, as an index of autonomic, sympathetic neuronal activity causing changes in blood flow and sweating, in turn triggered by emotional response in the brain. Researchers Dean Radin and Dick Bierman have published a series of well-controlled studies using electrodermal activity to look for emotional responses to images presented at random times on a computer screen. They found that emotional images elicited responses half a second to two seconds before the images appeared. They termed the effect pre-sentiment because the subjects were not consciously aware of the emotional feelings; non-conscious emotional sentiment (i.e. feelings) appeared to be referred backward in time.

In 2011, Daryl Bem published "Feeling the future: Experimental evidence for anomalous retroactive influences on cognition and affect" in the mainstream *Journal of Personality and Social Psychology.* The article reported on 8 studies showing statistically significant backward time effects, most involving non-conscious influence of future emotional effects (e.g. erotic or threatening stimuli) on cognitive choices. Mossbridge et al. (2012) published a meta-analysis of 26 reports published between 1978 and 2010 showing backward time effects, and concluded the results were valid. Moreover they pointed to findings in mainstream neuroscience which show backward time effects but are not reported.

In the famous double slit experiment in quantum physics, quantum entities (e.g. photons, electrons) can behave as either waves, or particles, depending on the method chosen to measure them. John Wheeler described a thought experiment in which the measurement choice (by a conscious human observer) was delayed until after the electron or other quantum entity passed though the slits, presumably as either wave or particle. Wheeler suggested the observer's delayed choice could retroactively influence the behavior of the electrons, e.g. as waves or particles. The experiment was eventually performed and confirmed Wheeler's prediction; conscious choices can affect previous events, as long as the events were not consciously observed in the interim.

In 'delayed choice entanglement swapping', originally a thought experiment proposed by Asher Peres (2000), Ma et al. (2012) went a step further. In entanglement swapping, two pairs of unified/entangled particles are separated, and one from each pair is sent to two measurement devices, each associated with a conscious observer ('Alice' and 'Bob', as is the convention in such quantum experiments). The other entangled particle from each pair is sent to a third observer, Victor. How Victor *decides* to measure the two particles (as an entangled pair, or as separable particles) determines whether Alice and Bob observe them as entangled (showing quantum correlations) or separable (showing classical correlations). This happens even if Victor decides after Alice's and Bob's devices have measured them (but before Alice and Bob consciously view the results). Thus Victor's conscious choice affects behavior of previously measured, but unobserved, events. Entanglement apparently includes not only spooky action at a distance, but spooky action on past events. Anton Zeilinger, senior author on the Ma et al. study, said: "Within a naïve classical worldview, quantum mechanics can even mimic an influence of future actions on past events".

Such influences in the brain can allow real-time conscious control of our actions, seen as deviation from Hodgkin-Huxley neuronal behavior (Figure 14). With quantum brain biology, consciousness does not come too late. Free will is possible.



Figure 14. As in Figure 4, Integrate-and-fire neuronal behaviors. a. The Hodgkin-Huxley model predicts integration, narrow threshold potential and low temporal variability in firing at the proximal axon (AIS) b. Recordings from cortical neurons in awake animals (Naundorf et al. 2006) show a large variability in effective firing threshold and timing. Some additional factor, perhaps related to consciousness ('C') exerts causal influence on firing and behavior, and may include backward time referral.

6. Tuning the brain

Orch OR has been skeptically viewed on the basis of 'decoherence' (i.e. random, 'un-orchestrated' OR). Technological quantum computers require extreme cold, near absolute zero temperature, to avoid thermal vibrations which appear to disrupt delicate quantum effects. Critics said the brain is simply too 'warm, wet and noisy' for functional quantum effects.

Orch OR countered theoretically that coherence akin to Bose-Einstein condensation, and described for biological systems by Herbert Fröhlich, converted thermal energy to coherent vibrations, somewhat like a laser. Quantum spin transfer through aromatic rings was shown to be promoted by heat, not disrupted (Ouyang & Awschalom, 2003), and beginning in 2006, evidence began to accrue for warm temperature quantum coherence in photosynthesis proteins (Engel et al, 2007). Recently, room temperature Bose-Einstein condensation has been demonstrated (Plumhof et al 2014). The brain is not too 'warm' for functional quantum effects.

Orch OR also suggested microtubule quantum coherence originated in isolated, non-polar, 'hydrophobic' regions within tubulin ('quantum channels'), shielded from polar, aqueous interactions. At such quantum sites, anesthetic molecules selectively erase consciousness, acting by quantum London forces. The brain is not too 'wet' for functional quantum effects, at least not in 'dry' quantum channels. Is the brain too 'noisy'? Seemingly random electrical fluctuations occur continuously throughout the brain, embedded as background in the EEG. The fluctuations emanate mostly from neuronal post-synaptic membrane potentials which don't reach threshold for axonal firing. According to standard neuroscience doctrine, such activity is irrelevant, as firings are all that matter, and dendritic-somatic 'noise' (though it constitutes 'integration') is ignored as irrelevant. Is it really?

The 'noise' is seen at all levels—neuronal, network, and the entire brain. While appearing locally random, brain electrical noise, or 'ongoing activity', is highly synchronized, or correlated (Arieli et al, 1996). The fluctuations are precisely the same everywhere. In pyramidal neurons, simultaneous recording of 'noise' in soma and apical dendrite (micron separation) show 'isopotentiality', near-perfect correlation (Yaron-Jakoubovitch et al 2008). Could correlated 'noise' have a function? Perhaps dendritic-somatic 'noise' is essential, or at least related to, cognition and consciousness (Pockett, 2000; McFadden, 2002). Perhaps brain noise is, as it has been said, "the brain orchestra warming up". Orch OR suggests correlated brain 'noise' originates from deeper level, finer scale quantum vibrations in microtubules inside neurons.



Figure 15. Five frequency bands of microtubule and brain activity plotted on a log scale. Starting at right, E and D are gigahertz and megahertz resonance frequencies found in individual microtubules (Sahu et al. 2013a, 2013b). B, C and D are kilohertz, tens of kilohertz and megahertz resonance frequencies detected from microtubule bundles inside active neurons (Bandyopadhyay 2014). A is the EEG spectrum put in 'by hand'. The 5 bands are self—similar and separated evenly by ~3 orders of magnitude, suggesting a harmonic system. EEG (A) may be derived as inverse harmonics, or 'beats' of higher frequency microtubule vibrations.

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Brain noise (and measurable EEG) derive from local field potentials due to post-synaptic trans-membrane potentials of roughly 100 millivolt fluctuations, mediated by ion fluxes through membrane protein channels. (Axonal firing potentials, or 'spikes', contribute only in a small way to noise and EEG.) Bandyopadhyay's megahertz and kilohertz electric field fluctuations from microtubule bundles inside neurons of 40 to 50 millivolts are sufficient to influence and regulate membrane potentials. Hameroff and Penrose (2014) suggested interference between microtubules vibrating at slightly different megahertz, or kilohertz, frequencies would give rise to slower 'beat' frequencies, seen as membrane potential fluctuations in EEG or brain noise. EEG is the tip of an iceberg of brain activity.

Thus brain activity relevant to cognition and consciousness may occur at various spatiotemporal scales, moving and combining, like music. Sequences of events at different frequencies, in some cases harmonically related, appear to be anchored by resonances inherent in microtubule lattice geometry. By Penrose OR, Orch OR events are also ripples, or rearrangements in fundamental spacetime geometry. Orch OR connects conscious brain activities to processes in the fine scale structure of the universe.

Within the brain, neuronal and microtubule vibrations span 10 orders of magnitude (Figure 15), and may be directly relevant to mental states. Microtubule vibrations inside brain neurons offer therapeutic opportunities for mood, cognition and neurological disorders.

Modern psychopharmacology aimed at modulating mental states, mood and cognitive function, based on the standard computationalist approach in neuroscience, has as its targets neuronal membrane receptor and channel proteins, and thus may be somewhat misguided. For example the antidepressant Prozac aims to prolong action of the neurotransmitter serotonin at its synaptic receptors (by inhibiting its 'reuptake'). The membrane-mediated effect is immediate, but mood improves only after several weeks, apparently allowing dendritic-somatic microtubules to reorganize (Bianchi et al, 2009).

Anti-anxiety benzodiazepine drugs such as Valium, Versed and Xanax are said to act by enhancing binding of GABA (gamma-amino-butyric acid), the brain's primary inhibitory neurotransmitter, to its membrane 'GABA receptor' proteins. But benzodiazepine molecules have several non-polar rings, directly inhibit microtubules in mitosis (Troutt et al. 1995), and are likely to enter neurons and bind in microtubule quantum channels. Similarly, opiate drugs which cause euphoria bind to opiate receptors, but also enter neurons and likely bind in microtubules. While receptor binding occurs, mood-altering drugs may act to tune microtubule vibrations and mellow the music.

Psychedelic drugs are also highly non-polar, contain indole electron resonance rings, and able to enter neurons. Potency of such molecules correlates with their ability to donate electron resonance energy (Kang, and Green; Snyder, and Merrill), thus perhaps promoting microtubule quantum vibrations at higher frequencies, and vibrational resonances over many scales.

Anesthetics have opposite effects, selectively erasing consciousness while sparing non-conscious brain functions. They include numerous gas molecules whose potency correlates precisely with solubility in a nonpolar, 'olive oil' medium, e.g. as found in lipids, and protein hydrophobic interiors. Franks and Lieb (1984) showed that anesthetics act in non-polar, hydrophobic regions of proteins (not in lipids), presumably membrane proteins, with receptors for acetylcholine, serotonin, glycine and GABA the most likely candidates. But despite decades of widespread searching, particular membrane receptors or channels mediating anesthetic action have not been found.

In 2006, Rod Eckenhoff's lab at University of Pennsylvania showed that anesthetics such as halothane bind to ~70 proteins in brain neurons, roughly half membrane proteins, and half cytoskeletal proteins including tubulin. Following anesthetic exposure, genetic expression of tubulin, but not of any membrane proteins, was altered. Genomic and proteomic evidence point to microtubules as the site of anesthetic action. Emerson et al. (86) used fluorescent anthracene as an anesthetic in tadpoles, and showed cessation of tadpole behavior occurs specifically via anthracene anesthetic binding in tadpole brain microtubules. Despite prevailing assumptions, actual evidence suggests anesthetics act on microtubules, not membrane receptors and channels to erase consciousness.

Thus modern psychopharmacology may be aiming at the wrong targets, thus explaining why it isn't more successful in treating mental state disorders. A primary reason membrane receptors and channels LECTURES

are studied is that their effects (drug binding, conformational change, channel opening) are measurable. Until recently, there was no assay for microtubule function other than polymerization states of assembly/ disassembly. Now however resonance vibrations, e.g. in megahertz, have been discovered, and drugs may be assayed for their effects on microtubule resonance spectra inside neurons. New vistas await in the study of drug effects on microtubule vibrations.

Another avenue to treating mental states and cognitive dysfunction comes through noninvasive brain stimulation techniques. Among these are transcranial magnetic stimulation ('TMS'), transcranial electrical direct current stimulation ('TDcS') and transcranial ultrasound stimulation ('TUS'), all of which have shown promise and interesting effects. Among these, only TUS can be narrowly focused to target specific, deeper brain regions (Legon et al. 2014).

Ultrasound consists of mechanical vibrations above human hearing threshold (~20,000 Hz), and is usually used in the low megahertz (10⁶ to 10⁷ Hz) for medical imaging, passing through the body and echoing back off surfaces. TUS consists of low intensity, sub-thermal levels of ultrasound administered at the scalp which safely penetrates skull and reaches the brain sufficiently to be echoed back to provide an image of the brain surface and sulci. As microtubules have megahertz vibrational resonances, TUS with proper settings might be expected to enhance microtubule resonance, and thereby affect microtubule functions related to cognition and mental states. Indeed, focused TUS enhances sensory discrimination in human volunteers (Legon et al, 2014), and unfocused TUS improved mood in chronic pain patients (Hameroff et al. 2013).

At the cellular level in embryonic neurons, ultrasound promotes growth of neurites leading to formation of axons, dendrites and synapses (Raman). At the level of tubulin, ultrasound promotes microtubule assembly. As traumatic brain injury involves disrupted microtubules, synapses and circuits, and as Alzheimer's disease and post-operative cognitive dysfunction (cognitive decline after anesthesia in elderly), TUS may be useful for all these disorders.

Traumatic memory is an important factor in psychotherapy (e.g. posttraumatic stress disorder). Some suggest eliciting a traumatic memory and then over-writing it at that time with a positive memory (Lane et al). Since synaptic membrane proteins are too short-lived to store and encode memory, and microtubules appear likely to do so, psychotherapy combined with TUS aimed at microtubule vibrations may be optimal.

To erase or over-write traumatic memory, to change the music and re-tune the tubules, combinations of pharmacology, psychotherapy and TUS (e.g. aimed at microtubule vibrations in amygdala, hippocampus and pre-frontal cortex) may be optimal. As the Beatles sang, "Take a sad song and make it better".

7. Conclusion

The mainstream materialist approach to brain function in neuroscience and philosophy suggests that consciousness and cognition emerge as higher order network effects from complex computation among relatively simple neurons. The fine grain of conscious and cognitive information is conveyed at the neuronal level by axonal firings and synaptic transmissions mediated entirely by membrane proteins.

This approach has failed. Neuronal computational networks fail to account for (1) cognitive phenomenal aspects of single cell organisms like paramecium which swim, learn, find food and mates and have sex, all without synaptic connections, using their cytoskeletal microtubules for sensory processing and motor actions, (2) phenomenal subjective aspects of consciousness (the 'hard problem'), (3) free will as real-time conscious control, neuronal activity correlating with perception occurring after seemingly conscious response, relegating consciousness to epiphenomenal 'helpless spectator', (4) memory, as membrane proteins determining synaptic sensitivity are transient, and yet memories can last lifetimes, (5) molecular mechanisms for drugs affecting consciousness including anesthetics, which selectively erase consciousness, but despite popular belief, do not act on membranes, and (6) scientific plausibility for nonlocality, e.g. so-called telepathy, pre-cognition, near death/out-of-body experiences, and afterlife. These are generally stated to be impossible because they cannot be scientifically explained by the mainstream view based on neuronal-based computation. But the mainstream materialist view can't really explain anything about consciousness. And materialism itself is illusory, as particles repeatedly coalesce from quantum possibilities.
In spiritual and idealist approaches, consciousness has in some sense always existed in the universe, being in some way intrinsic to its very makeup. Some such views place consciousness as primary, omnipresent, with matter and the world manifesting within an all-pervading consciousness. But such approaches themselves are as yet untestable and unfalsifiable, essentially putting consciousness outside science.

Orch OR is based on deeper level quantum vibrations in microtubules inside neurons, quantum vibrations which occur in the fine scale structure of spacetime geometry. Orch OR provides a bridge between the two approaches, and an opportunity to treat mental disorders by tuning microtubule quantum vibrations

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References

Arieli, A., Sterkin A., Grinvald, A., Aersten A. 1996, "Dynamics of Ongoing Activity: Explanation of the Large Variability in Evoked Cortical Responses," *Science* 273 (5283), 1868–1871.

Aspect, A., Grangier, P., Roger, G. 1982, "Experimental Realization of Einstein-Podolsky-Rosen-Bohm Gedanken Experiment: A New Violation of Bell's Inequalities," *Physical Reviews Letters* 48:91-94.

Barrow, J.D., Tipler, F.J. 1986, *The Anthropic Cosmological Principle*, Oxford: Oxford University Press.

Bem, D.J. 2012, "Feeling the Future: Experimental Evidence for Anomalous Retroactive Influences on Cognition and Affect," *Journal of Personality and Social Psychology* 100, 407-425.

Bennett, C.H., Wiesner, S.J. 1992, "Communication via 1- and 2-particle Operators on Einstein-Podolsky-Rosen States," *Physical Reviews Letters* 69:2881-84.

Bianchi, M., Shah, A.J., Fone, K.C., Atkins, A.R., Dawson, L.A., Heidbreder, C.A., et al. 2009, "Fluoxetine Administration Modulates the Cytoskeletal Microtubular System in the Rat Hippocampus," *Synapse* 63:359–64. Carter, B. 1974, "Large Number Coincidences and the Anthropic Principle in Cosmology," *IAU Symposium 63: Confrontation of Cosmological Theories with Observational Data, Dordrecht: Reidel*, 291–298.

Chalmers, D.J. 1996, *The Conscious Mind - In Search of a Fundamental Theory*, New York: Oxford University Press.

Churchland, P.S. 1981, "On the Alleged Backwards Referral of Experiences and its Relevance to the Mind-body Problem," *Philosophy of Science* 48:165-81.

Craddock, T., St George, M., Freedman, H., Barakat, K., Damaraju, S., Hameroff, S, et al. 2012, "Computational Predictions of Volatile Anesthetic Interactions with the Microtubule Cytoskeleton: Implications for Side Effects of General Anesthesia," PLoS ONE 7(6): e37251.

Craddock, T., Tuszynski, J., Chopra, D., Casey, N., Goldstein, L., Hameroff, S., et al. 2012, "The Zinc Dyshomeostasis Hypothesis of Alzheimer's Disease," PLoS ONE 7 (3): e33552.http://dx.doi.org/10.1371/journal.pone.0033552.

Craddock, T., Tuszynski, J., Hameroff, S. 2012, "Cytoskeletal Signaling: Is Memory Encoded in Microtubule Lattices by CaMKII Phosphorylation?" PLoS Comput Biol 8(3): e1002421.

Crick, F.C., Koch, C. 2001, "A Framework for Consciousness," *Nature Neuroscience* 6:119-26.

Dennett, D.C. 1991, Consciousness Explained, Boston: Little, Brown.

Dennett, D.C., Kinsbourne, M. 1991, "Time and the Observer: The Where and When of Consciousness," *Behavioral and Brain Sciences* 15:183-247.

Dennett, D.C., Kinsbourne, M. 1992, "Time and the Observer: The Where and When of Consciousness," *Behavioral and Brain Sciences* 15:183-247.

Dustin, P. 1985, Microtubules, 2nd ed. New York: Springer-Verlag.

Einstein, A., Podolsky, B., Rosen, N. 1935, "Can Quantum Mechanical Descriptions of Physical Reality be Complete?" *Physical Review* 47:777–80.

Emerson, D., Weiser, B., Psonis, J., Liao, Z., Taratula, O., Fiamengo, A., et al. 2013, "Direct Modulation of Microtubule Stability Contributes to Anthracene General Anesthesia," *J Am Chem Soc* 135(14):5398.

Engel, G.S., Calhoun, T.R., Read, E.L., Ahn, T.K., Mancal, T., Cheng, Y.C., et al. 2007, "Evidence for Wave-like Energy Transfer Through Quantum Coherence in Photosynthetic Systems," *Nature* 446:782–6.

Everett, H. 1983, "Relative State Formulation of *Quantum Mechanics*," *Quantum Theory and Measurement*, Wheeler, J.A., Zurek, W.H., Editors. Princeton: Princeton University Press. Originally in Reviews of Modern Physics 29 (1957):454-62.

Franks, N.P., Lieb, W.R. 1982, "Molecular Mechanisms of General Anesthesia," *Nature* 316:349-51.

Fröhlich, H. 1968, "Long-range Coherence and Energy Storage in Biological Systems," *International Journal of Quantum Chemistry* 2:641-9.

Fröhlich, H. 1970, "Long-range Coherence and the Actions of Enzymes," *Nature* 228:1093.

Fröhlich, H. 1975, "The Extraordinary Dielectric Properties of Biological Materials and the Action of Enzymes," *Proceedings of the National Academy of Sciences* 72:4211-15.

Hagan, S., Hameroff, S., Tuszynski, J. 2002, "Quantum Computation in Brain Microtubules? Decoherence and Biological Feasibility," *Physical Reviews* E 65:061901.

Hameroff, S.R., Watt, R.C. 1982, "Information Processing in Microtubules," J Theor Biol 98:549-61.

Hameroff, S.R., Penrose, R. 1996, "Conscious Events as Orchestrated Spacetime Selections," *Journal of Consciousness Studies 3*(1):36-53. http://www.u.arizona. edu/~hameroff/penrose2.

Hameroff, S.R., Penrose, R. 1996, "Orchestrated Reduction of Quantum Coherence in Brain Microtubules: A Model for Consciousness," *Toward a Science of Consciousness: The First Tucson Discussions and Debates* 507-540. Hameroff, S.R., Kaszniak, Scott, A.C., Editors. Cambridge: MIT Press. Also published 1996 in *Mathematics and Computers in Simulation* 40:453-480. http://www.consciousness.arizona.edu/hameroff/or.html.

Hameroff, S. 2003, "Time, Consciousness and Quantum Events in Fundamental Space-time Geometry," Buccheri, R., Saniga M. *The Nature of Time: Physics, Geometry and Perception.* Proceedings of a NATO Advanced Research Workshop.

Hameroff, S., Trakas, M., Duffield, C., Annabi, E., Gerace, M.B., Boyle, P. et al. 2013, "Transcranial Ultrasound (TUS) Effects on Mental States: A Pilot Study," *Brain Stimul* 3(6):409–15.

Hameroff, S.R., Penrose, R. 2014, "Consciousness in the Universe – Review of the Orch OR Theory," Phys Life Rev. <u>http://www.sciencedirect.com/science/article/pii/</u>S1571064513001188.

Hayes, D., Griffith, G.B., Engel, G.S. 2013, "Engineering Coherence Among Excited States in Synthetic Heterodimer Systems," Science 340(6139):1431–4.

Hildner, R., Brinks, D., Nieder, J.B., Cogdell, R.J., van Hulst, N.F. 2013, "Quantum Coherent Energy Transfer Over Varying Pathways in Single-light Harvesting Complexes," *Science* 340(639):1448–51.

Hodgkin, A., Huxley, A. 1952, "A Quantitative Description of Membrane Current and its Application to Conduction and Excitation in Nerve," J Physiol 117:500–44. http://dx.doi.org/10.1371/journal.pcbi.1002421.

Huxley, T.H. 1893, 1986, "Method and Results: Essays."

Koch, C., Crick, F.C.R. 2001, "The Zombie Within," Nature 411:893.

Koch, C. 2004, *The Quest for Consciousness:* A Neurobiological Approach, Englewood: Roberts and Co.

Kornhuber, H.H., Deecke, L. 1965, "Hirnpotential Andrugen Bei Willkurbewegungen und Passiven Bewungungen des Menschen: Bereitschaftspotential und Reafferente Potentiale Pflugers," *Archiv* 284:1-17. Kurzweil, R. 2013, How to Create a Mind. *The Secret of Human Thought Revealed*, New York: Viking Press.

Lamme, V.A.F., Roelfsema P.R. 2000, "The Distinct Modes of Vision Offered by Feed-forward and Recurrent Processing," *Trends Neurosci* 23 (11):571–579.

Lane, R.D., Ryan, L., Nadel, L., Greenberg, L. 2013, "Memory Reconsolidation, Emotional Arousal and the Process of Change in Psychotherapy. *New Insights from Brain Science Behavioral and Brain Science*," Forthcoming.

Lee, U., SeungWoo, M.D., Noh, G., Baek S., Choi, B., Mashour, G. 2013, "Anesthesiology," *Perioperative Medicine* 118 (6):1264–1275.

Legon, W., Sato, T.F., Opitz, A., Mueller, J., Barbour, A., Williams, A., Tyler, W.J. 2014, "Nature," *Neuroscience* 17:322–329.

Libet, B., Alberts, W.W., Wright, W., Delattre, L., Levin, G., Feinstein, B. 1964, "Production of Threshold Levels of Conscious Sensation by Electrical Stimulation of Human Somatosensory Cortex," *Journal of Neurophysiology* 27:546-78.

Libet, B., Alberts, W.W., Wright, E.W., Feinstein, B. 1967, "Response of Human Somatosensory Cortex to Stimuli below Threshold for Conscious Sensation," *Science* 158:1597-1600.

Libet, B., Wright, E.W., Jr., Feinstein, B., Pearl, D.K. 1979, "Subjective Referral of the Timing for a Conscious Sensory Experience," *Brain* 102:193-224.

Libet, B., Gleason, C.A., Wright, E.W., Pearl, D.K. 1983, "Time of Conscious Intention to Act in Relation to Onset of Cerebral Activity (Readiness Potential): The Unconscious Initiation of a Freely Voluntary Act," *Brain* 106:623-42.

Matsuyama, S., Jarvik, L. 1989, "Hypothesis: Microtubules, A Key to Alzheimer Disease," *Proc Natl Acad Sci USA* 86(20):8152–6.

McFadden, J. 2002, "The Conscious Electromagnetic Field Theory: The Hard Problem Made Easy," *J. Conscious. Stud.* 9 (8):45–60.

Mossbridge, J., Tressold, P., Utts, J. 2012, "Predictive Physiological Anticipation Preceding Seemingly Unpredictable Stimuli: A Meta-analysis," *Front Psychol* 17 doi: 10.3389/fpsyg.2012.00390.

Naundorf, B., Wolf, F., Volgushev, M. 2006, "Unique Features of Action Potential Initiation in Cortical Neurons," *Nature* 440:1060–3.

Ouyang, M., Awschalom, D.D. 2003, "Coherent Spin Transfer Between Molecularly Bridged Quantum Dot," *Science* 301:1074–1078.

Penrose, R. 1989, The *Emperor's New Mind*. 1st ed. Oxford: Oxford University Press. Penrose, R. 1994, *Shadows of the Mind*: A Search for the Missing Science of

Consciousness, Oxford: Oxford University Press.

Penrose, R., Hameroff, S.R. 1995, "What Gaps? Reply to Grush and Churchland," *J Conscious Stud* 2:98–112.

Penrose, R. 1996, "On Gravity's Role in Quantum State Reduction," *General Relativity and Gravitation* 28(5):581-600.

Penrose, R. 2004, *The Road to Reality: A Complete Guide to the Laws of the Universe*, London, Jonathan Cape.

Plumhof, J.D., Stoferle, T., Mai, L., Scherf, U., Mahrt, R.F. 2014, "Room-temperature Bose-Einstein Condensation of Cavity Exciton-polaritons in a Polymer," *Nature Materials* 13:247-252; doi: 10.1038/nmat3825.

Pockett, S. 2000, The Nature of Consciousness: A Hypothesis, New York: iUniverse.

Rasmussen, S., Karampurwala, H., Vaidyanath, R., Jensen, K., Hameroff, S. 1990, "Computational Connectionism within Neurons: A Model of Cytoskeletal Automata Sub-serving Neural Networks," *Physica* D 42:428–49.

Sahu, S., Ghosh, S., Ghosh, B., Aswani, K., Hirata, K., Fujita, D., et al. 2013, "Atomic Water Channel Controlling Remarkable Properties of a Single Brain Microtubule: Correlating Single Protein to its Supramolecular Assembly," *Biosens Bioelectron* 47:141–8.

Sahu, S., Ghosh, S., Hirata, K., Fujita, D., Bandyopadhyay. A. 2013, "Multi-level Memory-switching Properties of a Single Brain Microtubule," *Applied Physics Letter* 102:123701.

Stapp, H.P. 1993, *Mind, Matter and Quantum Mechanics.* Berlin: Springer Verlag. Tononi, G. 2012, PHI: *A Voyage from the Brain to the Soul*, Pantheon Books: New York.

Troutt, L.L., Spurck, T.P., Pickett-Heaps. 1995, "The Effects of Diazepam on Mitosis and the Microtubule Cytoskeleton II. Observations on Newt Epithelial and PtK1 Cells," *Protoplasma* 189(1,2):101-112.

Whitehead, A.N. 1929, Process and Reality, New York: Macmillan.

Whitehead, A.N. 1993, Adventure of Ideas, London: Macmillan.

Yaron-Jakoubovitch A., Jacobson G.A., Koch, C., Segev, I., Yarom, Y. 2008, "A Paradoxical Isopotentiality: A Spatially Uniform Noise Spectrum in Neocortical Pyramidal Cells," *Front Cell Neurosci* 13(2):3; doi: 10.3389/neuro.03.003.2008 (eCollection 2008).

DECODING FUNCTIONAL INFORMATION AT MACROSCOPIC AND MESOSCOPIC SCALES IN THE HUMAN BRAIN: FROM BASIC RESEARCH TO CLINICAL APPLICATIONS

Rainer Goebel*

Introduction

Since its invention 20 years ago, functional magnetic resonance imaging (fMRI) has become one of the most widely used and probably the publicly most visible non-invasive technique to measure brain activation. fMRI has played a central role in the development of cognitive neuroscience, and several new fields, including social neuroscience, neuroeconomics and genetic imaging, may not have developed had it not been for the unique opportunities afforded by fMRI. The particular strengths of this technique are in its spatial resolution and fidelity, ability to reach deep subcortical structures and whole-brain coverage, enabling the mapping of functionally connected networks and the extraction of information from activation patterns that are distributed across different brain areas. Functional brain imaging has substantially contributed to our understanding of specialised areas and large-scale networks in the human brain. This has also allowed "brain reading" applications relating distributed activity patterns to mental states. Recent real-time brain reading applications even provide new therapeutic applications of fMRI. While successful, fMRI currently targets a level of resolution that does not allow inferring the sub-categorical feature representations used by the brain. I will argue below that understanding mesoscopic functional organizations within brain areas is now in reach when using ultra-high magnetic field scanners (7 Tesla and higher). These devices allow submillimeter functional resolution opening the possibility to study the human brain at the level of cortical columns and cortical layers.

^{*} Faculty of Psychology and Neuroscience, Maastricht University, The Netherlands.

Real-time fMRI

In order to enable neurofeedback and brain-computer interface (BCI) applications, measured fMRI data needs to be processed online, i.e. during functional scanning; data analysis should preferentially operate in real-time, i.e. analysis for a newly measured functional volume should be completed before the next functional volume becomes available. Real-time processing (as opposed to near real-time fMRI), thus, restricts processing time to a maximum duration (volume time-to-repeat (TR)) that is defined by the temporal interval between successive functional volumes, which typically assumes values between 1 and 3 seconds. The requirement for incremental analysis in limited time windows is in contrast to conventional fMRI analyses processing data offline, i.e. data analysis only starts after the fMRI scanning session has actually ended without specific restrictions in calculation time. Recent real-time fMRI (rt-fMRI) studies use sophisticated software (Goebel et al., 2010; Weiskopf et al., 2012) employing analysis pipelines that include almost all preprocessing and (statistical) analysis steps used in conventional offline analysis.

Clinical fMRI neurofeedback applications

fMRI-based neurofeedback (fMRI-NF) has the potential to open up radically new paths to translation (Linden, 2012; Sulzer et al., 2013). During fMRI-NF training, participants receive feedback on their brain activity in real-time and are instructed to change this activation. This change is normally a simple up- or down-regulation, but could also entail changing the activation difference between two areas, their correlation, or the output of a multivariate pattern classification algorithm. The "haemodynamic" delay between neural activity and the vascular response that contributes to the fMRI signal, which is approximately five seconds, does not pose an obstacle when participants are informed of this delay (Weiskopf et al., 2004). compared to external stimulation techniques (e.g. transcranial magnetic stimulation), neurofeedback has the attractive characteristic of enabling the patients themselves to control their brain activity and thus contributing to their experience of self-efficacy, which is an important therapeutic factor in many neuropsychiatric disorders (Bandura, 1997). In our first psychiatric application of rt-fMRI neurofeedback (Linden et al., 2012), we trained patients with depression to up-regulate brain networks responsive to positive affective stimuli. This paradigm was modelled on our previous work with healthy participants, which had shown that the neurofeedback component is required for reliable control over emotion networks (Johnston et al., 2011). The eight patients who underwent this fMRI-NF protocol for four sessions improved significantly on the 17-item Hamilton Rating Scale for Depression, and this clinical improvement was not observed in eight control patients who engaged in a protocol of positive emotional imagery (matched to the fMRI-NF protocol for intervention and assessment times and affective stimuli) outside the scanner.

In another study we showed that successful up-regulation of the supplementary motor area (SMA) in early stage parkinson (PD) patients may lead to clinical benefits (Subramanian et al., 2011). In this study, five PD patients were trained to up-regulate SMA activity using rt-fMRI neurofeedback. The patients practiced the strategy employed in the scanning environment at home for a period of 2-6 months. A second neurofeedback session ensued, where the same training procedure was implemented again. The experimental group (but not a control group engaging in motor imagery in the scanner without receiving feedback) successfully activated the SMA during functional runs. Furthermore, participants in the experimental group showed significant improvements (37%) on a global measure of motor functions in Parkinson's disease (UPDRS-part III). Improvement in limb bradykinesia was observed in four out of the five participants, which was supported by the findings on a finger-tapping task. In contrast, no clinical benefits were reported for the control group.

In a recent study (Zilverstand et al., 2014) we could show that providing rt-fMRI neurofeedback has a facilitator effect on anxiety regulation in patients with spider phobia. The implemented neurofeedback training in spider phobia facilitated anxiety regulation by enabling patients to observe which regulation (re-appraisal) strategy increased activation in the regulatory network, and lead to a reduction of hyperactivation in the anxiety network throughout the session.

A communication BCI based on real-time fMRI

In brain-computer interface (BCI) applications, separate commands can be encoded by employing different cognitive brain functions. Since different cognitive states evoke spatially distinct brain activation patterns that can be disentangled by rt-fMRI analysis techniques, the encoder's original intention can be derived. We have exploited this to build a hemodynamic communication BCI (Sorger et al., 2012) that decodes 27 distinct states from single-trial spatio-temporal activity patterns. By decoding these states online as letters of the alphabet (see figure 1), the developed system provides the possibility for patients with severe motor impairments to 'write' words on the screen letter-by-letter with high accuracy. The subjects engaged in three different mental tasks (e.g. mental drawing, mental calculation, mental singing). In order to encode 27 distinct spatio-temporal patterns, these 3 mental tasks started at 3 different shifted times within a window and for 3 different durations. This and similar BCIs based on hemodynamic (vs neuroelectric) brain signals may constitute an important alternative communication means, for example for patient populations that do not benefit from approaches based on electroencephalography (EEG).



Figure 1. Principle of rt-fMRI based brain-computer interface enabling robust motorindependent communication.

The next frontier - Mesoscopic functional brain imaging

With standard fMRI at 3 Tesla, we can see specialised brain areas, including "expert" regions for colour, visual motion, faces, words, language, planning, memory and emotions. This level of neuroimaging has revealed an amazing organisation of the brain that is similar, but not identical, across individuals. This is often referred to as the macroscopic level of brain organisation. We still, however, know little about the representations coded *inside* each specialised brain area and how complex features emerge from combinations of simpler features when we move from one area to the next. With high-field MRI scanners (7 Tesla and beyond) and optimised MR pulse sequences, the achievable functional resolution reaches to the sub-millimetre level (500–1000 microns). Note that such a resolution is much more difficult to obtain for functional images than for anatomical images, where sub-millimetre resolution is limited to about 2 millimetres.

This increase in functional spatial resolution per se would probably not substantially advance our knowledge of the brain's functional organisation if neurons were distributed randomly within a specialised brain area. If, however, neurons that code for similar features are clustered into functional units with an extent of about 1 millimetre, then an increase in spatial resolution into the sub-millimetre range would not only reflect a quantitative step forward but would also establish a fundamental qualitative improvement. According to the seminal work on animals by the Nobel Prize winners Hubel and Wiesel (1969) and other scientists. the mammalian brain indeed seems to be organised in a set of "vertical units", also called cortical columns, spanning from the pial surface to the white matter. As a universal cortical organisation principle, such cortical columns seem to form the basic building blocks of complex distributed representations. Like letters of the alphabet, functional columnar-level units could form the basic features of an area's "coding alphabet" that would represent information relevant for a specialised brain area. In the motion-selective area V5, the basic features ("letters") would be columns coding for different directions of motion, whereas in the fusiform face area (FFA) the basic features could code for face parts and their relative

constellation, e.g. "shape of nose", "distance between eyes" or "colour of lips". Just as words are formed from combinations of letters, so too would different entities within a specialised brain area (e.g. different individual faces represented in FFA) be coded by a specific distributed activity pattern across the area's cortical columns. My core research vision is that substantial progress could be achieved in understanding the brain if we were able to measure and understand these columnar-level representations within specialised brain areas. I believe that this columnar-level code can indeed be "cracked" by adequately combining clever experimental designs, sub-millimetre fMRI, sophisticated data analysis tools and computational modelling.

I refer to this level of brain imaging to the *mesoscopic* level of functional brain organization. Thanks to the clustering of neurons with similar response properties into functional units, studying cortical columns seems to be the right level to reveal the principles that the brain uses to code information. This is important because, if the investigation at the neuronal level were the only way to learn about representations in the brain, using high-field imaging to zoom into specialised areas would become less important. Fortunately, the first evidence is now emerging that high-field neuroimaging is indeed able to reveal representations at the columnar level. We have recently performed a columnar-level study, showing topographic images on the columnar-level organisation of motion area V5 for the first time (Zimmermann et al., 2011).

We recently obtained encouraging results from feature-level (subcategorical) decoding of visual mental imagery (Emmerling et al., 2014): We could successfully decode one out of four imagined directions of motion. These recent results are not only relevant to advance our neuroscientific knowledge but would also enable advanced braincomputer interfaces. In a typical BCI setup as described above for communication (Sorger et al., 2012) the user is asked to perform one of a number of different specific kinds of mental imagery (e.g. imagine to move the hand vs. imagine to sing a song) that would correspond to different information entities that the user wants to encode (e.g. to steer the cursor on the screen to the left vs. to the right, or to send a letter of the alphabet). The BCI then classifies these different categories of mental imagery based on the acquired brain activation data and executes the associated intended actions. However, the possibility of columnarlevel sub-categorical decoding would allow intention expressions that are much more natural than with current BCIs: the imagery of rightward visual motion (instead of imagining to sing a song) could make a cursor on the screen go to the right. We will explore this possibility in our future research.

Moving from the macroscopic (system) level neuroimaging to the mesoscopic level of cortical columns and layers in as many areas as possible will lead to a deeper understanding of how the structure of the human mind emerges from feature representations and their interactions in the brain, and might enable more natural rt-fMRI-based brain computer interfaces.

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References

Bandura A. Self-efficacy: the exercise of control. New York: W.H. Freeman; 1997.

Emmerling T, Zimmermann J, Sorger B, Frost M, Goebel, R. (2014). Decoding the direction of imagined visual motion using 7T high-field fMRI reveals individual strategies. Submitted for publication.

Goebel R, Zilverstand A, Sorger B (2010) Real-time fMRI-based brain computer interfacing for neurofeedback therapy and compensation of lost motor functions. *Imaging in Medicine*, 2, 407-415.

Hubel, D. H., and Wiesel, T. N. (1969). Anatomical demonstration of columns in the monkey striate cortex. *Nature*, 221, 747-750.

Johnston S, Linden DE, Healy D, Goebel R, Habes I, Boehm SG (2011). Upregulation of emotion areas through neurofeedback with a focus on positive mood. *Cogn Affect Behav Neurosci*, 11, 44-51.

Linden DE (2012). The challenges and promise of neuroimaging in psychiatry. *Neuron*, 73, 8-22.

Linden DEJ, Habes I, Johnston SJ, Linden S, Tatineni R, Subramanian L, et al. (2012): Real-time self-regulation of emotion networks in patients with depression. *PLoS One*, 7, e38115.

Subramanian L, Hindle JV, Johnston S, et al. (2011). Real-time functional

magnetic resonance imaging neurofeedback for treatment of Parkinson's disease. J Neurosci, 31, 16309-16317.

Sulzer J, Haller S, Scharnowski F, Weiskopf N, Birbaumer N, Blefari ML, Bruehl AB, Cohen, LG, deCharms RC, Gassert R, Goebel R, Herwig U, LaConte S, Linden D, Luft A, Seifritz E, Sitaram R (2013). Real-time fMRI Neurofeedback: Progress and Challenges. *Neuroimage*, 76, 386-399.

Weiskopf N, Scharnowski F, Veit R, Goebel R, Birbaumer N, Mathiak K. (2004). Self-regulation of local brain activity using real-time functional magnetic resonance imaging (fMRI). *J Physiol Paris*, 98, 357-373.

Weiskopf N (2012). Real-time fMRI and its application to neurofeedback. *Neuroimage*, 62, 682-692.

Zilverstand A., Sorger B, Sarkheil P, Goebel R (2014). Neurofeedback based on functional magnetic resonance imaging facilitates anxiety regulation in spider phobia. Submitted for publication.

Zimmermann, J., Goebel, R., De Martino, F., van de Moortele, P.F., Feinberg, D., Adriany, G., Chaimov, D., Shmuel, A., Uğurbil, K. and Yacoub, E. (2011). Mapping the organization of axis of motion selective features in human area MT using high-field fMRI. *PLoS One*, 6, e28716.

MIND-MATTER INTERACTIONS IN SEVERE BRAIN INJURY AND COMA

Vanessa Charland-Verville * & Steven Laureys *

Abstract

The past fifteen years have provided an unprecedented collection of discoveries that bear upon our scientific understanding of recovery of consciousness in the human brain following severe brain damage. Highlighted among these discoveries are unique demonstrations that patients with little or no behavioral evidence of conscious awareness may retain critical cognitive capacities and the first scientific demonstrations that some patients, with severely injured brains and very longstanding conditions of limited behavioral responsiveness, may nonetheless harbor latent capacities for recovery. Included among such capacities are particularly human functions of language and higher-level cognition that either spontaneously or through direct interventions may reemerge even at long time intervals or remain unrecognized. When patients in "persistent vegetative state" (recently also coined unresponsive wakefulness syndrome) show minimal signs of consciousness but are unable to reliably communicate the term minimally responsive or minimally conscious state (MCS) is used. MCS was recently subcategorized based on the complexity of patients' behaviors: MCS+ describes high-level behavioral responses (i.e., command following, intelligible verbalizations or non-functional communication) and MCS- describes low-level behavioral responses (i.e., visual pursuit, localization of noxious stimulation or contingent behavior such as appropriate smiling or crying to emotional stimuli). Patients who show non-behavioral evidence of consciousness or communication only measurable via ancillary testing (i.e., functional MRI, positron emission tomography, EEG or evoked potentials) can be considered to be in a functional locked-in syndrome. An improved assessment of brain function

^{*} Cyclotron Research Center & CHU Neurology Department, University of Liège, Belgium.

in coma and related states is not only changing nosology and medical care but also offers a better-documented diagnosis and prognosis and helps to further identify the neural correlates of human consciousness. Taken together, recent studies show that awareness is an emergent property of the collective behavior of frontoparietal top-down connectivity. Within this network, external (sensory) awareness depends on lateral prefrontal/ parietal cortices while internal (self) awareness correlates with precuneal/ mesiofrontal midline activity. Of clinical importance, this knowledge now permits to improve the diagnosis, prognosis and treatment of patients with disorders of consciousness, which currently remains very challenging. New technological advances now also permit to show command-specific changes in fMRI, EEG or eye-pupil measurements providing motorindependent evidence of conscious thoughts and in some cases even of communication. We will conclude by discussing related ethical issues and the challenge of improving our clinical care and quality of life in these challenging patients with disorders of consciousness.

Reducing consciousness to two dimensions

At present there is no generally accepted definition of consciousness (Baars, Ramsoy, & Laureys, 2003). As clinicians, we will reduce the complexity of this term and define consciousness operationally, separating two main components: wakefulness and awareness (Figure 1) (Steven Laureys, 2005a). Wakefulness has been shown to critically depend upon the functional integrity of subcortical arousal systems over 50 years ago (e.g., see Damasio & Meyer, 2009). The level of wakefulness can be estimated by simple behavioral criteria based on eye opening ranging from absent, over stimulus-induced to spontaneous sustained eye opening. For instance, every night when falling asleep, we experience a decrease of the level of wakefulness up to the point we lose awareness of our environment. Awareness is more difficult to define and more challenging to assess behaviorally (Majerus, Gill-Thwaites, Andrews, & Laureys, 2005). We have recently proposed to reduce the phenomenological complexity of awareness into two further components: external awareness, namely everything we perceive through our senses (what we see, hear, feel, smell and taste), and *internal* awareness or stimulus-independent thoughts.

Interestingly, the switch between the external and internal milieu was found not only to characterize overt behavioral reports but also had a cerebral correlate (Vanhaudenhuyse et al., 2011). In particular, it was shown that behavioral reports of internal awareness were linked to the activity of midline anterior cingulate/mesiofrontal areas as well as posterior cingulate/precuneal cortices. Conversely, subjective ratings for external awareness seem to correlate with the activity of lateral frontoparieto-temporal regions (Figure 2). These findings highlight that the anticorrelated pattern between the internal and external awareness systems is of functional relevance to conscious cognition. Similar reductions in external awareness systems have been also shown for nonresponsive conditions, such as deep sleep and anesthesia (for a review see Heine et al., 2012). Taken together these studies indicate that the two awareness networks mediate (at least partially) conscious ongoing under the functions of a wide "global neuronal workspace" (Baars, et al., 2003; Dehaene & Changeux, 2011)

Over the past fifteen years we have increased our understanding of the neural correlates of awareness (Laureys & Schiff, 2012). The study of patients with disorder of consciousness (DOC) provides unique opportunities to determine the sufficient and possibly the necessary conditions for conscious cognition to happen. Patients in a coma are unconscious because, by definition, they cannot be awakened even when intensely stimulated. Patients will not remain in coma for months or years in contrast to what is sometimes reported in the media (Racine, Amaram, Seidler, Karczewska, & Illes, 2008). In a number of cases, patients will show such a massive brain damage that all brainstem function will be irreversibly lost and evolve to brain death (Laureys, 2005b). Those patients who will show a good recovery after coma classically will do so within the first days or weeks after the insult. A substantial fraction of coma patients will recover near-normal function of the subcortical "wakefulness network" (located in the brainstem) while remaining without external signs of awareness. This condition of eyes-open wakefulness was coined "persistent vegetative state" in the 1970s (Jennett & Plum, 1972) and more recently it has been described in more neutral descriptive terms as "unresponsive wakefulness syndrome" (Laureys et al., 2010). Vegetative/unresponsive (VS/UWS) patients classically breathe spontaneously and can make a wider range

of movements than can be seen in coma. Depending on the partial or full recovery of subcortical wakefulness networks and brainstem function they can show spontaneous or stimulus-induced eve opening, blinking to visual threat; have auditory startle responses or orient the eyes or head to stimuli; show stereotyped posturing, normal flexion withdrawal to noxious stimulation or grasping; show gag, deglutition, oral reflexes or vocalizations. The recovery of inconsistent but reproducible signs of awareness, in the absence of functional communication or object use, coins the diagnosis of minimally conscious state (MCS). Depending on the complexity of these behaviors it was recently proposed that MCS patients be subcategorized as MCS- when only showing simple non-reflex movements, such as visual pursuit, orientation to pain or non-contingent behavior (e.g., smiling to the presence of a family member and not to others) and MCS+ when patients recover the ability to respond to simple commands (e.g., move your feet) (Bruno, Vanhaudenhuyse, Thibaut, Moonen, & Laureys, 2011; Gosseries et al., 2011).

The study of coma and related states has shown that consciousness is not an emergent property of sensory cortical activation in isolation. Auditory stimulation with simple clicks in MCS patients activated widespread temporal auditory areas and most importantly lead to functional connectivity changes with the external awareness network (Boly et al., 2004). Similar activation and connectivity changes were observed in normal conscious controls but not in VS/UWS patients were activation was limited to isolated low-level auditory cortices, functionally disconnected from the external awareness network (Laureys et al., 2000). Novel technological developments now permit to assess the directionality of this long-range cortico-cortical connectivity. Using dynamic causal modeling on auditory oddball evoked potential data obtained with highdensity EEG, it was shown that only MCS patients (but not VS/UWS patients) showed feedback or top-down connections from higher-order frontal associative areas to hierarchically lower-level auditory regions (Boly et al., 2011). A study combining transcranial magnetic stimulation with simultaneously recorded EEG confirmed the importance of long-range connectivity from the posterior parietal associative cortex. Only MCS and not VS/UWS patients showed such long-range connectivity changes. This technique also permitted to longitudinally follow connectivity changes in

patients who recovered (or failed to recover) from VS/UWS (Rosanova et al., 2012). These early functional connectivity studies highlight the importance of connectivity measurements in the emergence of human conscious awareness.

Clinical interest

To efficiently evaluate the patients' level of consciousness is of paramount importance. For clinicians dealing with acute or chronic DOCs, the main challenge is to disentangle between "reflex" or nonpurposeful behavior from any "voluntary" or "willed" behavior. Currently, behavioral assessment is still considered to be the "gold standard" for detecting signs of consciousness at the bedside [15]. Many different scales have been developed to assess patients who are recovering from coma, and this last decade has particularly been focusing on the differential diagnosis between VS/UWS and MCS. Providing accurate diagnosis through the use of specialized scales allows for optimal clinical management (i.e., rehabilitation needs, pharmacological treatment, and end-of-life decisions). To date, the most complete and sensitive scale available to detect signs of consciousness, and thus to disentangle between VS/UWS from MCS, is the revised version of the Coma Recovery Scale (CRS-R) by Joseph Giacino and his collaborators (Bruno, Ledoux, et al., 2011; Giacino, Kalmar, & Whyte, 2004; Schnakers et al., 2009; Seel et al., 2010). It is important to stress that when aiming to assess the patients' level of consciousness, we are limited to make inferences based on motor responses (Sanders, Tononi, Laureys, & Sleigh, 2012). Most of the time this works fine but in some cases, consciousness can be present in the absence of consistent motor responsiveness.

Using neuroimaging techniques as complementary diagnostic and prognostic tools

To address this issue, clinicians now rely on other strategies to add more objectivity to their clinical assessment. With the advent of functional neuroimaging (functional MRI and PET) and electrophysiology (EEG and event related potentials), the study of residual brain function in

patients with a DOC has provided unique insights on the underlying brain mechanisms accounting for the presence of awareness (Laureys & Boly, 2008). For instance, it is thought that consciousness does not require the whole brain's activity, but rather that some areas are more critical than others to support consciousness. FDG-PET studies have demonstrated that when patients recover from coma to VS/UWS, they recover the wakefulness network (encompassing brainstem and basal forebrain) which explains the restoration of sustained spontaneous or stimulus-induced eye opening and of autonomic functions including spontaneous breathing (Laureys, Owen, & Schiff, 2004). However, recovery from VS/UWS does not coincide with near-normal metabolic activity in overall brain function. Voxel-based analyses between brain metabolic scans obtained in awake yet unaware VS/UWS patients compared to healthy controls (betweensubject) or comparisons with recovery of awareness (within-subject) have highlighted the critical role of the widespread fronto-temporo-parietal associative cortical network (Thibaut et al., 2012).

Within this "global workspace", the posterior midline regions encompassing precuneus and adjacent posterior cingulate cortex seem to form a critical hub. Indeed, these areas are the most metabolically active cortical regions in normal conscious waking, and are mostly impaired in patients in coma or VS/UWS whereas they are minimally active in MCS patients. Its critical role in consciousness was confirmed by a much mediatized case of "miracle recovery from coma" named Terry Wallis (Schiff et al., 2007). Nineteen years after his traumatic brain injury this patient was still considered "vegetative" and started to speak. When carefully examining the patient's medical files it became clear he was in a MCS already months after the trauma. Using MRI and diffusion tensor imaging in Mr. Wallis, Schiff and collaborators reported axonal regrowth, nearly two decades after the acute insult, in the aforementioned posterior midline structures (Voss et al., 2006). This case not only illustrates the problem of misdiagnosing DOCs if merely based on behavioral unstandardized tools (Schnakers et al., 2009) but also the possibility of neural plasticity even many years after the acute insult (Demertzi et al., 2011). More recent fMRI studies have confirmed these findings and demonstrated a consciousness-dependent non-linear breakdown in functional connectivity of the so-called default mode "midline core"

network when comparing normal consciousness to MCS, VS/UWS and comatose states (Vanhaudenhuyse et al., 2010).

Recently, the so-called "active" functional neuroimaging or event-related potential paradigms have been developed to assess motorindependent brain responses to commands (i.e., active paradigms) and in absence of external stimulation (i.e., passive paradigms). First, such "active" mental imagery paradigms have been developed using fMRI. In a collaborative effort between Cambridge and Liège, healthy volunteers were asked to perform a series of tasks (e.g., imagine singing a song in your head or imagine your mothers' face). The most robust and reproducible patterns of brain activation were obtained using motor imagery (i.e., imagine playing tennis) and spatial navigation (*i.e.*, imaging walking around in your house), leading to the predicted activation of supplementary motor cortex and parahippocampal areas, respectively (Boly et al., 2007). Using this tool, both teams together with Cornell University, have identified a series of severely brain damaged patients who were clinically diagnosed as being VS/UWS or MCS- and who yet showed robust fMRI evidence of response to command, and consequently conscious awareness (Bardin et al., 2011; Monti et al., 2010; Owen et al., 2006). In one of these cases, functional communication could even be established by explaining to the patient to do the motor imagery task to communicate "yes" and the spatial navigation task to communicate "no". This patient, a 22-year old man who was sent to Liège for a one-week diagnostic assessment, is another example of clinical misdiagnosis. Indeed, this patient had the clinical diagnosis of VS/UWS while standardized behavioral assessments showed that he was actually in a MCS (Monti, et al., 2010). To a series of simple questions (e.g., is your father's name Alexander) the automated user-independent analysis of the acquired fMRI data classified the brain's responses as a "yes" or "no" answer. Correct answers were obtained and reported by the blinded examiners for five consecutive questions. Only for the last question no answer could be elicited merely due to absent brain activation. As a consequence, this patient could be considered as being in a functional locked-in syndrome, given it was only functional neuroimaging that permitted to establish the yes-no communication to closed questions (in contrast to classical locked-in syndrome where an eye-coded yes-no communication can be established) (Bruno et al.,

2011). Evidently, these results (Monti, et al., 2010) should be seen as a proof of concept rather than a practical communication tool. As soon as the patient was taken out of the MRI machine, no communication whatsoever was possible.

Second, the so-called "passive" functional neuroimaging as the main advantages of measuring brain functioning at rest without requiring any participation from the patients (*e.g.*, language comprehension and/ or production or motor responses) nor sophisticated experimental setup. The use of these fMRI paradigms also permitted to highlight particular brain activation linked to the different states of consciousness. Resting state connectivity studies have demonstrated that a resting brain is characterized by coherent fluctuations in the blood-oxygen- level-dependent (BOLD) signal. The midline frontoparietal or default-mode network (DMN), comprising cortical regions that are known to be more active during rest (encompassing precuneus/posterior cingulate cortex, mesiofrontal/anterior cingulate cortex, and temporoparietal junction areas), has been shown to be informative of cognitive function (Greicius, Krasnow, Reiss, & Menon, 2003; Mevel et al., 2010) and to be correlated with bedside behavioral assessment (Soddu et al., 2011).

To complement these approaches, transcranial magnetic stimulation (TMS) together with high-density EEG is now employed to evaluate effective connectivity (*i.e.*, the influence one neural system exerts over another) at the bedside. According to theoretical models of consciousness, effective connectivity represents a basic requirement for consciousness and means that multiple, specialized areas of the brain (i.e., the thalamocortical system) must engage in rapid causal interactions (Laureys, 2005; Tononi & Koch, 2008). TMS/EEG measures report that, in VS/UWS patients, a simple and local electrical response is obtained after stimulating the brain, indicating a breakdown of effective connectivity like previously observed in unconscious sleeping or anaesthetized subjects (Ferrarelli et al., 2010; Massimini et al., 2005; Rosanova, et al., 2012). In contrast, TMS/EEG in MCS patients will trigger much more complex activations in the brain that will involve sequentially distant cortical ipsilateral and contralateral areas to the site of stimulation, similar to activations recorded in LIS patients (Rosanova, et al., 2012).

Finally, MRI is also used for prognosis purposes. Recently,

quantitative diffusion tensor imaging (DTI) techniques have been shown to outperform clinical markers in predicting 1-year functional outcome at the individual-patient level in patients with traumatic (Galanaud et al., 2012) or anoxic (Luyt et al., 2012) brain injury. Therefore, DTI-MRI techniques can offer a unique opportunity to quantify the structural integrity of the white matter, and can also quantify the primary and secondary axonal damage encountered in DOCs (Voss et al., 2006).

Brain computer interfaces

In addition to the detection of signs of consciousness, braincomputer interfaces (BCIs), recordings of brain signals might also enable self-expression in non-communicative patients with motor deficits (Kubler & Kotchoubey, 2007; Laureys & Boly, 2008). BCIs have classically been developed for LIS and other pathologies involving severe motor deficits (e.g., amyotrophic lateral sclerosis) in order to provide a means of interaction with their environment. In DOCs, BCIs using active paradigms are now developed to allow patients to express their consciousness and to communicate. For example, a remarkable case of a behaviorally diagnosed VS/UWS patient who could correctly answer autobiographical yes-no type questions (e.g., "Is your name John?"), by producing specific brain activations through mental imagery tasks (*i.e.*, to say yes, imagine yourself playing tennis; to say no, imaging yourself moving around in your house) in the MRI with the previously reported paradigm (Monti et al., 2010). Therefore, this revolutionary finding strikingly demonstrated the possibility of establishing binary communication using patients' brain responses alone. Hence, portable and cheaper EEG-based equivalents (e.g., Cruse et al., 2011; Cruse et al., 2012; Lulé et al., 2012), brain computer interfaces (BCI), have been developed for more routine clinical use (for recent review see Chatelle et al., 2012). Furthermore, a pupil size-dependent device has been recently proposed as a communication tool for patient with LIS. The device allows pupil measurements by a bedside camera when patients are performing a cognitively demanding task to signal their responses. Furthermore, using the same protocol, the authors demonstrated command-following for a MCS patient, suggesting its potential as a diagnostic tool for patients who can't demonstrate their

awareness at the bedside (Stoll et al., 2013). It is important to stress that the absence of brain activation to commands cannot be taken as proof of absence of consciousness and frequently false negative results have been reported in MCS+ patients (*e.g.*, Cruse, et al., 2012). Repeated fMRI and EEG BCI assessments would be needed to increase the confidence for true negative findings. In addition, we also need to tackle the problem of false positives, namely the fact that unconscious patients may show artifact or noise-related activation (Soddu et al., 2011). Future studies should deal with these issues in large patient cohort and also assess testretest variability of these novel technologies in this specific context.

Treatment in DOCs

Following severe brain damage, pharmacological agents can be given to counteract disturbances of specific neurotransmitter systems. Pharmacological treatments of patients currently aim to improve arousal levels and recovery of consciousness. For instance, amantadine and zolpidem have previously been reported to produce beneficial effects in some adults and pediatric populations with a DOC. More research is needed to determine which treatment would provide the best neurological outcome regarding the patient's etiology, diagnosis time since injury and overall condition. Large multi-center studies, using common behavioral metrics combined with state-of-the-art neuroimaging and/or electrophysiology techniques are expected to shed more light on the underlying mechanisms of these drug treatments and eventually determine an evidence-based model for the pharmacokinetics and pharmacodynamics of these agents in severely brain injured, non-communicative patients. In a more invasive way, global yet specific cerebral functional identification of thalamocortical connectivity has led to the development of thalamic deep brain stimulation paradigms for the treatment of post-traumatic MCS patients (Schiff, et al., 2007). A successful deep-brain stimulation case was reported in 2007 when a 6-year-post-injury patient recovered complex cognitively mediated behavioral patterns after the application of bi-lateral thalamic electrical stimulation (Schiff et al., 2007). This case report showed that deep-brain stimulation could improve arousal level and fluctuations as well as promoting more complex behavioral responsiveness as measured

with the CRS-R. Very recently, a double-blind sham-controlled crossover design was conducted to assess the effects of left dorsolateral prefrontal cortex transcranial direct current stimulation (tDCS) on CRS-R scores in severely brain-damaged patients with a DOC. Anodal and sham tDCS were delivered in randomized order over the left dorsolateral prefrontal cortex for 20 minutes in VS/UWS and MCS patients assessed at least 1 week after acute traumatic or non-traumatic insult. When assessed with the CRS-R after the anodal stimulation, 43% of MCS patients showed an improvement (*i.e.*, showed a clinical sign of consciousness never observed before). The study showed that a single session of short duration tDCS stimulation could transiently improve consciousness as measured by CRS-R assessment in MCS patients.

Ethical framework

DOCs raise a lot of ethical debates. First, one of the most debatable issues about this population is pain perception. The International Association of Pain Specialists (IAPS) defines it as "an unpleasant sensory and emotional experience associated with real or potential tissue damage" (Bekinschtein et al., 2011). Thus pain is a first-person experience and classic pain assessments require the verbal feedback of the patients. When it comes to DOCs, the question of pain perception is far more complex since they are unable to communicate their feelings and possible pain experiences. Detecting and treating pain represents important medical and ethical considerations, especially in severely brain-injured patients, thus neuroimaging and behavioral studies can help to address the question. Since pain represents a conscious first person perception, nociception is a more appropriate term that should be used regarding patients with DOC. As discussed previously in this review, on a neurofunctional perspective, it appears that MCS patients show a pain-matrix activation that is, although reduced, similar to what is seen in healthy volunteers while VS/UWS patients do not show this higher-order, widespread brain activation. Since the communication between associative brain areas and networks represent one key component of conscious awareness, it has been suggested that unconscious patients would not feel pain like the MCS patients and healthy volunteers do. These results obviously have

major consequences on patients' daily care and management. Despite these findings, according to a recent European survey, still high rates of medical doctors (56%) and para- medical professionals (68%) believe that VS/UWS do feel pain (Demertzi et al., 2009). These attitudes may have major consequences in patients' care management and especially in cases where VS/UWS patients are withdrawn from life-support treatment. In these cases patients may be left without administration of analgesic drugs during their dying process. Moreover, patients could experience pain without demonstrating any behavioral sign of such discomfort.

As well as the high rate of misdiagnosis of the altered states of consciousness highlighted above in this paper, nociception and pain could also be easily missed in this non-communicative population. Therefore, pain prophylaxis and treatment have been proposed for all patients suffering from DOCs (Schnakers, Faymonville, & Laureys, 2009; Schnakers & Zasler, 2007). To date, the presence or absence of nociception was inferred via motor responses following noxious stimulation, such as stereotypical responses, flexion withdrawal and localization responses (Schnakers & Zasler, 2007). In DOCs, only a clear localization to noxious stimulation is considered to be an indicator of conscious perception (Giacino et al., 2002). In order to accurately nonverbally assess nociception in this challenging population, a behavioral scale has been proposed for the first time. The Nociception Coma Scale (NCS) assesses behavioral responses at rest, during daily nursing care and during nociceptive stimulation (Schnakers et al., 2010). Recently, a revised version of the NCS has been proposed (NCS-R). The NCS-R encompasses motor, verbal and facial behaviors, excluding the previous visual subscale that was found to be uninformative of the patient's level of discomfort since the behaviors included in the subscale were frequently observed in response to non-noxious situations. According to this new version, the need of adequate pain management is recommended at a total cut-off score of 4 (on a maximum of 9) or higher (Chatelle, Majerus, Whyte, Laureys, & Schnakers, 2012). A second significant ethical challenge concerns the perceived quality of life of patients with DOC. Healthy individuals and medical professionals sometimes assume that their quality of life might be so poor that it is not worth living. To address the question, a survey on quality of life has been proposed to LIS patients. Although the LIS is not considered to be part of the DOCs, this pathological condition is often misdiagnosed as being such and might represent one of the cruelest physical disabilities. On 65 LIS patients interviewed, 47 self-reported a meaningful quality of life, while a minority of 17 patients rated themselves as being unhappy (Bruno et al., 2011). Moreover, demand for euthanasia is surprisingly infrequent in chronic LIS patients (Laureys et al., 2005). Indeed, less than 30% of the chronic LIS patients would report the wish to die or suicidal thoughts (Laureys, et al., 2005). As healthcare practionners, these findings stress the importance of leaving our personal attitudes and beliefs aside when dealing with severely disabled patients. Indeed, contrary to popular creed, it seems that life is worth living even in cases of severe disabilities. Biased clinicians interpretations of the patients' conditions might modify medical treatment plans and influence families in inappropriate ways.

Conclusion

Studying VS/UWS patients has shown that consciousness seems to emerge from a collective critical cortico-thalamo-cortical network dynamic, involving the frontoparietal global workspace (Laureys et al., 2002). At present, it remains controversial whether consciousness should be considered as a binary all-or-none phenomenon or continuous (Seth, Dienes, Cleeremans, Overgaard, & Pessoa, 2008). Based on clinical experience and on recent evidence from careful studies in normal healthy volunteers (e.g., Sergent & Dehaene, 2004) we here consider consciousness on a continuous non-linear scale. Our clinical boundaries are increasingly being challenged by neuroimaging or electrophysiology studies in patients with DOC who show motor-independent signs of awareness or communication. Such advances are naturally accompanied by legitimate neuroscientific and ethical queries, such as on pain perception and management as well as end-of-life options (Demertzi et al., 2011; Demertzi et al., 2012; Jox, Bernat, Laureys, & Racine, 2012a; Kuehlmeyer, Borasio, & Jox, 2012). In the future, efforts should be made towards consciousness classification metrics, where system-level functional neuroimaging and electrophysiology will provide an objective means to better characterize the underlying mechanisms accounting for conscious

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cognition and its recovery after severe acquired brain injury. Despite the best clinical assessment, we are still limited to make inferences about consciousness based on motor responsiveness, possibly leading to an underestimation of patients' awareness.

As we have previously highlighted, disentangling between conscious and VS/UWS patients represents a major challenge that can generate severe consequences. It is to these latter problematic challenges that the ethical and legal end-of-life issues of withholding and withdrawal of life-sustaining treatment are related (Celesia, 2000; Jennett, 2005). The rate of misdiagnosis among the altered states of consciousness is still very high; therefore, the use of behavioral scales in parallel with the increasingly powerful neuroimaging technologies will help to refine our understanding and definition of DOCs thus, leading to a more accurate diagnosis and prognosis. The rapidly growing neuroscientific findings on DOCs must be taken into account for patient's future care needs and to promote adequate policies to keep up with the findings (Jox, Bernat, Laurevs, & Racine, 2012b). In fact, new findings in consciousness research have led to the redefinition of clinical criteria for diagnosis and bring to the clinician new knowledge about patient's recovery and prognosis (Fins, 2008). Because most of these reported complementary para-clinical procedures remain mainly investigational, clinicians must be aware of the level of evidence supporting the research findings and of the unavoidable ethical and social issues involved.

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Figure 1. Figure illustrating an oversimplification of the two main components of consciousness: wakefulness (the level of arousal) and awareness (the level of consciousness).

Adapted with permission from Laureys (2005). The neural correlate of (un)awareness: lessons from the vegetative state. *Trends Cogn Sci*, 9(12), 556-559.



Figure 2. An oversimplified distinction of human awareness into awareness of the environment and of self-related mentation. Experimental works suggests that these two components have two distinct functionally alternating cerebral correlates. The external awareness network (areas in red) encompasses mainly lateral bilateral dorsolateral prefrontal cortices and posterior parietal cortices. The internal awareness network (areas in blue) includes mainly midline posterior cingulate/precuneual regions and anterior cingulate/medial prefrontal cortices. Apart from cortico-cortical connectivity, connectivity with subcortical structures, such as with the thalamus is considered to be essential to support wakefulness and ongoing conscious processing.

Adapted with permission from Laureys (2007). Eyes open, brain shut. *Sci Am*, 296(5),84-89 and Vanhaudenhuyse et al. (2011). Two distinct neuronal networks mediate the awareness of environment and of self. *J Cogn Neurosci*, 23(3),570-578.

References

Baars, B., Ramsoy, T. Z., & Laureys, S. (2003). Brain, conscious experience and the observing self. *Trends Neurosci*, 26(12), 671-675.

Bardin, J. C., Fins, J. J., Katz, D. I., Hersh, J., Heier, L. A., Tabelow, K., . . . Voss, H. U. (2011). Dissociations between behavioural and functional magnetic resonance imaging-based evaluations of cognitive function after brain injury. *Brain*, 134(Pt 3), 769-782. doi: 10.1093/*brain*/awr005

Bekinschtein, T. A., Coleman, M. R., Niklison, J. 3rd, Pickard, J. D., Manes, F. F. (2008). Can electromyography objectively detect voluntary movement in disorders of consciousness? *J Neurol Neurosurg Psychiatry*, 79(7), 826-828.

Boly, M., Coleman, M. R., Davis, M. H., Hampshire, A., Bor, D., Moonen, G., . . . Owen, A. M. (2007). When thoughts become action: an fMRI paradigm to study volitional brain activity in non-communicative brain injured patients. *NeuroImage*, 36(3), 979-992. doi: 10.1016/j.neuroimage.2007.02.047

Boly, M., Faymonville, M. E., Peigneux, P., Lambermont, B., Damas, P., Del Fiore, G., . . . Laureys, S. (2004). Auditory processing in severely brain injured patients: differences between the minimally conscious state and the persistent vegetative state. *Arch Neurol*, 61(2), 233-238.

Boly, M., Garrido, M. I., Gosseries, O., Bruno, M. A., Boveroux, P., Schnakers, C., . . . Friston, K. (2011). Preserved feedforward but impaired top-down processes in the vegetative state. *Science*, 332(6031), 858-862. doi: 10.1126/*science*.1202043

Bruno, M. A., Bernheim, J. L., Ledoux, D., Pellas, F., Demertzi, A., & Laureys, S. (2011). A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: happy majority, miserable minority. *BMJ Open*, 1(1), e000039. doi: 10.1136/ *bmjopen*-2010-000039

Bruno, M. A., Ledoux, D., Lambermont, B., Damas, F., Schnakers, C., Vanhaudenhuyse, A., . . . Laureys, S. (2011). Comparison of the Full Outline of UnResponsiveness and Glasgow Liege Scale/Glasgow Coma Scale in an intensive care unit population. *Neurocrit Care*, 15(3), 447-453. doi: 10.1007/s12028-011-9547-2

Bruno, M. A., Vanhaudenhuyse, A., Thibaut, A., Moonen, G., & Laureys, S. (2011). From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: recent advances in our understanding of disorders of consciousness. *J Neurol*, 258(7), 1373-1384. doi: 10.1007/s00415-011-6114-x

Celesia, G. G. (2000). Persistent vegetative state: clinical and ethical issues. *Suppl Clin Neurophysiol*, 53, 460-462.

Chatelle, C., Chennu, S., Noirhomme, Q., Cruse, D., Owen, A. M., & Laureys, S. (2012). Brain-computer interfacing in disorders of consciousness. *Brain Inj.* doi: 10.3109/02699052.2012.698362

Chatelle, C., Majerus, S., Whyte, J., Laureys, S., & Schnakers, C. (2012). A sensitive scale to assess nociceptive pain in patients with disorders of consciousness. *J Neurol Neurosurg Psychiatry.* doi: 10.1136/jnnp-2012-302987

Cruse, D., Chennu, S., Chatelle, C., Bekinschtein, T. A., Fernandez-Espejo, D., Pickard, J. D., . . . Owen, A. M. (2011). Bedside detection of awareness in the vegetative state: a cohort study. *Lancet*, 378(9809), 2088-2094. doi: 10.1016/S0140-6736(11)61224-5

Cruse, D., Chennu, S., Chatelle, C., Fernandez-Espejo, D., Bekinschtein, T. A., Pickard, J. D., . . . Owen, A. M. (2012). Relationship between etiology and covert cognition in the minimally conscious state. *Neurology*, 78(11), 816-822. doi: WNL.0b013e318249f764

Damasio, A., & Meyer, K. (2009). Consciousness: An overview of the phenomenon and of its possible neural basis. In S. Laureys & G. Tononi (Eds.), *The neurology of consciousness: Cognitive neuroscience and neuropathology*. (pp. 3-14). Oxford, UK: Academic Press.

Dehaene, S., & Changeux, J. P. (2011). Experimental and theoretical approaches to conscious processing. *Neuron*, 70(2), 200-227. doi: 10.1016/j.neuron.2011.03.018

Demertzi, A., Ledoux, D., Bruno, M.-A., Vanhaudenhuyse, A., Gosseries, O., Soddu, A., . . . Laureys, S. (2011). Attitudes towards end-of-life issues in disorders of consciousness: a European survey. *J Neurol*, 258(6), 1058-1065. doi: 10.1007/s00415-010-5882-z

Demertzi, A., Racine, E., Bruno, M. A., Ledoux, D., Gosseries, O., Vanhaudenhuyse, A., . . . Laureys, S. (2012). Pain perception in disorders of consciousness: neuroscience, clinical care, and ethics in dialogue. *Neuroethics*, 1-14. doi: 10.1007/s12152-011-9149-x

Demertzi, A., Schnakers, C., Ledoux, D., Chatelle, C., Bruno, M. A., Vanhaudenhuyse, A., . . . Laureys, S. (2009). Different beliefs about pain perception in the vegetative and minimally conscious states: a European survey of medical and paramedical professionals. *Prog Brain Res*, 177, 329-338. doi: 10.1016/S0079-6123(09)17722-1

Demertzi, A., Schnakers, C., Soddu, A., Bruno, M.-A., Gosseries, O., Vanhaudenhuyse, A., & Laureys, S. (2011). Neural plasticity lessons from disorders of consciousness. *Front Psychol*, 1, 1-7. doi: 10.3389/fpsyg.2010.00245

Ferrarelli, F., Massimini, M., Sarasso, S., Casali, A., Riedner, B. A., Angelini, G., . . . Pearce, R. A. (2010). Breakdown in cortical effective connectivity during midazolam-induced loss of consciousness. *Proceedings of the National Academy of Sciences USA*, *107*(6), 2681-2686. doi: 10.1073/pnas.0913008107

Fins, J. J. (2008). Neuroethics and neuroimaging: moving toward transparency. *The American journal of bioethics*: AJOB, 8(9), 46-52. doi: 10.1080/15265160802334490

Galanaud, D., Perlbarg, V., Gupta, R., Stevens, R. D., Sanchez, P., Tollard, E., . . . Puybasset, L. (2012). Assessment of white matter injury and outcome in severe

brain trauma: a prospective multicenter cohort. *Anesthesiology*, 117(6), 1300-1310. doi:10.1097/ALN.0b013e3182755558

Giacino, J. T., Ashwal, S., Childs, N., Cranford, R., Jennett, B., Katz, D. I., . . . Zasler, N. D. (2002). The minimally conscious state: definition and diagnostic criteria. *Neurology*, 58(3), 349-353.

Giacino, J. T., Kalmar, K., & Whyte, J. (2004). The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. *Arch Phys Med Rehabil*, 85(12), 2020-2029.

Gosseries, O., Bruno, M. A., Chatelle, C., Vanhaudenhuyse, A., Schnakers, C., Soddu, A., & Laureys, S. (2011). Disorders of consciousness: what's in a name? *NeuroRehabilitation*, 28(1), 3-14. doi: 10.3233/NRE-2011-0625

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proc Natl Acad Sci* U S A, 100(1), 253-258. doi: 10.1073/pnas.0135058100

Heine, L., Soddu, A., Gomez, F., Vanhaudenhuyse, A., Tshibanda, L., Thonnard, M., . . . Demertzi, A. (2012). Resting state networks and consciousness. Alterations of multiple resting state network connectivity in physiological, pharmacological and pathological consciousness states. *Frontiers in Psychology*, 3, 1-12. doi: 10.3389/ fpsyg.2012.00295

Jennett, B. (2005). Thirty years of the vegetative state: clinical, ethical and legal problems. *Progress in brain research*, 150, 537-543. doi: 10.1016/S0079-6123(05)50037-2

Jennett, B., & Plum, F. (1972). Persistent vegetative state after brain damage. A syndrome in search of a name. *Lancet*, 1(7753), 734-737.

Jox, R. J., Bernat, J. L., Laureys, S., & Racine, E. (2012a). Disorders of consciousness: responding to requests for novel diagnostic and therapeutic interventions. *Lancet Neurol*, 11(8), 732-738. doi: S1474-4422(12)70154-0

Kubler, A., & Kotchoubey, B. (2007). Brain-computer interfaces in the continuum of consciousness. *Curr Opin Neurol*, 20(6), 643-649. doi: 10.1097/WCO.0b013e3282f14782

Kuehlmeyer, K., Borasio, G. D., & Jox, R. J. (2012). How family caregivers' medical and moral assumptions influence decision making for patients in the vegetative state: a qualitative interview study. *J Med Ethics*. doi: medethics-2011-100373

Laureys, S. (2005). The neural correlate of (un)awareness: lessons from the vegetative state. *Trends Cogn Sci*, 9(12), 556-559. doi: 10.1016/j.tics.2005.10.010

Laureys, S. (2005b). Science and society: death, unconsciousness and the brain. *Nat Rev Neurosci*, 6(11), 899-909.

Laureys, S., Antoine, S., Boly, M., Elincx, S., Faymonville, M. E., Berre, J., . . . Maquet, P. (2002). Brain function in the vegetative state. *Acta Neurol Belg*, 102(4), 177-185.

Laureys, S., & Boly, M. (2008). The changing spectrum of coma. *Nat Clin Pract Neurol*, 4(10), 544-546.

Laureys, S., Celesia, G. G., Cohadon, F., Lavrijsen, J., Leon-Carrion, J., Sannita, W. G., . . . Dolce, G. (2010). Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. *BMC Med*, 8, 68. doi: 10.1186/1741-7015-8-68

Laureys, S., Faymonville, M. E., Degueldre, C., Fiore, G. D., Damas, P., Lambermont, B., . . . Maquet, P. (2000). Auditory processing in the vegetative state. *Brain*, 123(8), 1589-1601.

Laureys, S., Owen, A. M., & Schiff, N. D. (2004). Brain function in coma, vegetative state, and related disorders. *Lancet Neurol*, 3(9), 537-546.

Laureys, S., Pellas, F., Van Eeckhout, P., Ghorbel, S., Schnakers, C., Perrin, F., . . . Goldman, S. (2005). The locked-in syndrome : what is it like to be conscious but paralyzed and voiceless? *Prog Brain Res*, 150, 495-511. doi: 10.1016/S0079-6123(05)50034-7

Laureys, S., & Schiff, N. D. (2012). Coma and consciousness: paradigms (re)framed by neuroimaging. *NeuroImage*, 61(2), 478-491. doi: 10.1016/j. neuroimage.2011.12.041

Lulé, D., Noirhomme, Q., Kleih, S. C., Chatelle, C., Halder, S., Demertzi, A., . . . Laureys, S. (2012). Probing command following in patients with disorders of consciousness using a brain-computer interface. *Clin Neurophysiol*, in press.

Luyt, C. E., Galanaud, D., Perlbarg, V., Vanhaudenhuyse, A., Stevens, R. D., Gupta, R., . . . Puybasset, L. (2012). Diffusion tensor imaging to predict long-term outcome after cardiac arrest: a bicentric pilot study. *Anesthesiology*, 117(6), 1311-1321. doi:10.1097/ALN.0b013e318275148c

Majerus, S., Gill-Thwaites, H., Andrews, K., & Laureys, S. (2005). Behavioral evaluation of consciousness in severe brain damage. *Prog Brain Res*, 150, 397-413.

Massimini, M., Ferrarelli, F., Huber, R., Esser, S. K., Singh, H., & Tononi, G. (2005). Breakdown of cortical effective connectivity during sleep. *Science*, *309*(5744), 2228-2232. doi: 10.1126/science.1117256

Mevel, K., Grassiot, B., Chetelat, G., Defer, G., Desgranges, B., & Eustache, F. (2010). [The default mode network: cognitive role and pathological disturbances]. *Rev Neurol*, *166*(11), 859-872. doi: 10.1016/j.neurol.2010.01.008

Monti, M. M., Vanhaudenhuyse, A., Coleman, M. R., Boly, M., Pickard, J. D., Tshibanda, L., . . . Laureys, S. (2010). Willful modulation of brain activity in disorders of consciousness. *N Engl J Med*, 362(7), 579-589. doi: 10.1056/NEJMoa0905370

Monti, M. M., Vanhaudenhuyse, A., Coleman, M. R., Boly, M., Pickard, J. D., Tshibanda, L., . . . Laureys, S. (2010). Willful modulation of brain activity in disorders of consciousness. *N Engl J Med*, 362(7), 579-589. doi: 10.1056/NEJMoa0905370

Owen, A. M., Coleman, M. R., Boly, M., Davis, M. H., Laureys, S., & Pickard, J. D. (2006). Detecting awareness in the vegetative state. *Science*, 313(5792), 1402.

Racine, E., Amaram, R., Seidler, M., Karczewska, M., & Illes, J. (2008). Media coverage of the persistent vegetative state and end-of-life decision-making. *Neurology*, 71(13), 1027-1032. doi: 10.1212/01.wnl.0000320507.64683.ee

Rosanova, M., Gosseries, O., Casarotto, S., Boly, M., Casali, A. G., Bruno, M. A., . . . Massimini, M. (2012). Recovery of cortical effective connectivity and recovery of consciousness in vegetative patients. *Brain*, 135(Pt 4), 1308-1320. doi: 10.1093/*brain*/awr340

Sanders, R. D., Tononi, G., Laureys, S., & Sleigh, J. W. (2012). Unresponsiveness not equal unconsciousness. *Anesthesiology*, 116(4), 946-959. doi: 10.1097/ALN.0b013e318249d0a7

Schiff, N. D., Giacino, J. T., Kalmar, K., Victor, J. D., Baker, K., Gerber, M., . . . Rezai, A. R. (2007). Behavioural improvements with thalamic stimulation after severe traumatic brain injury. *Nature*, 448(7153), 600-603.

Schnakers, C., Chatelle, C., Vanhaudenhuyse, A., Majerus, S., Ledoux, D., Boly, M., . . . Laureys, S. (2010). The Nociception Coma Scale: a new tool to assess nociception in disorders of consciousness. *Pain*, 148(2), 215-219. doi: 10.1016/j. pain.2009.09.028

Schnakers, C., Faymonville, M. E., & Laureys, S. (2009). Ethical Implications: Pain, coma, and related disorders. In W. P. Banks (Ed.), Encyclopedia of consciousness (Vol. 1, pp. 243-250). Oxford: Elsevier.

Schnakers, C., Vanhaudenhuyse, A., Giacino, J., Ventura, M., Boly, M., Majerus, S., . . . Laureys, S. (2009). Diagnostic accuracy of the vegetative and minimally conscious state: clinical consensus versus standardized neurobehavioral assessment. *BMC Neurol*, 9, 35. doi: 10.1186/1471-2377-9-35

Schnakers, C., Vanhaudenhuyse, A., Giacino, J. T., Ventura, M., Boly, M., Majerus, S., . . . Laureys, S. (2009). Diagnostic accuracy of the vegetative and minimally conscious state: clinical consensus versus standardized neurobehavioral assessment. BMC *Neurol*, 9, 35.

Schnakers, C., & Zasler, N. D. (2007). Pain assessment and management in disorders of consciousness. *Curr Opin Neurol*, 20(6), 620-626. doi: 10.1097/ WCO.0b013e3282f169d9

Seel, R. T., Sherer, M., Whyte, J., Katz, D. I., Giacino, J. T., Rosenbaum, A. M., . . . Zasler, N. (2010). Assessment scales for disorders of consciousness: evidencebased recommendations for clinical practice and research. *Arch Phys Med Rehabil*, 91(12), 1795-1813. doi: 10.1016/j.apmr.2010.07.218

Sergent, C., & Dehaene, S. (2004). Is consciousness a gradual phenomenon? Evidence for an all-or-none bifurcation during the attentional blink. *Psychol Sci*, 15(11), 720-728. doi: PSCI748 [pii] 10.1111/j.0956-7976.2004.00748.x

Seth, A. K., Dienes, Z., Cleeremans, A., Overgaard, M., & Pessoa, L. (2008). Measuring consciousness: relating behavioural and neurophysiological approaches. *Trends Cogn Sci*, 12(8), 314-321. doi: S1364-6613(08)00151-4 Soddu, A., Vanhaudenhuyse, A., Demertzi, A., Bruno, M. A., Tshibanda, L., Di, H., . . . Noirhomme, Q. (2011). Resting state activity in patients with disorders of consciousness. *Funct Neurol*, 26(1), 37-43.

Soddu, A., Vanhaudenhuyse, A., Demertzi, A., Marie-Aurelie, B., Tshibanda, L., Di, H., . . . Noirhomme, Q. (2011). Resting state activity in patients with disorders of consciousness. *Funct Neurol*, 26(1), 37-43.

Stoll, J., Chatelle, C., Carter, O., Koch, C., Laureys, S., & Einhauser, W. (2013). Pupil responses allow communication in locked-in syndrome patients. *Curr Biol*, 23(15), R647-648. doi: 10.1016/j.cub.2013.06.011

Thibaut, A., Bruno, M. A., Chatelle, C., Gosseries, O., Vanhaudenhuyse, A., Demertzi, A., . . . Laureys, S. (2012). Metabolic activity in external and internal awareness networks in severely brain-damaged patients. *J Rehabil Med*, 44(5), 487-494. doi: 10.2340/16501977-0940

Tononi, G., & Koch, C. (2008). The neural correlates of consciousness: an update. *Ann N Y Acad Sci*, 1124, 239-261. doi: 10.1196/annals.1440.004

Vanhaudenhuyse, A., Demertzi, A., Schabus, M., Noirhomme, Q., Bredart, S., Boly, M., . . . Laureys, S. (2011). Two distinct neuronal networks mediate the awareness of environment and of self. *J Cogn Neurosci*, 23(3), 570-578. doi: 10.1162/jocn.2010.21488

Vanhaudenhuyse, A., Noirhomme, Q., Tshibanda, L. J., Bruno, M. A., Boveroux, P., Schnakers, C., . . . Boly, M. (2010). Default network connectivity reflects the level of consciousness in non-communicative brain-damaged patients. *Brain*, 133(Pt 1), 161-171. doi:10.1093/brain/awp313

Voss, H. U., Uluç, A. M., Dyke, J. P., Watts, R., Kobylarz, E. J., McCandliss, B. D., . . . Schiff, N. D. (2006). Possible axonal regrowth in late recovery from the minimally conscious state. *J Clin Invest*, *116*(7), 2005-2011.

RELIGIOUS AND ATHEISTIC MINDBRAINS

Adolf Tobeña *

Abstract

Recent hostilities between evolutionary biology and religious activism are used as an entrance into the neurobiology of religiosity, agnosticism and atheism. Frontiers of neuroanatomical and neurophysiological research are discussed selecting those findings which appear more promising to anchor the neural substrates of spirituality and transcendence traits as well as nonreligious postures within the workings of specific neural circuits and networks. This is a long-range endeavour which has only started a challenging itinerary though it may offer more substantial fruits than the perennial doctrinal clashes across the hiatus (negligible, in a lot of minds) between science and faith.

Keywords: Religiosity, Spirituality, Transcendence, Atheism, Brain, Neuroimage

Atheistic buses against religious memes

In 2006, Richard Dawkins¹ and Daniel Dennet² simultaneously began an antireligious campaign from the skeptical ranks of biology. With a highly combative style by Dawkins and a bit more detached by Dennet, the duet united forces together with outstanding activists of the secularism rooted in science³ to sever religious resurgence in the cultural panorama of our era. Besides books, essays, web discussions and tours of conferences on one side or the other of the Atlantic, they sponsored a variety of campaigns with nontrivial impact, although that which left a longer lasting trail was that of the "*atheist bus*" that circulated through some of the most important cities of the world. The harmony between these

^{*} Dept. Psychiatry and Forensic Medicine, School of Medicine, Universidad Autónoma de Barcelona, Spain.
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two leaders of antireligious thinking should not be surprising, because some years earlier Dennett⁴ had already put forth a thesis on the nature of the religion that gravitated on the notion of memetic transmission of Dawkins⁵.

In spite of his strict darwinian approach, Dawkins has always defended that in order to decipher the origins of religiousness, the flexible processes of cultural transmission (imitation and early instruction in children, and the training of habits, persuasion and seduction from adolescence to adulthood) are much more important than the chromosomal filters that pave the way to natural selection or to sexual selection. Thus, the proposal of infective "meme" (functional units of the cultural replication), to explain the dissemination of religious beliefs. God, the Gods, or any notion related with the sacred, constitute, according to this, ideation artifacts having great invasiveness with a specific function: to promote order and stability in the complex surroundings where the humans should resist and prosper. The essential scripts of all religion (the "nuclear memes," according to this hypothesis), contain a simplified but coherent description of the world that facilitates its understanding and meaning. They serve to erect *bastions of confidence* that have the guarantee of the supreme authority. The religious beliefs would be, consequently, cognitive spells at the service of the expectancy in a comforting regularity. From this derives their contribution to the thought tuning and fraternity between members of the devotional community. This *leverage of safety* is the essential attribute shared by all the sacred narratives, whether from the monotheistic or polytheistic religious traditions or, on the contrary, from "secular" assumptions (philosophical or scientific) on the ordered essence, although unreachable for human periscopes, of the universe and its phenomena². To brace the memetic conjecture of the genesis of the religions, Dennett departed from biological requirements for these ideational typologies⁶⁻⁹ although from a conventional approach⁴: religions are "social systems whose participants avow beliefs in a supernatural agent or agents to whom they owe obedience and respect."

The core of the definition therefore lies in the belief, in the conviction that there is a higher authority that actively regulates the future of existence. Religion is summarized in the belief, in the faith in omniscient agents or all-powerful forces. In turn, the sum of individuals with a shared belief shapes the devotional social system. By this dissection, Dennet avoids all need to cope with the experiential¹⁰ and temperamental¹¹ elements of religiousness (transcendence, spirituality, harmony, serenity, compassion, meekness, submission, credulity, empathic communion), in order to concentrate on the cognitive core of the subject. He needs to do it in this way to apply, without difficulties, the memetic conjecture: the notion of the cognitive, contagious and long-lasting device. However, with this, he rules out (or only touches upon the topic), neurobiological or genetic incursions that have already been made into the affective/emotional attributes of religiousness and their variability based on temperamental typologies^{12, 13}. The result of this elimination, which Dennet fully shares with Dawkins, is, in my view, disappointing. They use memetic vectors for cultural replication that besides being insufficient to substantiate the genesis of the religiousness, leave untouched the origins of the "atheist meme," the agnostic or the irreverent. Phenotypal varieties that also thrive, by the way, in the world (although much less). On the other hand, when they arrive to the sphere of the shared belief (the shelter of the social convention and uniting ideology), they liquidate the question promptly to go into the details of the representational stage (the belief in the belief in God), as a means of connection to explain the power of religious meme². The problem is that these eye-catching pirouettes continue to be useless as explanatory tools.

Canadian Carmelites, Tibetan monks and exceptional experiences

Neuroscientific incursions into the devoted person's brain and into that of the unbelievers are generating increasingly suggestive findings. One of the pioneer studies was conducted with the collaboration of 15 Carmelite nuns belonging to a Canadian community¹⁴ who were asked to try to reproduce the experience of an autobiographic episode of "union with God," while their brain was being scanned using a Functional Magnetic Resonance (fMRI). All of them had experienced mystic moments, throughout their lives, moments they described as the most intense and profound experience of their existence. They formed a group having variable age (between 23 and 64 years), with a time of dedication to the

Carmelite vocation ranging from 2 to 37 years. During the mystic remembrance session in the scanner the nuns went through different phases, including those of rest-habituation with their eyes closed, moments to remember harmonious episodes with a loved person and those of remembrance of the experience with the merger with God. They achieved a good recall of these experiences, up to the point of reliving sensations of timelessness and spatial disconnection together with incomparable fullness and pleasure which, in two cases, culminated with the "divine presence" during the scanning. The results obtained from comparing cerebral activations and deactivations regarding control conditions (rest and amicable empathy) denoted a "mystical" pattern that recruited several brain systems. Regions of the orbitofrontal cortex, caudate and upper and lower parietal areas, in both hemispheres, were preferentially activated. All this agrees with the complex experiences in which some peculiar corporeal and spatial perceptions are combined with pleasure and serene and intense well-being, in circumstances of disconnection regarding external stimuli and with little reflexive elaboration. The brain activation pattern, definitively, brings to mind those registered in women in love when they look at a photograph images of their loved one in the peak of infatuation¹⁵. It is not trivial that these results have appeared concordant, between the exceptional experience of the "divine union" and the much more worldly and frequent one, although not necessarily less powerful, of the "loving fusion." In addition to confirming old suspicions on the erotic component of the mystical exaltation, these data indicate that we are seeing phenomena comparable to other human experiential reactions that may be object of an empirical approach.

Using cerebral mapping methods by the registry of electroencephalographic (EEG) activity, the electrical changes that are self-induced in Buddhist monks with a dilated experience in the meditation techniques have been studied¹⁶. In a study conducted in Nepal by a North American team, that had the approval and counseling of the Dalai Lama, the monks that entered into deep meditation recreating a state of unconditional love/compassion for the creatures of this world enormously increased the EEG gamma frequencies (between 25-42Hz) of great amplitude, in comparison with university students with much more limited training in these meditation techniques. This spectacular increase of the EEG gamma frequency band (which in other experiments has been linked with highly focalized consciousness), occurred, above all, in lateral fronto-parietal regions, in both hemispheres, and tended to last beyond the meditative session up to the point of presenting differences at rest compared to the controls. Consequently, these are data that indicate that some procedures of modification of the states of consciousness associated to profound empathic experiences and "religious" rapport induce long-lasting changes in the electrical activity of the cerebral cortex. This type of work has had continuity and some studies suggest that the changes after prolonged training in meditative techniques may give rise to structural changes in particular brain regions^{17, 18}.

It remains to be seen if these findings will remain firm, although the exploratory breach is already open and it does not seem to be a bad beginning to detect phenomena related with abnormalities or singularities in the states of consciousness. It may be well to remember that in the principal monotheistic religions, the culminating moment of the revelation was produced under peculiar consciousness circumstances. Specifically, in all of them, there was the phenomenon of the "mountainous" revelation. This agrees with many cases of walking travelers who have experienced singular experiences within condition of altitude, hypoxia and exaggeration of the visual perspective, there being clinical repercussions in many cases¹⁹.

All of this can be connected with classical neurological observations, based on sporadic though well-studied clinical cases, which had linked focal epilepsies of the temporal lobe with an accentuated tendency to religiousness together with other temperamental peculiarities as hyper-graphy or preference for gallant and asexual modalities of love²⁰. There are studies^{21,22} of clinical case series that confirm this relation together with the proclivity to experience mystic experiences: episodes of very singular self-consciousness whose contents are, frequently, universal love-compassion or perceptions of fusion with the "final essence of the cosmos". The intimate peace, serenity and pleasant sense of fullness are usual tonalities of mood states during these episodes.

Such "journeys" towards borders of dilution/expansion of the ordinary consciousness is that which has been searched for by those hungry for exceptional experiences who, at different times, have dared to take highly active psychedelic substances to alter their perceptions and thou-

ght flow. A good part of these potions so venerated by archaic shamans and by their contemporary emulators, alter the serotonergic functionality in the brain while inducing abnormalities in other subtle gears of the chemical neuroregulation. In this sense, the finding¹² of a team from the Institute Karolinska, in Stockholm, was seminal: when they studied several cerebral targets using molecular markings with positron emission tomography, they found that the availability of the 5-HT1A serotonin receptors presented consistent relationships with standardized religiousness scales in males. That is, in ordinary young Swedish the greater their tendency to spirituality and transcendence, the lower was the availability of these receptors in the frontal cortex, hippocampus and raphe nuclei, which generally results in greater serotonergic function. Spirituality and self-transcendence (when we perceive that we are something more than the surroundings of our physical being or that we can separate ourselves from it), can be experienced both by believers and non-believers: one can feel anointed to God or to all nature and feel that one's body is fused with the universe as a whole.

The laboratory studies of mystical peaks triggered by psychodelic agents declined after some pioneering attempts at the sixties of the last century. Such approach has been revived lately by Roland Griffiths, at the John Hopkins University, Baltimore, administering psylocibin to volunteers in a well-controlled series of experiments²³. The findings are stunning: single doses of this potent pro-serotonergic agent provoked deep physiological, affective and consciousness changes that left traces which can be measured more than one year after the session. The subjects described the episode as the most intense and meaningful experience in their lives. Applying similar procedures a British team has found ²⁴, from fMRI scans obtained during the psylocibin peak induction, that these profound effects correlate with strong de-activations and disconnections of brain areas and networks that sustain the continuity and coherence of consciousness, at rest.

"Religious-spiritual" variations and neural anomalies

Italian investigators from the University of Udine linked a specific zone of the parietal cortex of the brain to the grade of religiousness and the experience of transcendence. They studied changes of self-transcendence and spirituality feelings in patients with brain tumors²⁵. The work was conducted with a large sample of encephalic tumors (neural or meningeal cancers) in patients who were classified by the type and location of the brain tumors: patients with tumors in the anterior zone of the brain (frontal and temporal cortexes), or the posterior one (occipital and parietal cortexes). The results were distinctive: patients with parietal cortex tumors presented superior religiousness to the others. That is, a greater proportion of these patients considered themselves to be deeply spiritual. This effect was accentuated after the removal of the tumor, suggesting that a decrease in the neural volume and work in this brain area causes an increase in religiousness. It must be stressed that religiousness indexes did not depend on age, education, gender and cognitive or emotional capacities. The increase in religiousness was related with the malignancy of the tumor and its growth rhythm within the posterior parietal cortex.

The fact that the posterior parietal cortex is responsible for representing the different parts of the body to be able to perceive our body as a whole, in relation to the contextual environment, is well known. For example, patients with lesions in this zone (due to the presence of tumors or trauma, vascular accidents or other reasons) have problems to coordinate parts of their body in space, or feel that some parts of their body do not belong to them. These findings suggest that this brain area has additional functions. The authors propose that the reduction of the parietal cortex activity may be related to the experiences of dilution of corporal limits during self-awareness perception that some persons go through in the climax of the spiritual experiences.

In a subsequent study ²⁶ with 24 normal catholics the same group tried to show if a transient inactivation of these brain areas induced similar augmentations in religiousness-spirituality measures. They applied pulses of Transcranial Magnetic Stimulation to restricted zones of inferior parietal lobe, dorsolateral prefrontal cortex and the brain vertex, as a control site, to investigate whether implicit religious-spiritual representations measured through an Implicit Association Test, can be modified by a "virtual lesion". They detected a specific increase of religiousness-spirituality after the inhibition of inferior parietal cortex thus suggesting a causative role in inducing such changes. In contrast, inhibition of dor-

sal prefrontal cortex led to widespread effects encompassing variations in other self-concepts which were used as comparisons. This represents an elegant confirmation, in a small sample of individuals from one religious tradition, of the role that a particular zone of the inferior parietal lobe may play in religiousness-spirituality. There are, moreover, concordant neuroimaging findings that are not based on variations resulting from gross alterations of the brain tissue or its ordinary functionality.

From neuroimaging studies to the genetics of religiousness

The first normative study on the anatomical variability of defining regions of the brain cortex and its links with religiousness scores was conducted in 40 healthy adult North Americans (20 from each gender) by structural magnetic resonance scans¹³. The measurements of religiousness made it possible to obtain large vectors that had covariations with zonal volumes from the brain cortex: thus, the "experience of a close relation with God," covariated positively with volumes of the anterior and middle zones of the temporal lobes; the "fear of divine rage" covariated negatively with the orbitofrontal and parietal region volume; and the "pragmatism and religious skepticism" with parietal regions (the right precuneus especially). On the other hand, "religious education during childhood" did not show any relation with cortical volume, which makes it possible to rule out that those links could be due to differences in the religious training and practice received (the possible incidence of factors such as age, educational or economic level and intake of toxic agents that could affect brain volume was discarded). This morphological study has been accompanied by many functional fMRI studies that measure the changes of regional activity or connectivity between cerebral cortex areas and other brain sites to statements with religious or irreligious content and also distinguishing between believers and non-believers^{27, 28, 29}.

As a whole, the results have tended to indicate that there are regions and networks involved in the processing of religious-type beliefs and experiences and that they can be assigned to the mentalization circuits of the "social brain": that is, the systems in charge of putting one's ideation processes and those of others in tune (or out of tune). A direct deduction follows: mentalizing deficits should undermine such cognitive intuitions and lead to less belief in religious ideas. Ara Norenzayan team has found precisely that in autistic adolescents and by measuring mentalizing skills in large samples of Canadians and American adolescents they showed that their differences in religiosity were mediated by basic mentalizing abbilities³⁰. Furthermore, the fact that the parietal regions of the precuneus have been demonstrated to be crucial in the most genuine and personal prayer³¹ confers them an additional value as crossroad to differentiate between the tendencies to accentuate spirituality or to irreligious pragmatism/empiricism. In another order of things, the findings that have found atrophic changes in the hippocampus, in advanced ages, in individuals who have suffered sudden spiritual reconversions or in the non--believers, manifest that the known antistress action of religion coverage can be followed by brain scans³¹.

We should therefore conclude that there is more than enough data to link religious proclivity with singularities of the ordinary and extraordinary brain functioning. Consequently it could be expected that findings in regards to the genetic marking of religiosity will not be long in coming. Studies with well-controlled samples of twins have well established that the religious propensity, in its temperamental components, carry a modest, although not trivial, genetic weight³²⁻³⁵ this being an influence manifested in estimations of hereditability of about 40%. The first genes that have been related with this temperamental proclivity (and therefore, with a neural organization favoring the states of consciousness illustrated above) have not offered sufficiently firm replications³⁶. However, there are other highly promising ones that are related with some of the previously mentioned links of neurochemical regulation³⁷. Nonetheless, it must be acknowledged that the subject is complex and that it is not at all urgent. There are many other targets that merit an indisputable priority in biomedical research. Therefore, it seems sensible to adopt a waiting attitude for confirmatory results that may take time to arrive, although surprises that have occurred in other fields during undirected incursions (genetics of human linguistic skills, for example) should not be ruled out.

God in the hands of biology?

Advances in brain imaging techniques have favored the resurgence of enquiries to study how the brain processes spirituality-religiousness. In fact, a campaign of empirical investigations dedicated to the "neuroscience of religiosity" is fully ongoing. It aims to elucidate the mechanisms of spirituality, transcendence and mystical tendencies from a neurobiological point of view. It is assumed that this type of experience is mediated by the brain, without aiming to discredit the value of the religious beliefs for the devout. Many of the investigators who work in this area do not consider that revealing the neural substrate of spirituality involves undermining the relevance of the notion of God or other sacred concepts or icons. It would be naive to do it when it has even been possible to demonstrate that intense religious beliefs may involve advantages in the focused attentional processing and the automatic erasing of errors by the brain^{38, 39}.

Therefore, it seems that the ambitious campaigns of Dawkins¹, Dennet² and their allies are also not headed on the way to harvesting greater successes. I stated at the start that this duet began daring initiatives to tackle the greening of theistic proselytism in some educational settings in the USA particularly. Many other activists³ joined this because it is in this area nowadays where the strongest apprehensions crackle in the face of the progression of the corrosive machinery of biology. It is here, precisely where the alarms go off and arouse the most fierce antiscientific resistances. The slogan to open hostilities and unite activists is simple and effective: give to biology that which is incumbent to it and reserve to God that which is of God. Or, this is, do not let biology penetrate into the folds of the spirit.

In the European world, there is, however, no hurry to enter into these fights insofar as the debates on the question of divine intervention in the future of the cosmos and in the diversification of the forms of nature, including the human mind and their beliefs, are rare. Apparently, in our cultural panorama, there are no creationists or combative theists, who aim to derogate the teachings of biology in secondary education or in the University. According to authorized voices, our societies are a model of accommodation to the tendencies of progress in all settings, from transgressor social changes to the absorption of scientific knowledge and therefore it is not necessary to debate that. Among us, prac-

tically everyone affirms a strong evolutionist position. At the same time and in similar percentages (everybody more or less illustrated) proclaims strong "antibiologist" or "antireductionist" convictions. That is, Darwin is accepted, but not the derivations of his ideas⁴⁰⁻⁴¹. However, I fear that these postures reflect the usual desert now disguised with the appearance of pseudo-cosmopolitism of societies that were suddenly enriched, thus allowing them the possibility of traveling (in low cost airlines) throughout the world. There are many signs of it. I even dare to postulate that the categorical contradiction is not such: in our places, almost everyone continues to be stonily theist (with many and renovated invocations, that is) and they find no problem in placing the tag of divine ahead of the evolutive processes. In other words, biology, as everything in this valley of tears, continues in the hands of God and should thus continue for the solace of old and new inquisitors. Thus, we are where we used to be in spite of the incessant progress in the discerning of the neural devices of religiosity and the unbelieving skepticisms^{8, 11, 30, 42, 43}.

References

1. Dawkins R. The god delusion. London: Bantam Books, 2006.

2. Dennet DC. Breaking the spell: religion as a natural phenomenon.New York: Viking, 2006.

3. Harris S. The end of faith: religion, terror and the future of reason. New York: WW Norton and Co, 2004.

4. Dennet DC. Appraising grace: what evolutionary good is God? The Sciences. 1997 Jan-Feb; 39-44.

5. Dawkins R. The selfish gene. New York: Oxford University Press, 1997.

6. Atran S. In God we trust: the evolutionary landscape of religion. New York: Oxford University Press, 2002.

7. Boyer P. Religion explained: the evolutionary origins of religious thought. New York: Basic Books, 2002.

8. Boyer P. Religious thought and behaviour as by-products of brain function. Trends in Cognitive Sciences. 2003, 7,3, 120-124.

9. Burkert W. Creations of the sacred: tracks of biology in early religions. Cambridge (Mass.): Harvard University Press, 1996.

10. James W. The varieties of religious experience: a study on human nature. NY: Simon and Shuster, 1902.

11. Tobena A. Devots i descreguts: biologia de la religiositat. Valencia: UV, 2013.

12. Borg J, Andre B, Soderstrom H, Farde L. The serotonin system and spiritual experiences. The American Journal of Psychiatry, 2003,160, 1965-1969.

13. Kapogianis D, Barbey ASM, Krueger F, Grafman J. Neuroanatomical variability of religiosity. PloSOne. 2009, 4, 9, e7180.

14. Beauregard M, Paquette V. Neural correlates of a mystical experience. Neuroscience Letters. 2006, 405,186-190.

15. Tobena A. El cerebro erotico: rutas neurales de amor y sexo. Barcelona: La Esfera de los Libros, 2006.

16. Lutz A, Greichar LL, Rawlings NB, Ricard M, Davidson RJ. Long.term meditators self-induce high amplitude gamma synchrony during mental practice, PNAS. 2004 101, 46, 16369-16373.

17. Holzel BK, Carmody J, Vangel M, Congleton CH, Yerramsetti SM, Gard T, et al. Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Research: Neuroimaging. 2011,19,1, 36-43.

18. Lazar SW, Kerr CC, Waserman RH, Gray JR, Greve DN, Treadway MT, et al. Meditation experience is associated with increased cortical thickness. Neuroreport. 2005, 16, 17, 1893-1897.

19. Arzy S, Idel M, Landis T and Blanke O. Why revelations have occurred on mountains?: linking mystical experiences and cognitive neuroscience. Medical Hypothesis. 2005, 65, 841-845.

20. Ramachandran VS, Hirstein W, Armel KC, Tecoma E, Iragui V. Theneural basis of religious experience. Society of Neuroscience Abstracts. 1998, 23, 519-521.

21. Hansen BA, Brodtkorb E. Partial epilepsy with "ecstatic seizures". Epilepsy and Behavior. 2003, 4, 667-673.

22. Wuerfel J, Krishnamoorthy ES, Lemiuex L, Koepp M, Tebarz von Elst L, Trimble MR. Religiosity is associated with hippocampal but not amygdala volumes in patients with refractory epilepsy. Journal of Neurology, Neurosurgery and Psychiatry, 2004, 75, 640-642.

23. Griffiths RR, Johnson MW, Richards WA, Richards BD, McCann U, Jesse R Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects, Psychopharmacology, 2011, 218, 649-665.

24. Carhart-Harris RL, Erritzoe D, Williams T, Stone JM, Reed LJ, Colasanti A, Tyacke RJ, Leech R, Malizia AL, Murphy K, Hobden P, Evans J, Feilding A, Wise RG, Nutt DJ Neural correlates of the psychedelic state as determide by fMRI studies with psylocibin, PNAS, 2012, 109, 6, 2138-2143.

25. Urgesi C, Agliotti SM, Skrap M, Fabro F. The spiritual brain: selective cortical lesions modulate human self-trascendence. Neuron. 2010, 65, 309-319.

26. Crescentini C, Agliotti SM, Fabbro F,Urgesi C Virtual lesions of the inferior parietal cortex induce fast changes of implicit religiousness/spirituality, Cortex, 2014, 54, 1-15

27. Harris S, Kaplan JT, Curiel A, Boookheimer SY, Iacoboni M, Cohen MS. The

neural correlates of religious and non-religious belief. PloSOne. 2009,4,10, e0007272.

28. Kapogianis D, Barbey AK, Su M, Zamboni G, Krueger F, Grafman J. Cognitive and neural foundations of religious belief. PNAS. 2009, 106, 12, 4876-4881.

29. Kapogiannis D,Deshpande G, Krueger F,Thornburg MP, Grafman JH. Brain Networks Shaping Religious Belief. Brain Connectivity, 2014, 4, 1, 70-78.

30. Norenzayan A, Gervais WM, Trzesniewski KH, Mentalizing deficits constrain beliefs in a personal God. PLoSOne. 2012; 7, 5, e36880.

30. Schjoedt U, Stodkilde Jorgensen H, Geertz AW, Roepstorff A. High religious participants recruit areas of social cognition in personal prayer. Scan. 2009; 4, 199-207.

31. Owen AD, Hayward RD, Koenig HJ, Steffens DC, Payne ME. Religious factors and hippocampal atrophy in late life. PloSOne. 2011; 6, 3, e17006.

32. Kendler KS, Liu X, Gardner ChD, McCullough ME, Larson D, Prescott CA. Dimensions of religiosity and their relationship to lifetime psychiatric and substance use disorders. American Journal of Psychiatry. 2003; 160, 496-503.

33. Kirk KM, Eaves LJ, Martin N. Self-trascendence as a measure of spirituality in a sample of older Australian twins. Twin Research. 1999; 2, 81-87.

34. Koenig L, McGue M, Krueger RF, Bouchard TH. Religiousness, antisocial behavior and altruism: genetic and environmental mediation. Journal of Personality. 2008; 75, 2, 265-290.

35. Bradshaw M, Ellison CHG. Do genetic factors influence religious life?: findings from a behavior genetic analysis of twin siblings, Journal of Scientific Studies of Religion. 2008, 47, 4, 529-544.

36. Hamer D. The God gene: how faith is hardwired in our genes. New York: Doubleday, 2004.

37. Bachner-Melman R, Dina CH, Zohar AH, Constantini N, Larer E, Hoch S, Sella S, Nemanov L, Grishenko I, Lichtenberg P, Granot R, Epstein RP, AVPR1a and SLC6A4 gene polymorphisms are associated with creative dance performance. PloSGenetics. 2007; 1, 3, e42:0394-0403.

38. Inzlicht M, McGregor M, Hirsh JB, Nash K. Neural markers of religious conviction. Psychological Science. 2009; 20-3:385-92.

39. Inzlicht M, Tullet AM. Reflecting on God: religious primes can reduce neurophysiological response to errors. Psychological Science. 2010; 2, 8, 1184-1190.

40. Darwin Ch. The descent of man and selection in relation to sex. Princeton: Princeton University Press-Edition, 1871.

41. Darwin Ch. The expression of emotion in man and animals. New York: Appleton and Co.Edition, 1872.

42. Wilson DS. Darwin's cathedral: evolution, religion and the nature of society. Chicago: Chicago University Press, 2002.

43. Thagard P. The brain and the meaning of life. Princeton (New Jersey): Princeton University Press, 2010.

THE SENSE OF AGENCY AND ITS PLACE IN HUMAN EXISTENCE

Patrick Haggard *

Introduction

When you look around you, much of what you see is probably manmade. You are probably in a building, you are probably wearing clothes, you are reading on a computer or in a book. These facts all attest to a human ability to change the environment, to make things, to produce events and objects. We use the term 'agency' to refer to this ability. Agency can be accidental. For example, I can knock over your glass and spill your drink by an over-expansive gesture. But, in general, it is impossible to discuss agency without a concept of goal or purpose, or outcome. That is, we perform actions on the environment because of some reason, and to achieve some purpose. In psychology, the concept of purpose is often related to the concept of 'reward', but neo-Darwinian theories view all rewards and purposes as ultimately secondary to biological survival.

Animals change the world, as do humans. In a typical operant conditioning scenario, a rat or other animal will regularly learn to press a lever to get food. However, human agency appears almost unlimited relative to that of other species. The main reasons for this appear to be cognitive. First, the human brain can associate an action with an outcome that is highly remote in space and time. Second, the human brain can readily perform one action in order to facilitate another (for example, making a spade to facilitate cultivating a garden). Third, human agency can be remarkably distributed across agents, through mutual social exchange. For example, I can achieve my goal of getting to theatre by walking there, or I can ask you to drive me in your car. These flexibilities and extensions of agency seem central to key steps in human civilisation. For example, agriculture, technology and civic society can all be seen as products of agency.

^{*} Institute of Cognitive Neuroscience & Dept. Psychology, University College London, UK.

These facts of agency can perhaps explain why the recent evolutionary change in the human brain has lead to such striking biological success. The human brain has been able to change the world, within limits, to suit its purposes. However, such broad biological or anthropological statements belie what occurs at the moment of a single human instrumental action. A specific psychological experience of acting to produce a desired outcome seems essential to agency. For example, in one of the buildings I visit, I can press a button on a machine, and receive a cup of coffee. I know this relation from experience, and I re-experience it each time I get a coffee. In fact, without a specific experience of agency, it is hard to see how I would learn the functions of the machine, and how I would learn to keep going back to it, whenever I want a coffee. The same connection between experience and learning occurs in other instances of agency. It is hard to see why our first agricultural ancestors would continually plant seeds unless they had learned through experience that the act of planting would be associated with a later food reward.

In these examples, three distinct facts seem to be harmoniously aligned:

- 1. There is a causal relation between the organism's actions and some external event. This may be called the physical fact of agency.
- 2. The agent knows that this relation exists. This may be called the epistemic capacity for agency. It is a capacity, because this knowledge can be stored, and can be latent. An agent may know that they could cause a particular event, even if they are not currently doing so, and perhaps never will do so.
- 3. The agent experiences that they cause the external event. This may be called the psychological fact of agency.

Here we focus on the psychological fact. We use the term 'sense of agency' to describe the experience to which it refers. The importance of sense of agency in all human goal-directed action cannot be underestimated. Yet, because it is a ubiquitous feature of healthy adult human life, it can be hard to isolate and define. Psychiatric disorders provide a striking illustration of the importance of sense of agency in human existence. Most psychiatric disorders involve an abnormality in the sense of agency. The severely depressed abulic and apathetic patient shows a marked lack of sense of agency, leading to a severe reduction in energy and activity. What is the point of doing anything, if one's actions never have any effect, or never have any positive effect? Schizophrenic patients with positive symptoms also show a disorganised sense of agency. They often experience that they do not cause their own actions (passivity, delusion of control). In other circumstances, they overestimate their own agency (Blakemore, Wolpert, & Frith, 2000), for example believing that their thoughts can influence external events.

Explicit judgements of agency

There is widespread agreement on the causes of sense of agency. To experience a sense of agency, an agent must make an intentional action. The intention of the action is to produce that specific external event. For this reason, the phrase goal-directed action is also used. The agent must then register that the external goal event has occurred, and they must link its occurrence to the physical fact of their action. These processes of action, perception, and association support an experience of "I did that". Locke, for example, considered actions (he gives the example of murder in Ch XXIII, article 10) to be 'mixed modes', compounding the simple ideas of an action cause, and a subsequent effect (Locke, 1689). This associationist idea has received recent flesh in computational models of motor control. Originally developed as an engineering approach to computing neural motor commands, these models have recently offered an explicit causal account of the experience of agency. Briefly, intentional motor commands are used by an internal model within the brain to predict the likely consequences of action. If sensory information about a current external event matches this prediction, then there is an experience of agency. In essence, such 'comparator' models generate an experience of "I did that" by checking whether "that" is what should happen given a model of the consequences of "I did" (Synofzik, Vosgerau, & Newen, 2008).

In contrast, there is little consensus regarding the *consequences* of agency. Perhaps trivially, recognising oneself as the author of action is a consequence of the fact of agency. Explicit agency judgements of this kind are rare in everyday life, but have proved productive in laboratory studies. Interestingly, the scientific literature on explicit judgements of agency is strongly linked to self-recognition and self-awareness. One classic

paradigm involves the participant making an action, and viewing, with or without some spatiotemporal transformation, the consequences of the action. For example, Daprati and colleague (Daprati et al., 1997) asked participants to make a hand gesture, and judge whether a gesture that they simultaneously saw on a visual display did or did not correspond to the one they were making (the visual display might also show the movement of a confederate making similar actions in an adjacent room). The visual feedback thus corresponds to the "that" of "I did that". These studies have produced several interesting results. First, people routinely overestimate their own agency, regularly attributing to themselves movements that are not their own. Second, spatial transformations have rather little effect on judgements of agency (Fourneret & Jeannerod, 1998), while temporal delays between action and feedback lead to a strong reduction (Farrer et al., 2003). Third, disorganised and excessive acceptance of agency is commonly found in psychiatric disorders, and in particular in psychosis (Franck et al., 2001).

Indeed, one might define agency as "self-induced causation". These observations confirm a strong link between agency and normal selfawareness. In fact, such experiments are interestingly close to the classic rouge test (Gallup, 1970) that is used as an objective marker of selfawareness in animals. A visual marker (e.g., rouge lipstick) is placed on the skin of an animal who can view themselves in a mirror. If the animal reaches to the location of the rouge on their body, for example in an effort to remove it, this is taken as evidence that the animal realises that they see themselves in the mirror. Traditionally, this mirror self-recognition has been considered a test of 'body ownership': does the animal realise that the rouge is on its own body, and that it views its own body in the mirror. However, mirror self-recognition could also be a product of agency. For example, if the rouge is perceptually salient, it could trigger a reaching movement to explore it. This reaching movement might even be directed into the mirror, rather than at the corresponding body part. Once the animal views the visual consequences of its own movement, however, it has the essential association of "I did that". That is, there is knowledge of self-generated movement, and a visual experience of a corresponding event in the world (visual feedback of the movement of the arm). Even if the animal never reaches towards their own body and the rouge, they

might still recognise that their own actions lead to the pattern of visual feedback they observe. Associative agency could be sufficient for self-recognition, even without the strong link between the self and the visual body that the rouge test posits.

Implicit measures of sense of agency

How does being an agent with respect to an event alters one's experience of that event? This question has been investigated using implicit measures, such as time perception. The interval between an operant action and its subsequent outcome is perceived as being significantly shorter than the interval between a control event and the same outcome. That is, voluntary actions and their effects show a perceptual attraction across time, much as the associationist philosopher Hume might have predicted (Hume, 1760). In the 'intentional binding' paradigm, participants watch a rotating clock hand, and indicate the position on the clock at which they make a self-paced voluntary action such as a keypress. In separate blocks, they indicate the moment when they hear an auditory tone. In other blocks, these two events are linked through an operant action: participants decide for themselves when to make the keypress, and pressing the key causes the tone to occur 250 ms later. Participants again judge either the action, or the tone, in separate blocks.

The robust finding from such experiments is that the perceived time of action shifts towards the subsequent tone in operant blocks, relative to baseline blocks. In addition, the perceived time of the tone shifts earlier in time in operant blocks, towards the action that caused it, relative to baseline blocks. Thus, while the interval between action and tone is not measured directly, participants appear to perceive it as compressed, as if linking action and tone across time. Crucially, this binding is specific to intentional actions, since it is not found for involuntary or passive movements (Haggard, Clark, & Kalogeras, 2002; Kühn, Brass, & Haggard, 2013) or for two external events unrelated to intentional action (Cravo, Claessens, & Baldo, 2009; Haggard, Aschersleben, & Gehrke, 2002).



Figure 1. The intentional binding effect. Upper row: participants make a voluntary action, which is followed 250 ms later by an auditory tone. Middle row: The perceived time of a voluntary action that causes a tone is shifted towards the time of the tone, in comparison to measures taken during a baseline block where actions are not followed by tones. The perceived time of a tone is shifted back in time towards the action that caused it, relative to a baseline block where tones occur without any action. Lower row: these binding effects are reversed when voluntary movements are replaced by involuntary twitches caused by transcranial magnetic stimulation, and compared to their respective baselines.

Intentional binding therefore offers a potentially useful proxy measure of sense of agency. Importantly, it does not require a narrative of agency, or any explicit judgment of agency. Therefore, the general tendency to overestimate one's own agency (Daprati et al., 1997), particularly for positive outcomes (Bandura, 1982) may have minimal effects on intentional binding. The process of binding itself appears to happen well below the level of conscious awareness. For example, Walsh and Haggard (2013) used a 150 ms action-tone interval, which unexpectedly lengthened or shortened after a number of trials. For the first few trials at a novel interval, participants' judgements of when the tone occurred did not reflect the actual time of its occurrence, but the time it would have been predicted to occur based on previous experience. Importantly, explicit judgements of agency obtained in parallel did not show any change. This result carries the important implication that the experience of agency must be learned in each new situation, and then continuously updated. Moreover, we are not necessarily conscious of this continual ongoing calibration of the experience of our own interaction with the world.

The neural basis of the sense of agency has been investigated in several studies. Studies of explicit judgement have not found any neural correlate of the sense of agency, but have repeatedly found that the angular gyrus of the parietal cortex is activated when participants feel they are not the agent over an external event (Chambon, Wenke, Fleming, Prinz, & Haggard, 2013; Farrer et al., 2003). Studies of implicit agency have suggested a frontal involvement. For example, perceptual compression of the interval between action and outcome was associated with activation of the medial frontal lobe (Kühn et al., 2013). Temporary disruption of the pre-Supplementary Motor Area in the medial frontal lobe produced a reduction in intentional binding (Moore, Ruge, Wenke, Rothwell, & Haggard, 2010). Moreover, a group of neurological patients with corticobasal degeneration showed a strong correlation between reduction in action binding towards a subsequent tone, and grey matter density in the pre-Supplementary Motor Area (Wolpe et al., 2013). It remains unclear whether intentional binding also involves a parietal component.

Agency and motivation

Human actions aim at goals, often biologically reasonable goals such as food, reproduction, security. Locke refers the 'uneasiness' that always begins a stirring of the will. In contrast, most studies of sense of agency have considered the direct sensorimotor experience of controlling either one's own actions, or some arbitrary outcome of one's own action, such as the auditory tone in intentional binding paradigms. Therefore, surprisingly little is known about the relation between agency and motivational factors such as outcome valence, and reward. Several results suggest a mental construction, or rather reconstruction, of one's own actions which is fundamentally evaluative. Two examples will suffice. First, the general tendency to overestimate one's own agency is further amplified when outcomes are positive. People are ready to accept credit for positive outcomes, while denying agency for negative outcomes, in LECTURES

a form of self-serving bias (Takahata et al., 2012). In addition, where the facts of agency are clear, people may reconstruct the valence of the outcome of an action, to avoid the unpleasant cognitive dissonance that comes from generating a bad outcome(Festinger, 1957). That is, the sense of agency appears to enhance self-efficacy.

We have recently investigated how the sense of agency varies with the affective value of action outcomes. Participants caused an emotionally positive (i.e., achievement, amusement), emotionally negative (i.e., fear, disgust) or neutral sounds by making a simple keypress at a time of their own choosing. The intentional binding between keypress and sound was measured. Intentional binding was strongest for positive sounds, intermediate for neutral sounds, and weakest for negative sounds. Thus, not only do people readily attribute more positive outcomes to themselves, they also generate the primary experience of a closer association with a positive outcome, compared to a negative outcome (Yoshie & Haggard, 2013).



Figure 2. The binding between a voluntary action and its outcome depends on the affective valence of the outcome.

Finally, agency is itself motivating. Watching a young infant playing with a rattle, or a kitten with a ball of wool, suggests a fascinating and motivating experience is underway. However, establishing this point scientifically is not trivial. Eitam and colleagues (2013) recently showed that participants systematically prefer actions that produce outcome feedback, even when this feedback is irrelevant and uninformative for task performance. One interpretation may be that the experience of generating the feedback itself has motivational value.

Agency and learning/Agency and culture

Our own experience tells us that the sense of agency is largely acquired, rather than innate. Many people can remember first learning to ride a bicycle, for example. We suggest there are two levels of agency learning. First, individuals acquire a sense of agency over their own body and over external events as part of their motor development. A young baby's first interactions with the world appear relatively purposeless: it must discover that grasping an object and banging it against a surface makes a noise, and may also bring the reward of adult attention. Second, agency learning also has a cultural dimension. In his famous article of 1934 Marcel Mauss (Mauss, 1936) opined "J'appelle technique un acte traditionnel efficace". Mauss noted the important cultural transmission of particular forms of action, to achieve a desired goal. For example, particular dance forms are taught and learned, and have socio-anthropological significance in appeasing the gods etc. Thus, the capacity to change the world through instrumental action is not simply something that the individual discovers haphazardly for themselves, but is also culturally transmitted. Skills, trades and practices provide important examples. The motor action takes place to achieve particular goals within the social context of the world: "Acte technique, acte physique, acte magico-religieux sont confondus pour l'agent" (Mauss, 1936). By combining the capacity for instrumental action with the capacity to transfer to others the means to perform those actions, human societies achieve a remarkable ability to coordinate effort on a shared goal. It is this ability that has allowed us to construct our world to a much greater extent than any other animal.

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References

Bandura, A. (1982). Self-efficacy mechanism in human agency. *American Psychologist*, 37(2), 122–147. doi:10.1037/0003-066X.37.2.122

Blakemore, S. J., Wolpert, D., & Frith, C. (2000). Why can't you tickle yourself? *Neuroreport*, 11(11), R11–16.

Chambon, V., Wenke, D., Fleming, S. M., Prinz, W., & Haggard, P. (2013). An online neural substrate for sense of agency. *Cerebral Cortex (New York, N.Y.: 1991), 23*(5), 1031–1037. doi:10.1093/cercor/bhs059

Cravo, A. M., Claessens, P. M. E., & Baldo, M. V. C. (2009). Voluntary action and causality in temporal binding. *Experimental Brain Research*, 199(1), 95–99. doi:10.1007/s00221-009-1969-0

Daprati, E., Franck, N., Georgieff, N., Proust, J., Pacherie, E., Dalery, J., & Jeannerod, M. (1997). Looking for the agent: an investigation into consciousness of action and self-consciousness in schizophrenic patients. *Cognition*, 65(1), 71–86. doi:10.1016/S0010-0277(97)00039-5

Eitam, B., Kennedy, P. M., & Tory Higgins, E. (2013). Motivation from control. *Experimental Brain Research*, 229(3), 475–484. doi:10.1007/s00221-012-3370-7

Farrer, C., Franck, N., Georgieff, N., Frith, C. D., Decety, J., & Jeannerod, M. (2003). Modulating the experience of agency: a positron emission tomography study. *NeuroImage*, 18(2), 324–333.

Festinger, L. (1957). A theory of cognitive dissonance. Evanston, Ill.: Row, Peterson.

Fourneret, P., & Jeannerod, M. (1998). Limited conscious monitoring of motor performance in normal subjects. *Neuropsychologia*, 36(11), 1133–1140.

Franck, N., Farrer, C., Georgieff, N., Marie-Cardine, M., Daléry, J., d' Amato, T., & Jeannerod, M. (2001). Defective recognition of one's own actions in patients with schizophrenia. *The American Journal of Psychiatry*, 158(3), 454–459.

Gallup, G. G. (1970). Chimpanzees: Self-Recognition. *Science*, 167(3914), 86–87. doi:10.1126/science.167.3914.86

Haggard, P; Aschersleben, G; Gehrke, J; Prinz, W; (2002) Action, binding, and awareness. In: Prinz, W and Hommel, B, (eds.) Oxford University Press.

Haggard, P., Clark, S., & Kalogeras, J. (2002). Voluntary action and conscious awareness. *Nature Neuroscience*, 5(4), 382–385. doi:10.1038/nn827

Hume, D. (1760). *Enquiry concerning human understanding*. Edinburgh: Kincaid and Donaldson.

Kühn, S., Brass, M., & Haggard, P. (2013). Feeling in control: Neural correlates of experience of agency. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, 49(7), 1935–1942. doi:10.1016/j.cortex.2012.09.002

Locke, J. (1689). *An essay concerning human understanding*. London: G. Routledge. Mauss, M. (1936). Les techniques du corps. *Journal de Psychologie*, 32(3-4), 365–86.

Moore, J. W., Ruge, D., Wenke, D., Rothwell, J., & Haggard, P. (2010). Disrupting the experience of control in the human brain: pre-supplementary motor area contributes to the sense of agency. *Proceedings. Biological Sciences / The Royal Society*, 277(1693), 2503–2509. doi:10.1098/rspb.2010.0404

Synofzik, M., Vosgerau, G., & Newen, A. (2008). Beyond the Comparator Model: A Multi-Factorial Two-Step Account of Agency. *Consciousness and Cognition*, 17(1), 219–239.

Takahata, K., Takahashi, H., Maeda, T., Umeda, S., Suhara, T., Mimura, M., & Kato, M. (2012). It's Not My Fault: Postdictive Modulation of Intentional Binding by Monetary Gains and Losses. *PLoS ONE*, 7(12), e53421. doi:10.1371/journal. pone.0053421

Walsh, E., & Haggard, P. (2013). Action, prediction, and temporal awareness. *Acta Psychologica*, 142(2), 220–229. doi:10.1016/j.actpsy.2012.11.014

Wolpe, N., Moore, J. W., Rae, C. L., Rittman, T., Altena, E., Haggard, P., & Rowe, J. B. (2013). The medial frontal-prefrontal network for altered awareness and control of action in corticobasal syndrome. *Brain*, awt302. doi:10.1093/brain/awt302

Yoshie, M., & Haggard, P. (2013). Negative Emotional Outcomes Attenuate Sense of Agency over Voluntary Actions. *Current Biology*: CB, 23(20), 2028–2032. doi:10.1016/j.cub.2013.08.034

POSTER APRESENTADO PELA FUNDAÇÃO BIAL POSTER PRESENTED BY THE BIAL FOUNDATION

Resumo do poster apresentado pela Fundação Bial Abstract of the poster presented by the Bial Foundation

BIAL FOUNDATION GRANTS (1994-2014): BUILDING AN ONLINE DATABASE

Guedes, P.¹, Júdice, A.², Marinbo, S.^{1,3}, & Topa, H.¹

Objectives:

1. To build an online database accessible to the general public with nformation about the projects funded by the BIAL Foundation from 1994 o 2014.

2. To analyze the distribution of projects by major areas (Psychophysiology, Parapsychology) and subareas.

3. To analyze the scientific production resulting from the projects through bibliometric indicators.

Methods:

1. A database (ATHENA, developed by DID) was created including all the information available on each project, specifying Title, Researcher(s), Affiliation, and Publications. Within these, Results/Abstract, URL, Keywords, Document Type (e.g. final report, article, abstract, book), Full bibliographic reference (APA style, 6th edition), Times cited, Impact factor, and Indexation were indicated.

2. A categorization of the research topics was created for both of the major areas (Psychophysiology and Parapsychology), allowing a more systematic and consistent thematic classification throughout the projects.

3. Publications were analyzed by standard bibliometric methods using Scopus and ISI Web of Science and "Times cited" data was retrieved from Web of Science[™] Core Collection in March 2014.

¹ BIAL Foundation, Portugal.

² Inês de Castro Foundation, Portugal.

³ Faculty of Psychology and Education Sciences, University of Porto, Portugal.

Results:

A total of 461 projects have been funded by the BIAL Foundation from 1994 to 2014, in the areas of Psychophysiology (223 grants, 48.3%), Parapsychology (175 grants, 38%), and Joint (63 grants, 13.7%). A category system was created, resulting in 14 not mutually exclusive categories for Psychophysiology and 15 for Parapsychology. In Psychophysiology four categories stood out: Cognitive processes (49.3%), Brain (47.5%), Biopsychological problems (32.3%), and Emotion (23.8%). In Parapsychology the most representative categories were Extrasensory perception (48.6%), Paranormal belief (18.3%), Psychokinesis (17.7%), and Assessment tools (16.6%). For the projects joining both areas, the most frequent categories were Brain (44.4%), Altered states of consciousness (41.3%), and Extrasensory perception (28.6%). A total of 556 full indexed papers (Psychophysiology, 63.8%; Parapsychology, 27.9%; Joint, 8.3%), and 115 indexed abstracts (Psychophysiology, 91.3%; Parapsychology, 5.2%; Joint, 3.5%) were published.

Summary of Purposes and Conclusions:

The BIAL Foundation hopes the building of the present database will achieve two purposes: an internal purpose enabling evaluation of the productivity and significance of the projects funded. An external purpose that will enable the easy access by the general public to the work done by the BIAL Fellows and that will constitute a valuable tool for those interested in analyzing progress in the areas preferentially funded by the Foundation (Psychophysiology and Parapsychology), allowing the online search of scientific production in these areas. Since 2008, the projects show an increasing approximation of Psychophysiology and Parapsychology, suggesting a growing interest in the development of a multidisciplinary approach. Along the years, there has been a progressive and sustained increase of scientific production published in indexed journals.

Keywords: BIAL Foundation grants, Psychophysiology, Parapsychology, Online database, Bibliometry.

LISTA DE POSTERS POSTERS

Posters com resultados finais apresentados pelos bolseiros da Fundação Bial e/ou disponíveis em www.fundacaobial.com

Posters with final results presented by the Bial Foundation Fellows and/or available at www.fundacaobial.com

Resumos dos posters disponíveis em / Posters' abstracts available at www.fundacaobial.com

2004

108/04 – "A pilot study into the incidence of deathbed phenomena in nursing homes and hospices in Hampshire England, and in Rotterdam Holland"

Investigadores/*Researchers:* Prof. Peter Fenwick, Dr. Sue Brayne, Dr. Shirley Firth, Dr. Bart van de Lugt, Dr. Julian Candy, Dr. Frans Reynders, Mr. Frans Baar

Instituição/*Institution*: University Department of Mental Health, Royal Southampton Hospital, Hamphsire (UK)

Duração prevista/Estimated duration: 2008/11 - 2014/04

2008

20/08 – "Beyond anthropocentric empathy: ERP dynamics of empathy for non-human beings and ecosystems" – only abstract available

Investigadores/*Researchers:* Dr. José Raúl Naranjo Muradas, Dr. Verónica Sevillano Triguero, Prof. Juan I. Aragonés, Prof. Shihui Han Instituição/*Institution:* Department of Environmental Health Sciences, University Medical Centre Freiburg (Germany)

Duração prevista/Estimated duration: 2009/11 - 2014/04

42/08 – "Physiological markers of the sensory processing in the neonate"

Investigadores/*Researchers:* Dr. Adriana da Conceição Soares Sampaio, Dr. Maria de Góis Vicente Ramalho Eanes, Dr. Clédna Patrícia de Oliveira Silva, Dr. Hugo Miguel Braga de Almeida Tavares, Dr. Sara Cruz Instituição/*Institution:* CIPsi - Centro de Investigação em Psicologia, Universidade do Minho, Braga (Portugal) Duração/*Duration:* 2009/02 - 2013/02

81/08 – "Subjective Experiences Associated with Seizures" – only abstract available

Investigadores/*Researchers:* Prof. Bruce Greyson, Dr. Nathan B. Fountain, Prof. Donna K. Broshek, Ms. Lori L. Derr

Instituição/*Institution:* Division of Perceptual Studies, University of Virginia Health System (USA)

Duração/Duration: 2009/10 - 2012/10

85/08 – "Embodied Emotions. The impact of expertise in mindfulness on the automaticity in emotion regulation strategies detected by psychophysiological parameters and self-report in a laboratory setting" – only abstract available

Investigadores/*Researchers:* Dr. Susanne Müller, Prof. Ulrike Halsband Instituição/*Institution:* Department of Psychology/Neuropsychology, University of Freiburg (Germany)

Duração prevista/Estimated duration: 2009/09 - 2014/04

104/08 – "Lability and PK performance: Identifying the optimal conditions for PK-RNG effects in the laboratory using an I Ching task" Investigador/Researcher: Dr. Chris A. Roe

Instituição/*Institution*: Centre for the Study of Anomalous Psychological Processes [CSAPP], University of Northampton (UK) Duração/*Duration*: 2009/01 - 2013/09

105/08 – "Testing the Psi-mediated Instrumental Response theory using an implicit psi task"

Investigador/*Researcher:* Dr. Chris A. Roe Instituição/*Institution:* Centre for the Study of Anomalous Psychological Processes [CSAPP], University of Northampton (UK) Duração/*Duration:* 2009/01 - 2013/09

118/08 – "An Interpretative Phenomenological Analysis of Anomalous Experience at the End-of-Live" – only abstract available

Investigadores/*Researchers:* Dr. Craig D. Murray, Dr. Joanne Murray Instituição/*Institution:* Division of Health Research, Lancaster University (UK) Duração prevista/*Estimated duration:* 2009/11 - 2014/04

126/08 – "Experience of Pain: functional changes induced by chronic pain in the neuronal circuits of reward and aversion"

Investigadores/Researchers: Prof. Vasco Miguel Clara Lopes Galhardo, Prof. Deolinda Maria Valente Alves de Lima Teixeira, Dr. Clara Maria Pires Costa Bastos Monteiro, Dr. Hélder Cardoso Cruz, Dr. Maria Leonor Godinho, Dr. Daniela Seixas, Dra. Sónia Margarida Dourado Instituição/*Institution:* IBMC – Instituto de Biologia Molecular e Celular, Porto (Portugal)

Duração/Duration: 2009/03 - 2013/10

135/08 – "Electrophysiological Correlates of Learning New Faces: A study with event-related potentials and skin-conductance responses" Investigadores/*Researchers:* Dr. Isabel Maria Barbas dos Santos, Dr.

Christopher Alexander Longmore, Dr. Jorge Manuel Costa Oliveira Instituição/*Institution:* Laboratório de Psicologia Experimental e Aplicada (PsyLab) do Centro de Investigação em Educação e Ciências do Comportamento (CIECC), Universidade de Aveiro, Departamento de Ciências da Educação (Portugal)

Duração prevista/Estimated duration: 2009/05 - 2014/04

136/08 – "Psychophysiological Markers of Externalizing Personality in Non-Clinical and Criminal Populations"

Investigadores/*Researchers:* Dra. Isabel Maria Barbas dos Santos, Dr. Jorge Manuel Costa Oliveira, Dr. Paula Emanuel Rocha Martins Vagos, Prof. Nick Anthony DeFilippis

Instituição/*Institution:* Laboratório de Psicologia Experimental e Aplicada (PsyLab) do Centro de Investigação em Educação e Ciências do Comportamento (CIECC), Universidade de Aveiro, Departamento de Ciências da Educação (Portugal)

Duração/Duration: 2009/01 - 2014/02

141/08 – "Neural and Computational Mechanisms of Conscious and Unconscious Decisions Under Uncertainty"

Investigadores/*Researchers:* Dr. Edward Vul, Prof. Nancy Kanwisher, Prof. Joshua Tenenbaum

Instituição/*Institution:* Department of Psychology, University of California, San Diego, CA (USA)

Duração/Duration: 2010/11 - 2014/02

180/08 – "Emotional influences on psychophysiological indices of focused attention and response anticipation in social anxiety: A combined neuroimaging and electroencephalographic study"

Investigadores/*Researchers:* Dr. Yoko Nagai, Prof. Hugo Critchley, Dr. Marcus Gray

Instituição/Institution: Clinical Imaging Sciences Centre, Brighton and Sussex Medical School, University of Sussex (UK)

Duração prevista/Estimated duration: 2009/10 - 2014/04

189/08 – "Exploration of the Effect of Local Geomagnetic Activity and Tibetan Buddhist Meditation on Psychic Awareness"

Investigadores/*Researchers:* Dr. Serena M. Roney-Dougal, Dr. Adrian Ryan Instituição/*Institution:* Psi Research Centre, Glastonbury, Somerset (UK) Duração/*Duration:* 2009/10 - 2013/07

2010

01/10 – "Neurocognitive Correlates of the Out-of-Body Experience and Kindred Hallucinations of Embodiment and the 'Self'"

Investigador/*Researcher:* Dr. Jason John Braithwaite Instituição/*Institution:* Selective Attention and Awareness Laboratory (SAAL) Behavioural Brain Sciences centre, School of Psychology,

University of Birmingham (UK)

Duração/Duration: 2011/03 - 2013/05

08/10 – "Hallucination Experience and Psi (Phase II): New Psychological, Psychopathological, Psychophysiological and Transcultural Approach"

Investigadores/Researchers: Dr. Alejandro Enrique Parra, Dr. Romina Ileana Mielgo, Dr. Irma Juana Caputo Instituição/Institution: Universidad Abierta Interamericana, Facultad de Psicología, Buenos Aires (Argentina) Duração/*Duration*: 2011/03 - 2013/01

21/10 - "Effects of intentionally enhanced tea on mood"

Investigadores/*Researchers:* Prof. Yung-Jong Shiah, Dr. Dean Radin Instituição/*Institution:* Psychology Department of Kaohsuing Medical University, Kaohsuing, (Taiwan) Duração/*Duration:* 2011/04 - 2012/11

32/10 – "Facilitating healthy ageing: Investigating neuroprotective effects of mindfulness"

Investigadores/*Researchers:* Dr. Peter Malinowski, Prof. Thomas Gruber, Dr. Cathy Montgomery

Instituição/*Institution:* Liverpool John Moores University, School of Natural Sciences and Psychology Byrom Street, Liverpool (UK) Duração/*Duration:* 2011/04 - 2013/05
37/10 – "Psychophysiological mechanisms of hierarchical novelty detection in the human auditory brain"

Investigadores/Researchers: Prof. Carles Escera, Dr. Sabine Grimm, Dr. Marc Recasens

Instituição/*Institution:* Research Institute for Brain, Cognition and Behavior (IR3C) and Department of Psychiatry and Clinical Psychobiology, Faculty of Psychology, University of Barcelona (Spain) Duração/*Duration*: 2011/04 - 2013/03

39/10 – "Paranormal Belief, Evaluation of Paranormal Experiences, Schizoptypy and Reality Testing"

Investigadores/*Researchers:* Dr. Neil Andrew Dagnall, Dr. Gary Munley, Dr. Andrew Parker, Dr. Kenneth Drinkwater

Instituição/*Institution:* The Manchester Metropolitan University, Research Institute of Health and Social Change, Faculty of Health, Psychology and Social Care, Dep. of Psychology, Manchester (UK) Duração/*Duration:* 2011/09 – 2013/11

42/10 – "Conscious Induction of Theta EEG Patterns by a Healing Procedure"

Investigadores/*Researchers:* Dr. Stefan Schmidt, Dr. Thilo Hinterberger Instituição/*Institution:* Center for Mindfulness, Meditation and Neuroscience Research, Institute of Environmental Health Sciences, University Medical Center Freiburg (Germany) Duração/*Duration:* 2011/11 – 2013/03

50/10 – "Trance: Cortical Representations" – only abstract available

Investigadores/*Researchers:* Dr. Alessandra Ghinato Mainieri, Dr. Julio Fernando Prieto Peres, Prof. Alexander Moreira de Almeida, Prof. Ute Habel, Dr. Nils Kohn

Instituição/*Institution:* Department of Psychiatry and Psychotherapy, RWTH Aachen University, Aachen (Germany) Duração/*Duration:* 2011/03 - 2013/05

252

55/10 – "The developmental and psychophysiological emergence of dreams and nightmares: state-dependent and state-independent fronto-cortical disconnectivity"

Investigadores/*Researchers:* Dr. Róbert Bódizs, Dr. Peter Daniel Simor, Dr. Piroska Sándor, Dr. Szilvia Csóka, Klára Horváth Instituição/*Institution:* Institute of Behavioural Sciences, Semmelweis

University, Budapest (Hungary)

Duração/Duration: 2011/03 - 2014/02

58/10 – "Somatic Psi vs. Survival Psi: A Quantitative Investigation of Mediums' Phenomenology comparing Psychic Readings and Ostensible Communication with the Deceased" – only abstract available Investigadores/*Researchers:* Dr. Julie Beischel, Dr. Adam J. Rock, Dr. Mark Boccuzzi, Dr. Michael Biuso Instituição/*Institution:* The Windbridge Institute for Applied Research in Human Potential, Tucson (USA)

Duração/Duration: 2011/03 - 2013/02

63/10 – "Mindful ageing. Avoiding age related cognitive decline"

Investigadores/*Researchers:* Prof. Isabel Pavão Martins, Prof. Nuno Lunet, Dr. Carolina Maruta, Dr. Clara Loureiro, Dr. Vanda Freitas, Dr. Joana Morgado, Dr. Sofia Reimão, Dr. Joana Tavares

Instituição/*Institution:* Laboratório de Estudos de Linguagem, Unidade Neurologica de Investigação Clínica, Faculdade de Medicina de Lisboa e Instituto de Medicina Molecular, Universidade de Lisboa (Portugal) Duração prevista/*Estimated duration:* 2011/04 - 2014/04

64/10 – "A psychophysiological investigation of semantic contributions to episodic memory" – only abstract available Investigadores/*Researchers:* Dr. Andrea Greve, Prof. Edward Wilding Instituição/*Institution:* Cardiff University Brain Research Imaging Centre (CUBRIC), School of Psychology, Cardiff University (UK) Duração/*Duration:* 2011/05 - 2013/12

66/10–"TheSpiritualBrain:neuropsychologicalandneurophysiologic investigations of Self-transcendence and Spirituality"

Investigadores/*Researchers:* Dr. Salvatore Maria Aglioti, Prof. Cosimo Urgesi, Dr. Franco Fabbro, Dr. Matteo Candidi, Dr. Fabio Campanella Instituição/*Institution:* Department of Psychology, University of Rome "La Sapienza", Rome (Italy)

Duração/Duration: 2011/04 - 2013/02

72/10 – "Neurocognitive mechanisms supporting the influence of memory on visual attention in healthy and disease"

Investigadores/*Researchers:* Dr. José Miguel Pinto Cardoso de Bourbon Teles, Dr. David Soto, Dr. Paul Bentley

Instituição/*Institution:* Centre for Neuroscience, Faculty of Medicine, Department of Neuroscience and Mental Health, Imperial College London (UK)

Duração/Duration: 2011/04 - 2013/10

74/10 – "The Psychobiological Effects of Yoga/Meditation in a Prison Population"

Investigadores/*Researchers:* Dr. Miguel Farias, Dr. Amy Bilderbeck Instituição/*Institution:* Department of Experimental Psychology, University of Oxford (UK)

Duração prevista/Estimated duration: 2012/02 - 2014/04

85/10 – "Importance of cognitive coping in facilitation of hypnorelaxation in stressed students and in anxious patients: holistic psycho-neuroendocrino-immunological analysis (Building telepathic contact with the inner adviser)"

Investigadores/*Researchers:* Prof. Margit Keresztes, Prof. Tibor Rudisch, Dr. Zoltán Kovács, Prof. János Tajti, Dr. János Gardi, Dr. Gyöngyi Serfőző Instituição/*Institution:* Dept. Biochemistry, Medical Faculty, University of Szeged, Szeged (Hungary)

Duração/Duration: 2011/03 - 2012/10

86/10 – "The different faces of one's self: Neural correlates of changes in selfidentity"

Investigadores/*Researchers:* Dr. Ana Tajadura-Jiménez, Dr. Emmanouil (Manos) Tsakiris Instituição/*Institution:* Department of Psychology, Royal Holloway University of London (UK) Duração/*Duration:* 2011/09 - 2012/10

94/10 – "Cortical and autonomic responses associated with accurate intuition" – only abstract available

Investigadores/*Researchers:* Prof. Paul J. Mills, Dr. Arnaud Delorme, Dr. Julie Beischel, Dr. Dean Radin, Dr. Rael Cahn Instituição/*Institution:* Institute of Noetic Sciences, California (USA) Duração/*Duration:* 2011/10 - 2013/04

96/10 - "The psychophysiology of positive psychology"

Investigadores/*Researchers:* Prof. Angela Clow, Dr. Lisa Thorn, Dr. Nina Smyth, Prof. Frank Hucklebridge

Instituição/*Institution:* Psychophysiology and Stress Research Group, Department of Psychology, University of Westminster, London (UK) Duração/*Duration:* 2011/06 - 2013/10

100/10 – "Replicating von Lucadou's Psycho-Physical Correlation Matrices"

Investigadores/*Researchers:* Prof. Harald Walach, Dr. Nikolaus von Stillfried

Instituição/*Institution:* Institute for Transcultural Health Sciences (INTRAG), European University Viadrina, Frankfurt Oder (Germany) Duração prevista/Estimated duration: 2011/11 – 2014/03

102/10 – "The Importance of the Rapid Eye Movement Sleep Stage for Creativity and for Creative Problem Solving"

Investigadores/*Researchers:* Prof. Ingegerd Carlsson, Per Davidson, Dr. Una Gustafsson, Dr. Markus Jansson-Frójmark, Prof. Sara Mednick, Dr. Marianne Ors Instituição/*Institution:* Department of Psychology, Lund University, Lund (Sweden)

Duração/Duration: 2011/07 – 2013/11

105/10 – "Analgesic Properties of Computer Games"

Investigadores/*Researchers:* Dr. Stephen Fairclough, Dr. Helen Poole Instituição/*Institution:* School of Natural Sciences and Psychology, Liverpool John Moores University, Liverpool (UK) Duração/*Duration:* 2011/09 – 2013/02

106/10 – "Mapping the Psychophysiology of Anxiety Responses Using Virtual Reality" – only abstract available

Investigadores/*Researchers:* Dr. Simon Dymond, Dr. Philip M. Newton, Dr. Bryan Roche Instituição/*Institution:* Department of Psychology, Wales Institute of Cognitive Neuroscience, Swansea University, Swansea (UK) Duração/*Duration:* 2011/07 - 2014/01

141/10 – "Pattern Classification of Emotion-Induced Physiological

Changes" – only abstract available Investigadores/*Researchers:* Dr. Julia Mossbridge, Dr. David Little Instituição/*Institution:* Northwestern University Visual Perception, Cognition, and Neuroscience Laboratory, Evanston (USA) Duração prevista/*Estimated duration:* 2011/04 - 2014/03

155/10 – "Memory for personal experience and the parietal cortex"

Investigadores/*Researchers:* Dr. Charlotte Russell, Dr. Paresh Malhotra, Dr. Adrian Williams

Instituição/*Institution:* Centre for Cognition and Neuroimaging, Department of Psychology, Brunel University, Uxbridge (UK) Duração prevista/*Estimated duration:* 2011/07 - 2014/03

157/10 – "Control of cognitive and emotional processing of faces by the frontal theta Rhythm"

Investigadores/*Researchers:* Dr. Alberto João Rodrigues Leal, Dr. Ricardo Jorge de Pina Ramos Machado Lopes, Dr. Patrícia Arriaga, Prof. Francisco Gomes Esteves

Instituição/*Institution:* Centro de Investigação e Intervenção Social, ISCTE-IUL, Lisboa (Portugal)

Duração prevista/Estimated duration: 2011/04 - 2014/04

170/10 – "The role of fusion of multisensory percepts in dynamic facial/body expressions: an fMRI study"

Investigadores/*Researchers:* Dr. Gina Maria Costa Caetano, Prof. Miguel Castelo-Branco, Prof. Beatrice de Gelder, Eng. Gregor Philipak

Instituição/*Institution:* Instituto Biomédico de Investigação de Luz e Imagem - IBILI-, Faculdade de Medicina, Universidade de Coimbra (Portugal)

Duração/Duration: 2011/04 - 2013/11

180/10 – "Neuronal mechanisms underlying sex hormone-dependent switching of sexual receptivity"

Investigadores/*Researchers:* Dr. Kensaku Nomoto, Dr. Susana Lima Instituição/*Institution:* Champalimaud Foundation, Lisboa (Portugal) Duração/*Duration:* 2011/05 - 2013/07

186/10 - "Brain Mechanisms of Placebo Analgesia"

Investigadores/*Researchers:* Prof. Magne Arve Flaten, Prof. Per M. Aslaksen, Prof. Torgil R. Vangberg, Dr. Odd Petter Eldevik, Prof. Jan Bergdahl, Dr. Sara Vambheim, Dr. Just C. Thoner Instituição/*Institution:* University of Tromsø and University Hospital of North Norway, Tromso (Norway) Duração/*Duration:* 2011/03 - 2014/02

190/10 - "The Sharefeld: A new standard for free response ESP research"

Investigadores/*Researchers:* Dr. Mario Varvoglis, Dr. Peter Bancel, Dr. Djohar Si Ahmed, Eng. Jean-Paul Bailly

Instituição/*Institution:* Institut Metapsychique International, Paris (France)

Duração/Duration: 2011/04 - 2013/09

191/10 – "Lucid dream induction by transcranial cortex stimulation: A test of the prefrontal hypothesis of lucid dreaming"

Investigadores/*Researchers:* Prof. Michael Schredl, Dr. Claudia Schilling, Dr. Ahmed Karim, Dr. Daniel Erlacher, Birgit Schütz

Instituição/Institution: Central Institute of Mental Health, Mannheim (Germany)

Duração/Duration: 2011/08 – 2012/10

199/10 - "Psychophysiology of Spiritual Transmission"

Investigadores/*Researchers:* Dr. Cassandra Vieten, Dr. Dean Radin, Dr. Marilyn Schlitz, Dr. Arnaud Delorme Instituição/*Institution:* Institute of Noetic Sciences, California (USA) Duração/*Duration:* 2011/09 – 2013/06

201/10 – "The effects of audience size and audience rating on field random number generator output: A case study of Japanese professional baseball"

Investigadores/*Researchers:* Dr. Takeshi Shimizu, Prof. Masato Ishikawa, Dr. Tatsu Hirukawa Instituição/*Institution:* Science Communicatoin Laboratory, Meiji University, Tokyo (Japan)

Duração/Duration: 2011/03 - 2012/10

206/10 – "Extrasensory Perception, Dissociation, and Motor Automatisms"

Investigadores/Researchers: Dr. John Palmer, Dr. Christine Simmonds-Moore

Instituição/*Institution:* Rhine Research Center, North Carolina (USA) Duração/*Duration:* 2011/03 - 2012/10

215/10 - "Vestibular contributions to self-awareness"

Investigadores/*Researchers:* Prof. Patrick Haggard, Dr. Elisa Raffaela Ferre **Instituição/Institution:** Institute of Cognitive Neuroscience, University College London (UK) Duração/*Duration:* 2011/10 - 2013/04

223/10 – "Exploring the relationship between the synaesthesias and anomalous experiences"

Investigadores/*Researchers:* Dr. Christine Simmonds-Moore, Dr. Carlos Alvarado, Dr. Nancy Zingrone, Ferrell Carpenter Instituição/*Institution:* University of West Georgia (USA) Duração/*Duration:* 2011/09 - 2013/05

231/10 – "Toward understanding visual awareness: An intracranial EEG study on transient suppression phenomena of conscious visual perception"

Investigadores/*Researchers:* Dr. Tonio Ball, Prof. Andreas Schulze-Bonhage, Prof. Ad Aertsen, Dr. Jörn Rickert, Markus Kern

Instituição/Institution: Epilepsy Center, University Hospital, Freiburg (Germany)

Duração prevista/Estimated duration: 2011/08 - 2014/04

238/10 – "Effect of the comprehensive Art of Living yogic breathing programme on brain function in correlation with physiological and psychological well-being"

Investigadores/*Researchers:* Dr. Sanja Kostrun, Dr. Irena Svenda, Dr. Kresimir Jergovic, Dr. Drazen Durch, Prof. Jagoda Doko Jelinic, Prof. Fahri Saatvcioglu, Dr. Alen Pticar, Dr. Sanja Kordic Instituição/*Institution:* Art of Living Croatia, Zagreb (Croatia) Duração prevista/*Estimated duration:* 2011/11 - 2014/04

2012

41/12 – "The Body beyond the body"

Investigador/*Researcher:* Prof. Marcello Costantini, Dr. Francesca Ferri Instituição/*Institution:* Department of Neuroscience and Imaging, University "G. d'Annunzio", Chieti (Italy) Duração prevista/*Estimated duration:* 2013/03 - 2014/03

46/12 - "Motivational Intensity in the Prefrontal Cortex"

Investigador/*Researcher:* Prof. Stephen Fairclough, Dr. Christopher Burns Instituição/*Institution:* School of Natural Sciences and Psychology, Liverpool John Moores University (UK)

Duração prevista/Estimated duration: 2013/03 - 2014/03

54/12 – "A Rasch Scaling Validation of a Core "Near-Death Experience (NDE)" A Critical Replication and Extension"

Investigador/*Researcher:* Dr. Rense Lange Instituição/*Institution:* Integrated Knowledge Systems, Inc., Illinois (USA) Duração prevista/*Estimated duration:* 2013/02 - 2014/03

127/12 – "An Investigation of the I Ching Using the Q-Sort Method and a PK-RNG Design"

Investigador/Researcher: Dr. Lance Storm

Instituição/*Institution:* Brain and Cognition Centre, School of Psychology, University of Adelaide and Australian Institute of Parapsychological Research, Incorporated, Gladesville (Australia)

Duração prevista/Estimated duration: 2013/03 - 2014/03

266/12 - "One ear is better than two; but why and when?"

Investigador/*Researcher:* Prof. Veena Kumari, Dr. Elena Antonova Instituição/*Institution:* Institute of Psychiatry (IoP), King's College London (UK)

Duração prevista/Estimated duration: 2013/03 - 2014/03

PALESTRANTES E MODERADORES SPEAKERS AND MODERATORS

PETER BANCEL Doutorado em Física. Até 2010 esteve envolvido no Global Conscious Project, Princeton, Nova Jérsia, EUA. Membro do *European Board Shambhala Europe*, Colónia, Alemanha. Membro da Direção do *Institut Intérnational Métapsychique*, Paris, França. Interesses científicos: correlações de dados aleatórios contínuos com eventos mundiais importantes, efeitos de consciência de massa e o *Global Consciousness Project*.

PhD, BSc, Physics. Until 2010 has been involved with the Global Conscious Project, Princeton, NJ, USA. Member of the European Board Shambhala Europe, Cologne, Germany. Membre Comité Directeur, Institut Intérnational Métapsychique, Paris, France. Research interests: correlations of continuous random data with major world events, effects of mass consciousness and the Global Consciousness Project.

DICK BIERMAN Regente (Jubilado) da Cadeira Heymans de Experiências Excecionais, Universidade de Humanísticas, Utrecht, Holanda. Doutorado em Física Experimental, Universidade de Amesterdão, Holanda. Interesses científicos: estudos da consciência, inteligência artificial, aprendizagem sob estados modificados de consciência (em especial durante o sono), papel das emoções não conscientes na tomada (intuitiva) de decisão, pré-sentimento (excitação corporal anómala, que precede acontecimentos emocionais), relação entre a física quântica e consciência.

Heymans Chair of Exceptional Experiences, University for Humanistics, Utrecht, The Netherlands (Emeritus). PhD in Experimental Physics, University of Amsterdam, The Netherlands. Research interests: consciousness studies, artificial intelligence, learning during altered states of consciousness (especially during sleep), non-conscious emotions and their role in (intuitive) decision-making, pre-sentiment (anomalous body arousal preceding emotional events), relation between quantum physics and consciousness.

MIGUEL CASTELO-BRANCO Professor de Biofísica e Matemática e Ciências da Visão e Diretor do IBILI e ICNAS, Universidade de Coimbra. Vários prémios na área das Neurociências. Dezenas de artigos publicados na área da Bioengenharia, Neurociência da Visão e Neurociência Clínica. Consultor (*peer-reviewer*) de várias revistas científicas nas áreas de Neurociências e Ciências da Visão. Secretário científico da Sociedade Europeia EVER (Ciências da Visão). Interesses científicos: neurociências sensoriais e cognitivas em populações saudáveis e doentes.

Professor of Biophysics and Mathematics and Visual Sciences and Director of IBILI and ICNAS, University of Coimbra. Several awards on Neuroscience. Dozens of papers published on Bioengineering, Visual Neuroscience and Clinical Neuroscience. Consultant (peer-reviewer) for several journals on Neuroscience and Visual Sciences. Scientific Secretary of the European Society EVER (Visual Sciences). Research interests: sensory and cognitive neuroscience in healthy and ill populations. **ALEXANDRE CASTRO-CALDAS** Professor de Neurologia, Diretor do Instituto de Ciências da Saúde da Universidade Católica Portuguesa, Lisboa. Foi Presidente da *International Neuropsychological Society*. Interesses científicos: literacia/iliteracia e ortografia e substratos neurobiológicos cerebrais, afasia e doença de Parkinson.

Professor of Neurology, Director of the Health Sciences Institute of the Catholic University of Portugal, Lisbon, Portugal. Past President of the International Neuropsychological Society. Research interests: literacy/illiteracy and orthography and brain neurobiological substrates, aphasia and Parkinson's disease.

VANESSA CHARLAND-VERVILLE Neuropsicóloga, integra o Grupo de Ciência do Coma, Centro de Investigação Cyclotron e Departamento de Neurologia, Hospital Universitário *CHU Sart Tilman*, Bélgica. Obteve o título de B.Sc. em Psicologia, Universidade de Montreal, e trabalhou na área das concussões desportivas em atletas profissionais de futebol e de hóquei. Mestre em Neurociências e Doutoranda em Ciências Médicas, Universidade de Liège, Bélgica. Interesses científicos: memórias póscoma e cognição, estudo comportamental e neurofuncional de estados alterados de consciência em doentes com lesão cerebral grave.

Neuropsychologist, part of the Coma Science Group, Cyclotron Research Centre and Neurology department, CHU Sart Tilman University Hospital, Belgium. She obtained her B.Sc. in Psychology, University of Montreal, and worked on sport concussions in professional football and hockey athletes. She then obtained her Master degree in Neurosciences and is currently doing her PhD in Medical Sciences at the University of Liège, Belgium. Research interests: post-coma memories and cognition, behavioral and neurofunctional study of altered states of consciousness in patients with severe brain injury.

AXEL CLEEREMANS Diretor de Investigação, Grupo da Consciência, Cognição e Computação, Universidade Livre de Bruxelas, Bélgica. Autor de múltiplos artigos científicos sobre aprendizagem implícita e consciência e editor dos livros "*The Unity of Consciousness: Binding, Integration and Dissociation*" e "*The Oxford Companion to Consciousness*". Membro da Real Academia da Bélgica. Interesses científicos: consciência e aprendizagem implícita, modelos de cognição consciente e não consciente, rede neuronal de processos cognitivos.

Research Director, Consciousness, Cognition & Computation Group, Université Libre de Bruxelles, Belgium. Author of numerous papers on implicit learning and consciousness and editor of the books "The Unity of Consciousness: Binding, Integration and Dissociation" and "The Oxford Companion to Consciousness". Member of the Royal Academy of Belgium. Research interests: consciousness and implicit learning, models of conscious and unconscious cognition, neural network of cognitive processes. **RUI COSTA** Médico Doutorado, Investigador do Programa Champalimaud de Neurociências, Fundação Champalimaud, Lisboa, Portugal. Investigador Convidado, *National Institutes of Health* (NIH), EUA. Diretor, Módulo de Neurociência, Programa Doutoral GABBA, Universidade do Porto, Portugal. Recebeu, entre outros, os Prémios *Seeds of Sciences Prize for Life Sciences* 2010, Portugal e o *Young Investigator Award, Society for Neurosciences* 2012, EUA. Interesses científicos: mecanismos moleculares, celulares e de sistemas de geração da ação, sequência e aprendizagem de competências, ações intencionais vs. hábitos, abordagem de diferentes níveis para o estudo das perturbações cognitivas e senso-motoras em modelos de rato (PD, TOC, NFI e autismo).

PhD, MD, Researcher, Champalimaud Neuroscience Program, Champalimaud Foundation, Lisbon, Portugal. Guest Researcher, National Institutes of Health, USA. Director, Neuroscience Module, GABBA Doctoral Program, University of Porto, Portugal. He received the Seeds of Sciences Prize for Life Sciences 2010, Portugal, and the Young Investigator Award, Society for Neurosciences 2012, USA, among others. Research interests: Molecular, cellular and systems mechanisms of action generation, sequence and skill learning, goal-directed actions versus habits, across-level approach to study cognitive and sensorimotor disorders in mouse models (PD, OCD, NFI and autism).

EBERHARD FETZ Professor de Fisiologia e Biofísica e de Bioengenharia, Universidade de Washington, Escola de Medicina, Seattle, EUA, e Chefe da Divisão de Neurociência, *Primate Research Center*, da mesma Universidade. Recebeu, entre outros, os prémios *Humboldt Research Award 2011*, NYAS e *Aspen Brain forum First Prize* in Neurotechnology 2010. Interesses científicos: estimulação e reabilitação cerebrais, interface cérebro-computador, controlo volitivo e neuropróteses.

Professor of Physiology and Biophysics and of Bioengineering, University of Washington, School of Medicine, Seattle (USA) and Head of Neuroscience Division, Primate Research Center at the same University. He received the Humboldt Research Award 2011 and NYAS and Aspen Brain forum First Prize in Neurotechnology 2010, among others. Research interests: brain stimulation and rehabilitation, brain-computer interface, volitional control and neuroprosthetics. **RAINER GOEBEL** Professor Catedrático de Neurociência Cognitiva, Faculdade de Psicologia e Neurociência, Universidade de Maastricht, Holanda. Diretor do *Maastricht Brain Imaging Centre* (M-BIC) e líder de equipa do grupo "*Neuromodeling and Neuroimaging*", *Netherlands Institute for Neuroscience (NIN), Royal Netherlands Academy of Arts and Sciences* (KNAW). Recebeu o prémio Heinz Maier Leibnitz Advancement Award 1993 em ciência cognitiva patrocinado pelo Ministro Alemão da Ciência e da Educação, e o prémio Heinz Billing Award 1994 pela Max Planck Society. Interesses científicos: representações neuronais no cérebro e o modo como estas são processadas para permitir funções percetivas e cognitivas específicas, aplicações clínicas nas interfaces cérebro-computador (ICC) e estudos de *neurofeedback*.

Full professor for Cognitive Neuroscience, Faculty of Psychology and Neuroscience, Maastricht University, The Netherlands. Director of the Maastricht Brain Imaging Centre (M-BIC) and team leader of the "Neuromodeling and Neuroimaging" group, Netherlands Institute for Neuroscience (NIN), Royal Netherlands Academy of Arts and Sciences (KNAW). He received the Heinz Maier Leibnitz Advancement Award 1993 in cognitive science sponsored by the German Minister of Science and Education and the Heinz Billing Award 1994 by the Max Planck Society. Research interests: neuronal representations in the brain and how they are processed to enable specific perceptual and cognitive functions, clinical applications in brain computer interfaces (BCls) and neurofeedback studies.

PATRICK HAGGARD Professor de Neurociência Cognitiva, University College, Londres, Reino Unido. Presidente da comissão de avaliação de investigação, *Fonds National de Recherche Scientifique*, Bélgica, e membro do Conselho Consultivo Científico, Unidade Max Planck CBS, Alemanha. Interesses científicos: ação humana voluntária, consciência corporal, correlações neurais da experiência de intervenção e da atividade cerebral e experiência consciente.

Professor of Cognitive Neuroscience, University College, London, UK. President of research evaluation committee, Fonds National de Recherche Scientifique, Belgium, and member of the Scientific Advisory Board, Max Planck CBS Unit, Germany. Research interests: human voluntary action, bodily awareness, neural correlates of the experience of agency and brain activity and conscious experience. **STUART HAMEROFF** Professor Jubilado, Departamento de Anestesiologia e Psicologia. Diretor, Centro para Estudos da Consciência, Universidade do Arizona, Tucson, EUA. Recebeu o prémio *Rustin Roy Award pela Chopra Foundation*. É coeditor do *Tucson Discussions and Debates – Toward a Science of Consciousness.* Interesses científicos: estudos da consciência, mecanismos moleculares da anestesia, memória e processamento de informação em microtúbulos, terapêutica por ultrassom transcraniano (TUS), biologia quântica.

Emeritus Professor, Departments of Anesthesiology and Psychology. Director, Center for Consciousness studies, University of Arizona, Tucson, Arizona, USA. He received the Rustin Roy Award by the Chopra Foundation. Co-editor of the Tucson Discussions and Debates – Toward a Science of Consciousness. Research interests: consciousness studies, molecular mechanisms of anesthesia, memory and information processing in microtubules, transcranial ultrasound therapy (TUS), quantum biology.

FERNANDO LOPES DA SILVA Professor Jubilado de Fisiologia Geral, Universidade de Amesterdão, Holanda, *Investigador Coordenador* do Instituto Superior Técnico (IST) de Lisboa e Professor Convidado da Faculdade de Medicina da Universidade de Lisboa. Interesses científicos: eletrofisiologia do cérebro, origens do fenómeno epilético, redes neuronais em relação com a memória, atenção e consciência.

Emeritus Professor of General Physiology, University of Amsterdam, The Netherlands, Head researcher of the Higher Technical Institute (IST) of Lisbon and Invited Professor of the Faculty of Medicine, University of Lisbon, Portugal. Research interests: electrophysiology of the brain, origin of epileptic phenomena, neuronal networks in relation to memory, attention and consciousness.

RUI MOTA CARDOSO Professor de Psicologia, Faculdade de Medicina, e Psiquiatra, Porto. Fundador da Sociedade Portuguesa de Psicossomática e da Sociedade Portuguesa de Psicodrama. Interesses científicos: relação terapêutica e medicina psicossomática.

Professor of Psychology, Faculty of Medicine, and Psychiatrist, Oporto, Portugal. Founder of the Portuguese Society of Psychosomatics and Portuguese Society of Psychodrama. Research interests: the therapeutic relationship and psychosomatic medicine. **ANDER RAMOS-MURGUIALDAY** Investigador cientista, Instituto de Psicologia Médica e de Neurobiologia Comportamental, Universidade *Eberhard Karls* de Tübingen e diretor do TECNALIA, Alemanha. Tem mais de 10 anos de experiência em ciência translacional desde a pesquisa básica até às aplicações clínicas. Interesses científicos: robótica e mecatrónica, neurofisiologia, neuroplasticidade, neuroprostética e neuroreabilitação usando técnicas de ICM (interface cérebro-máquina) aliadas à robótica.

Research Scientist, Institute of Medical Psychology and Behavioral Neurobiology, Eberhard Karls University of Tubingen and director of TECNALIA, Germany. He has more than 10 years-experience doing translational science from basic research to clinical applications. Research interests: robotics and mechatronics, neurophysiology, neuroplasticity, neuroprosthetics and neurorehabilitation using BMI (brain-machine-interfaces) techniques coupled with robotics.

DEAN RADIN Cientista sénior, *Institute of Noetic Sciences, Califórnia*, e Professor Adjunto, Departamento de Psicologia, *Sonoma State University*, Califórnia, EUA. Ex-Presidente da Parapsychological Association e membro do Conselho de Administração. Coeditor chefe do *Journal of Science and Healing*. A sua participação nos media inclui entrevistas na imprensa escrita, rádio, e televisão, e contribuições em documentários e em filmes. É autor e coautor de vários livros, um deles traduzido em Português – "*Entangled Minds*" (Mentes Entrelaçadas – Experiências extrassensoriais na realidade quântica). Interesses científicos: experiências de cura à distância através do espaço e do tempo, modelos de interação mente-matéria, consciência no mundo físico, retrocausalidade, precognição, meta-análise e análise exploratória de dados.

Senior Scientist, Institute of Noetic Sciences, California, and Adjunct Faculty, Department of Psychology, Sonoma State University, CA, USA. Past President of the Parapsychological Association and member of the Board of Directors. Co-editor-in chief of the Journal of Science and Healing. Broad media outreach includes print, radio and TV interviews and documentary and feature film contributions. He authored or co-authored various books, one of them translated in Portuguese – "Entangled Minds" (Mentes Entrelaçadas – Experiências extrassensoriais na realidade quântica). Research interests: distant healing experiments through space and time, models of mind-matter interaction, conscious in the physical world, retrocausation, precognition and meta-analysis and exploratory data analysis

NICK RAMSEY Professor de Neurociência Cognitiva, *Rudolf Magnus Institute for Neuroscience*, e de Neuroimagem Cognitiva e Psicologia Experimental, University Medical Center, Utrecht, Holanda. Coautor do livro "*Psychology in the brain*" (2013). Interesses científicos: estudo funcional do cérebro na epilepsia através da eletrocorticografia, interface cérebro-computador, métodos de imagem funcional (IRM de campo elevado – human 7 Tesla), imagem farmacológica e aplicações clínicas. Professor of Cognitive Neuroscience, Rudolf Magnus Institute for Neuroscience, and of Cognitive Neuroimaging and Experimental Psychology, University Medical Center of Utrecht, The Netherlands. Co-author of the book "Psychology in the brain" (2013). Research interests: functional brain research in epilepsy with electrocorticography, brain-computer interfacing, functional imaging methods (high field MRI – human 7 Tesla) and pharmacological imaging and clinical applications.

MÁRIO SIMÓES Professor de Psiquiatria e de Ciências da Consciência, Faculdade de Medicina de Lisboa. Diretor do Curso de Pós-Graduação em Hipnose Clínica e Experimental da Faculdade de Medicina de Lisboa. Interesses científicos: psicologia e psicofisiologia dos estados alterados de consciência, etnomedicina, experiências excecionais humanas e psicologia e espiritualidade.

Professor of Psychiatry and Consciousness Sciences, Faculty of Medicine of Lisbon, Portugal. Director of the Post-Graduation Course in Clinical and Experimental Hypnosis, Faculty of Medicine of Lisbon. Research interests: psychology and psychophysiology of altered states of consciousness, ethnomedicine, human exceptional experiences and psychology and spirituality.

ADOLF TOBEŃA Professor Catedrático de Psiquiatria e Presidente do Departamento de Psiquiatria e de Medicina Legal, Universidade Autónoma de Barcelona, Espanha. Recebeu, entre outros, o prémio Europeu "Estudio general" em Scientific Popularization 2004 (Universidade de Valência). É professor convidado nas Universidades de Londres, Groningen, Tel Aviv, Veneza e Córdoba (Argentina). Autor ou coautor de vários livros. Interesses científicos: biologia da religiosidade, valores, empatia e equidade, cérebro, poder, envelhecimento e lucidez.

Full Professor of Psychiatry and Chairman of the Department of Psychiatry and Forensic Medicine, Autonomous University of Barcelona, Spain. European Award "Estudio general" on Scientific Popularization 2004 (University of Valencia), among others. He is visiting professor at the Universities of London, Groningen, Tel Aviv, Venice and Córdoba (Argentine). Author or co-author of various books. Research interests: biology of religiosity, values, empathy and fairness, brain and power and aging and lucidity. HARALD WALACH Professor e Diretor do Institute of Transcultural Health Sciences, Universidade Europeia Viadrina, Frankfurt (Oder), Alemanha, onde também coordena o programa de formação pós-graduada para médicos em medicina complementar e estudos culturais. É coordenador da Secção Europeia do Programa *Brain, Mind, and Healing* (BMH) do Instituto Samueli. Fundou o Programa de Mestrado *Transpersonal Psychology and Consciousness Studies*, Universidade de Northampton, Reino Unido. Interesses científicos: avaliação de intervenções não convencionais, investigação em homeopatia, meditação atencional consciente ("*mindfulness*"), medicina complementar, auto-cura, efeitos placebo, meditação e interações não-locais entre sistemas.

Professor and Director of the Institute of Transcultural Health Sciences, European University Viadrina, Frankfurt (Oder), Germany, where he also coordinates a postgraduate training program for doctors in complementary medicine and cultural studies. He is Coordinator of the European section of the Brain, Mind, and Healing (BMH) Program of the Samueli Institute. Founder of the MSc Program of Transpersonal Psychology and Consciousness Studies, University of Northampton, UK. Research interests: evaluation of unconventional interventions, research in homeopathy, mindfulness, complementary medicine, self-healing, placebo effects, meditation and non-local interactions between systems.

CAROLINE WATT Investigadora Sénior Perrott-Warrick e Docente Sénior, Departamento de Psicologia, Universidade de Edimburgo, Escócia. *Past President da Parapsychological Association*, coautora do livro "*An Introduction to Parapsychology*" e autora de artigos em livros e revistas científicas na área da parapsicologia e de crenças paranormais. Interesses científicos: a psicologia e parapsicologia de experiências de sonhos pré-cognitivos, efeitos da expectativa do experimentador e do participante.

Perrott-Warrick Senior Researcher, and Senior Lecturer, Psychology Department, University of Edinburgh, Scotland. Past President of the Parapsychological Association, co-author of the book "An Introduction to Parapsychology" and author of journal articles on parapsychology and paranormal beliefs. Research interests: the psychology and parapsychology of precognitive dream experiences, experimenter and participant expectancy effects.

fundação

À Av. da Siderurgia Nacional • 2745-457 Coronado (S. Romão e S. Mamede) • Portugal Tel. + 351 22 986 6100 • Fax + 351 22 986 6199 • fundacao@bial.com • www.fundacaobial.com

2004

108/04 – "A pilot study into the incidence of deathbed phenomena in nursing homes and hospices in Hampshire England, and in Rotterdam Holland"

Investigadores/*Researchers*: Prof. Peter Fenwick, Dr. Sue Brayne, Dr. Shirley Firth, Dr. Bart van de Lugt, Dr. Julian Candy, Dr. Frans Reynders, Mr. Frans Baar

Instituição/Institution: University Department of Mental Health, Royal Southampton Hospital, Hamphsire (UK)

Duração prevista/Estimated duration: 2008/11 - 2014/04

Objectives: To examine the frequency, nature and possible causes of end of life experiences (ELEs), the training of carers in this little known area, and to compare the experiences of the dying in Holland and the UK.

Method: We questioned a palliative care team in London about the frequency and character of end of life phenomena. A 40 item questionnaire was constructed and validated by the palliative care workers. Two hospices and one nursing home in England, and three hospices in Rotterdam were identified. Ethical permission was given and carers who agreed to take part in the study completed the questionnaire, covering experiences encountered during the previous five years. They were then interviewed and during the coming year kept a diary recording experiences they heard. Prospectively, they again completed the questionnaire and had a further interview.

Results: Shortly before death ELEs are not infrequent, particularly deathbed visions (60%), transition to another reality, and deathbed coincidences. At death, shapes were seen leaving the body and light surrounding it. Mechanical interference, clocks stopping, and odd animal reactions were reported. Carers in England had received little training in ELEs, while over 70% of Dutch carers were trained. 80% of all carers believed ELEs were spiritual, 10% thought them due to medication or organic causes. There was no relationship to demographic factors or religious affiliation. Carers claimed ELEs were comforting to the dying and helped the grieving relatives.

Conclusion: ELEs are not uncommon. No cultural differences were found between UK and Holland. Neither country was aware of the full range of phenomena. Education in this area is essential, particularly for the medical profession.

Publications: Fenwick P., Lovelace H., Brayne S. Comfort for the Dying: five year retrospective and one year prospective studies of end of life experiences. 2010. *Arch. Gerontol. Geriatr.* Epub. PMID: 19913927. 51(2):173-9.

Brayne S., Farnham C., Fenwick P. Deathbed phenomena and their effect on a palliative care team: a pilot study. *American Journal of Hospice and Palliative Care* 2006. 23(1):17-24.

Brayne S., Fenwick P. The case for training to deal with end of life experiences. *European Journal of Palliative Care:* 2008, 15(3), 118-120.

Brayne S., Lovelace H., Fenwick P. End of life experiences and the dying process in a Gloucestershire Nursing Home as reported by nurses and care assistants. *American .Journal of Hospice and Palliative Care*. 2008. 25(3): 195-206.

Fenwick P. and Brayne S. End of life experiences: reaching out for compassion, communication and connection – meaning of deathbed visions and coincidences. *American. Journal of Hospice and Palliative Care.* 2011. 28(1):7-15.

Fenwick P., Lovelace H., Brayne S. End of life experiences and their implications for palliative care. *International Journal of Environmental Studies*. 2007. 3. 315-323.

Brayne S. and Fenwick P. *Nearing the End of Life. A Guide for Relatives and Friends of the Dying.* 2008. Published with the aid a grant from the Aim Foundation.

Brayne S. and Fenwick P. *End of Life Experiences. A Guide for Carers of the Dying.* 2008. Published with the aid of a grant from the Sheepdrove Trust.

Fenwick P. Non-local effects in the process of dying: can quantum mechanics help? *Neuroquantology*. 2010. 8(2).

Fenwick P and Fenwick E. The Art of Dying. 2008. Continuum. London

Keywords: End of life experiences, Deathbed visions, Training

2008

20/08 – "Beyond anthropocentric empathy: ERP dynamics of empathy for non-human beings and ecosystems" – only abstract available

Investigadores/*Researchers*: Dr. José Raúl Naranjo Muradas, Dr. Verónica Sevillano Triguero, Prof. Juan I. Aragonés, Prof. Shihui Han

Instituição/Institution: Department of Environmental Health Sciences, University Medical Centre Freiburg (Germany)

Duração prevista/Estimated duration: 2009/11 - 2014/04

Objectives: Previous research work suggests that empathy towards non-human beings is a reliable human attribute and that empathy is stronger towards phylogenetically closer animals. However, it is still not clear which are the neural mechanisms underlying empathy towards non-human beings. We aimed to investigate the neural processes of ecocentric empathy. This was realized by studying the EEG empathic response to visual stimulus showing humans, animals, plants and ecosystems in negative situations.

Method: Our approach included three different analyses:

- i) ERP analysis to detect temporally separated components associated to the empathic response.
- ii) Wavelets analysis to extract the spectral amplitude in the frequency range from 1 Hz to 40 Hz.
- iii) Source analysis using LORETA. A ROI analysis was done for seven different empathy-related regions of interests (ROIs) comprising bilateral ACC, anterior Insula (AI), IFG and the mPFC.

Results: The ERP time evolution of the empathic response has a triphasic structure: an early T1 (150-250 ms), an intermediate T2 (250-450 ms) and a late T3 (450-650 ms). Humans and animals in negative situations elicited a stronger empathic response compared to plants and ecosystems. Interestingly, empathic response to animals was stronger than to humans at T2 and T3. Wavelet analysis revealed that humans and animals in negative situations elicited temporo-parietal and fronto-central theta oscillations (3-8 Hz, centered at 5 Hz) with a maximum at around 225 ms. Plants and ecosystems images elicited a rather intermittent pattern of 10 Hz oscillations localized in occipito-temporal areas. The LORETA analysis revealed that the mPFC and ACC were strongly activated by images of animals in distress while the anterior Insula and the IFG were equally activated by images of humans and animals.

Conclusions: Our study suggests that humans may equally empathize with other humans and with animals in distress, while plants and ecosystems elicit a smaller emotional response. Besides, empathy for humans and animals recruits an overlapping set of brain areas which are differentially activated depending on the image content and are associated to different neural oscillatory regimes.

Keywords: Ecocentric empathy, ERP, Wavelet analysis, LORETA

42/08 – "Physiological markers of the sensory processing in the neonate"

Investigadores/*Researchers*: Dr. Adriana da Conceição Soares Sampaio, Dr. Maria de Góis Vicente Ramalho Eanes, Dr. Clédna Patrícia de Oliveira Silva, Dr. Hugo Miguel Braga de Almeida Tavares, Dr. Sara Cruz Instituição/*Institution*: CIPsi - Centro de Investigação em Psicologia, Universidade do Minho, Braga (Portugal) Duração/*Duration*: 2009/02 - 2013/02

Objective: With this project, we aim to identify physiological markers (central and neurovegetative nervous system measures) of sensorial processing in one-month-old infants (auditory and visual modalities) and correlate these psychophysiological responses with a) the neurobehavioral profile; and b) developmental level and mother-baby interaction at 12 months.

Method: A total of 61 caucasian circa one-month-old infants were assessed considering their visual and auditory ERP responses as well as their neurobehavioral profile. All infants were full-term with normal birth weight and Apgar score. The infants were recruited from Obstetric and Pediatric services of Woman's, Children's and Adolescent's Department of Hospital Pedro Hispano, Portugal and the informed consent was obtained from the parents. The Ethics Committee of the hospital approved the study. To elicit the psychophysiological response (the ERPs response and the cardiac, galvanic and respiratory activity) three visual and auditory stimuli intensities were design and offered to the newborn. For the visual modality we used the Grass PS33-Plus Photic Stimulator (Astro-Med Inc.) which delivers flashes of light that directly to the newborn's face (positioned at 50cm distance); the auditory paradigm was created in Presentation® software (Version 0.61.3, www.neurobs.com) and through speakers position at 20 cm from each newborn's ear the sounds were offered. For the ERPs data collection we used Quick-AmpTM System connected to ActicapTM with 32 electrodes (Brain Vision Products) and for the neurovegetative nervous system data collection, we used Biopac MP-150 (BIOPAC SYSTEM®, Santa Barbara, CA, USA) coupled with ECG 100C, RSP 100C and GSR 100C modules.

Results: Preliminary results indicate that the infants produced a different psychophysiological response to the visual and auditory stimuli. Regarding the ERPs, the primary components N1, P1 and P2 were clearly present in the ERP waveform. The N1 and P1 components latency was found to be predicting a better interactive and regulatory behavior in one-month-old infants. Likewise, considering the neurovegetative analysis, the infants who presented a better vasovagal regulation to the stimuli displayed a better interactive performance.

Conclusions: In full-term and healthy infants, different psychophysiological responses to auditory and visual stimuli predict a normal and organized interactive and regulatory behavior. However, an integrated assessment of different sensorial systems should be analyzed as they represent better behavioral marker of sensory processing.

Publications:

Góis-Eanes, M., Gonçalves, O., Caldeira-da-Silva, P., & Sampaio, A. (2012). Biological and Physiological Markers of the Tactile Sensorial Processing in Healthy Full-term Newborns. *Infant Mental Health*, pp.1-8.

Góis-Eanes, M., Cruz, S., Schuster, B., Gonçalves, O., & Sampaio, A. (2010, December). *Olfactory Event-Related Potentials in Infants*. Poster session presented at the Human Chemosensation 2010, Dresden, Germany. Conference.

Góis-Eanes, M., Cruz, S., Galdo, S., Gonçalves, O., & Sampaio, A. (2012). *Visual event-related potentials in healthy infants*. Poster session presented at the International Society for the Study of Behavioural Development 2012 Biennial Meeting, 8-12 de Julho. University of Alberta, Edmonton, Alberta, Canada. Conference.

Cruz, S., Ribeiro, E., Gonçalves, O., & Sampaio, A. *Physiological markers of neurobehavioral profiles: Evidence from visual and auditory evoked-potentials.* Poster session presented at the Society for Research in Child Development (SRCD) 2013 Biennial Meeting, 18-20 of April. Seattle, United States of America. Conference.

Scientific papers in preparation:

Visual Evoked-Potentials can predict better Social and Internal Regulation Behavior in One-month-old Infants.

Physiological Markers of Neurobehavioral Profiles – Evidence from Auditory Evoked-Potentials. Heart Rate and Respiration Frequency - Physiological Markers of Neurobehavioral Profiles.

Keywords: Infants, Psychophysiology assessment, Neurobehavioral assessment, Development

81/08 - "Subjective Experiences Associated with Seizures" - only abstract available

Investigadores/*Researchers:* Prof. Bruce Greyson, Dr. Nathan B. Fountain, Prof. Donna K. Broshek, Ms. Lori L. Derr

Instituição/Institution: Division of Perceptual Studies, University of Virginia Health System (USA) Duração/Duration: 2009/10 - 2012/10

Objectives: Alterations of consciousness are critical factors in the diagnosis of seizure disorders. With this alteration in consciousness, some persons report unusual experiences that may resemble spontaneous mystical experiences; and some persons report sensations of separating from the physical body that may resemble spontaneous out-of-body experiences. This study was designed to characterize these mystical and out-of-body-like subjective experiences associated with seizure activity.

Method: We interviewed 100 patients with seizures attending the University of Virginia Epilepsy Outpatient Clinic, regarding their recall of experiences associated with seizures. All patients interviewed, whether or not they spontaneously recalled subjective experiences associated with their seizures, were administered the Mysticism Scale, a validated instrument designed to measure intense experiences characterized by a sense of unity with the outside world and/or with "nothingness," which may or may not be interpreted religiously.

Results: 55% of the patients in this study recalled some subjective experience in association with their seizures, of whom 7 reported out-of-body experiences. We found no differentiating traits associated with patients' reports of out-of-body experiences, in terms of demographics, seizure risk factors and precipitants, localization and type of seizure, or neuropsychological functioning. Even in those few patients who report out-of-body experiences, such sensations are extremely rare events that do not occur routinely with their seizures. Most patients who reported out-of-body experiences described one or two experiences that occurred an indeterminate number of years ago. None of the patients' descriptions met the criteria for mystical experience. Although few features of mystical experience were reported in this study, those that were did not seem to be associated primarily with temporal lobe function, nor were they lateralized to either the right or left side. Mysticism Scale scores were not significantly associated with demographics, seizure risk factors and precipitants, localization and type of seizure, or neuropsychological functioning.

Conclusions: Both out-of-body experiences and mystical experiences occur very rarely in association with seizures. When they do occur, they are not differentially associated with any specific site in the brain; they are not differentially associated with any particular type of seizure; and they are not associated with any clinical measure of neuropsychological functioning.

Keywords: Seizures, Epilepsy, Mystical experience, Out-of-body experience

85/08 – "Embodied Emotions. The impact of expertise in mindfulness on the automaticity in emotion regulation strategies detected by psychophysiological parameters and self-report in a laboratory setting" – only abstract available

Investigadores/*Researchers*: Dr. Susanne Müller, Prof. Ulrike Halsband Instituição/*Institution*: Department of Psychology/Neuropsychology, University of Freiburg (Germany) Duração prevista/*Estimated duration*: 2009/09 - 2014/04

Objectives: Prior research showed that mindfulness plays an increasing role in the therapy of emotional disorders. It has been found that negative emotional states can be reduced by greater and non-judgemental awareness and acceptance. The current study yields to assess the relationship between longtime mindfulness practice and the physiological reaction (mainly of the heart rate) while watching fear-inducing film scenes.

Method: Two highly fear-inducing film scenes (*Strangers* and *Open Water*) were selected from a preceding study. While watching the scenes, the heart rate of the participants was recorded by a portable ECG-device. In order to investigate the relationship between mindfulness and physiological reaction the scenes were presented to 20 women of an average age of 41, 9 years. Half of the participants had never done any mindfulness practice, whereas the other half had daily experience for years (M = 15 years). The accuracy of emotional perception was measured via the correlation of subjective and actual heart rate changes as well as by means of self-reported emotional attention and clarity. The mindfulness component was indicated by low ratings on an emotion-regulation survey.

Results: An increased film-induced heart rate has been found (p < .01). This indicates good measurement of the fear reaction. Nevertheless, only one differentiation between the two groups could be found: Concerning the immediacy of the heart reaction while watching the film scene *Open Water*, the group with mindfulness practice showed a significantly earlier reaction to a fear stimulus (p < .05). Furthermore, a connection between heart rate and the general consumption of movies could be observed for the film *Strangers*. However, the results of the study did not necessarily confirm clearly beneficial effects of mindfulness. Due to this fact, the variety of mindfulness strategies and the only few differences between the two groups are proposed as possible influences on the observed effects.

Conclusions: Due to the well-found theoretical arguments supporting the assumed psychological mechanisms it seems promising to further inquire this still unanswered question within a pre-post study using improved instruments to measure the mindfulness components.

Keywords: Mindfulness, Physiological reaction, Heart rate, Fear, Film scenes

104/08 – "Lability and PK performance: Identifying the optimal conditions for PK-RNG effects in the laboratory using an I Ching task"

Investigador/*Researcher*: Dr. Chris A. Roe Instituição/*Institution*: Centre for the Study of Anomalous Psychological Processes [CSAPP], University of Northampton (UK) Duração/*Duration*: 2009/01 - 2013/09

Objectives: We proposed to build on the success of the Northampton approach to PK research that attempts to generate tasks that are engaging for participants and which have some personal meaning for them. This work has produced effect sizes described as 'remarkably strong'. That work would be extended here to address the following identified needs: a need to better articulate the construct of lability as an individual difference measure; to confirm previously reported interaction effects between sender and target system lability using an alternative PK testing paradigm so as to help rule out explanations in terms of methodological artifact; include measures of paranormal belief/confidence, anxiety and arousal; to explore the effects of experimenter-participant interaction and general laboratory ambience.

Method: Study 1 utilised a new PK testing program involving an I Ching divination task. Different sources of randomness (RNG, RND function in BASIC, and random numbers from published tables) were sampled to produce 3 hexagrams. Participants rated the applicability of all I Ching outcomes in advance using a Q-sort method. Study 2 was an on-line survey intended to produce a psychometrically robust measure of lability and to explore whether the construct was associated with spontaneous experience of PK phenomena. Study 3 used the refined Lability Scale from Study 2 in a further I Ching experiment, and also looked at the effects of stress and physiological arousal on performance. Study 4 retained was another I Ching RNG-PK experiment but focused on the impact upon task success of the interaction between participants and the researcher. Study 5 investigated the use of effort on the production of PK performance using a 'practice' and a 'test' I Ching trial. In the latter participants were encouraged to strive for a desired prediction along the lines suggested by Rubin and Honorton (1971).

Results: The general pattern of performance in Study 1 was in line with prediction, with highest ratings awarded to hexagrams selected by the most labile randomness source, and lowest for the most stabile source, the mean shifts were small and nonsignificant. A similar pattern was found for participant lability, and for the overall interaction. Study 2 produced a Lability Scale consisting of 71 items with acceptable overall internal reliability that incorporated five factors. Three of the factors, Intuitive Cognition, Egoorientated Cognition and Emotional Interpretation, predicted paranormal belief and psychokinetic experience scores. Study 3 also failed to replicate earlier interaction effects between participant and target system lability. Relationships between arousal measures and PK performance were inconsistent, but there were significant correlations between heart rate and low lability target system performance and between PSS and high lability performance. Study 4 also failed to find any lability interaction effect, and there were no differences found between the 'friendly' and 'formal' experimental conditions. Participant ratings of the quality of interaction were not associated with PK scores; experimenter assessments produced larger but still nonsignificant effect sizes. Study 5 did produce a significant interaction between individual lability levels and RNG lability levels ($F_{2,94} = 3.84$, p < 0.05). Performance in 'test' condition was significantly better than in the 'practice' condition for low and intermediate lability target systems, but not for high lability.

Conclusions: Only the final experiment gave rise to the proposed interaction effect, with the other three experiments giving outcomes that were very close to chance expectation. Internal effects offer somewhat more encouragement, with performance related to participant striving and suggestively to researcher ratings of experimenter-participant interaction. It would be interesting to see how other researchers might fare if attempting replications and the software and materials will be made freely available to interested parties.

Publications:

Journal papers - None as yet

Peer reviewed conference proceedings

Drennan, S.L., Roe, C.A., & Broughton, R.S. (2011). Labilty, paranormal beliefs and psychokinetic experiences: Development of the Lability scale using an online survey-based study. *Abstracts of presented papers: Parapsychological Association 54th Annual Convention, Curitiba, Brazil, August 18-21, 2011.* (pp. 25-26).

Roe, C.A., Martin, H., & Drennan, S. (2010). Effects Of Participant And Target System Lability Upon PK Performance Using An I Ching Task. *Abstracts of Presented Papers: The Parapsychological Association 53rd Annual Convention, Paris, France, July 22-25 2010.* (p. 23).

Other Conference presentations

Drennan, S.L. (2011). Lability, paranormal beliefs and psychokinetic experiences: A questionnaire-based survey. *Exploring the Extraordinary III Conference*, York, 23–25 Sept., 2011

Drennan, S.L., Roe, C.A., & Broughton, R.S. (2011). Lability, paranormal beliefs and psychokinetic experiences. *Paper presented at the Society for Psychical Research 35th International Conference*, Edinburgh University, 2-4 Sept.

Martin, H., Drennan, S.L., & Roe, C.A. (2010). Exploring Lability Interaction Between Individual And Situational Variables On PK-RNG Performance Using The I Ching. *Paper presented at the Society for Psychical Research 34th International Conference*, Sheffield University, 10-12 Sept.

Keywords: Psychokinesis, I Ching, Lability

105/08 - "Testing the Psi-mediated Instrumental Response theory using an implicit psi task"

Investigador/*Researcher*: Dr. Chris A. Roe Instituição/*Institution*: Centre for the Study of Anomalous Psychological Processes [CSAPP], University of Northampton (UK) Duração/*Duration*: 2009/01 - 2013/09

Objectives: We proposed to conduct four ESP experiments as a programmatic replication of earlier findings by Luke, Roe and Davison (2008) using an implicit psi task with contingent rewards. We planned to control for possible artifacts by rewriting the software and more directly test the PMIR theory by deriving and testing aspects of that model.

Method: Study 1 was a proof of principle replication of the Luke et al. protocol. The computer program was completely rewritten, but still presented participants with a 'personal preferences task': they were shown 15 sets of 4 abstract images and asked to indicate which was most aesthetically pleasing to them. In fact this was an implicit precognition task, and after each selection the program randomly chose one of the 4 images to be their precognitive 'target'; participants who achieved more hits than mean chance expectation were given a pleasant task as 'reward' and those scoring below MCE were given an unpleasant task as 'punishment'. Study 2 tested the PMIR prediction that the precognition task should be non-intentional in order to be effective Participants completed both non-intentional and intentional versions of the task with immediate, trial-by-trial feedback. The main focus of Study 3 was to explore the construct of latent inhibition by incorporating a more direct performance measure. The 'personal preferences task' was simplified in order to control for inherent differences in image attractiveness. Here, sets of 4 abstract images were replaced by mirror image pairs. Study 4 focused on individuals' underlying sensitivities to rewards or punishments by incorporating the BIS/BAS and SPSRQ scales. New stimuli were developed using sets of 4 versions of the same image, each rotated through 90 degrees. Finally effects on performance of experimenter-participant interactions were assessed.

Results: Study 1 Results indicated that participants scored nonsignificantly more hits than would be expected by chance alone. Performance was unrelated to scores on the luck scale, but there was a significant positive association with Openness to Experience [OE]. Study 2 findings were less encouraging, with participants performing at near-chance levels for both the non-intentional and intentional conditions. Unexpectedly, a significant negative relationship was found between the psi scores and OE levels of male participants, whereas a positive relationship with lability was observed for females only. Results of study 3 were more promising, with participants scoring suggestively above chance at the non-intentional precognition task. However, predicted relationships between psi and both Latent Inhibition and OE were not found. In Study 4 participants' non-intentional precognition hit rates were close to chance levels. Sensitivity to reward or punishment was not associated with outcome. However, ratings for participant relaxation, participant rapport, and participant positivity did correlate with psi performance.

Conclusions: Participants scored more hits than MCE in Studies 1 and 3, but scores in Studies 2 and 4 were very close chance. Combining all four studies together gives a positive but nonsignificant effect size for non-intentional precognition scores (Stouffer Z = .51), so the programme does not provide evidence in support of PMIR. Nevertheless, the overall effect size observed was greater than the mean effect size reported in Honorton and Ferrari's meta-analysis of forced-choice precognition studies, so there may be insufficient statistical power here. When combined with the original studies by Luke et al., the overall results remain highly significant (Stouffer z = 4.12, p = 0.000019).

Publications:

Journal papers

Hitchman, G.A., Roe, C.A., & Sherwood, S.J. (2012). A re-examination of nonintentional precognition with openness to experience, creativity, psi beliefs, and luck beliefs as predictors of success. *Journal of Parapsychology*, **76**(1), 109-145.

Published conference proceedings

Hitchman, G.A., Roe, C.A., & Sherwood, S.J. (2012). The Influence of Latent Inhibition on Performance at a Non-Intentional Precognition Task. *Abstracts of presented papers: Parapsychological Association 55th Annual Convention, Durham, North Carolina, August 9-12, 2012.*

Hitchman, G.A., Roe, C.A., & Sherwood, S.J. (2011). A re-examination of non intentional precognition with openness to experience, creativity, psi beliefs and luck beliefs as predictors of success. *Abstracts of presented papers: Parapsychological Association 54th Annual Convention, Curitiba, Brazil, August 18-21, 2011.* (pp. 13-14).

Other publications

Hitchman, G.A. (2012). *Testing the Psi-mediated Instrumental Response theory using an implicit psi task*. Unpublished PhD thesis, University of Northampton.

Other Conference presentations

Hitchman, G.A., Roe, C.A., & Sherwood, S.J. (2012). The effects of participant-experimenter interaction and sensitivity to rewards and punishments in a goal oriented non-intention precognition task. *Paper presented at the Society for Psychical Research 36th International Conference*, University of Northampton, 7-9 Sept. 2012.

Hitchman, G.A., Roe, C.A., & Sherwood, S.J. (2011). The relationship between lability and performance at intentional and nonintentional versions of an implicit PMIR-type psi task. *Paper presented at the Society for Psychical Research 35th International Conference*, Edinburgh University, 2-4 Sept.

Hitchman, G.A., Roe, C.A., & Sherwood, S.J. (2010). A replication of studies concerning PMIR, psi, beliefs about luck, paranormal beliefs, openness to experience and creativity. *Paper presented at the Society for Psychical Research 34th International Conference*, Sheffield University, 10-12 Sept.

Keywords: Psi-Mediated Instrumental Response, Implicit psi, Precognition

118/08 – "An Interpretative Phenomenological Analysis of Anomalous Experience at the End-of-Live" – only abstract available

Investigadores/*Researchers*: Dr. Craig D. Murray, Dr. Joanne Murray Instituição/*Institution*: Division of Health Research, Lancaster University (UK) Duração prevista/*Estimated duration*: 2009/11 - 2014/04

Objectives: The aim of the research was to explore the experience and meanings of anomalous experience surrounding end-of-life phenomena for family members and healthcare professionals.

Method: Interviews were conducted with bereaved adults and healthcare professionals. The transcribed data was analysed using Interpretative Phenomenological Analysis.

Results: Bereaved adults reported a variety of sense-of-presence experiences and how they attempted to make sense of these. Issues of validation, stigma, and positive self-perceptions were implicated in these participants mental wellbeing. Healthcare professionals spoke of the difficulties in managing the emotional impact of patients' ELEs and the value of acceptance in relation to unusual experiences.

Conclusions: Recommendations are made for service support for bereaved adults and healthcare professionals in achieving positive coping strategies in relation to ELEs.

Publications:

Keen, C., Murray, C., Payne, S. (2013). Sensing the presence of the deceased: A narrative review. *Mental Health, Religion & Culture, 16*(4), 384–402

Keen, C., Murray, C., Payne, S. (2013) A qualitative exploration of sensing the presence of the deceased following bereavement. *Mortality*, *18*(4), 339-357.

McDonald, C., Murray, C., Atkin, H. (in press) Palliative care professionals' experiences of unusual spiritual phenomena at the end of life. *Mental Health, Religion & Culture.*

Keywords: Bereavement, End-of-life, Meaning-making, Sense-of-presence

126/08 – "Experience of Pain: functional changes induced by chronic pain in the neuronal circuits of reward and aversion"

Investigadores/*Researchers*: Prof. Vasco Miguel Clara Lopes Galhardo, Prof. Deolinda Maria Valente Alves de Lima Teixeira, Dr. Clara Maria Pires Costa Bastos Monteiro, Dr. Hélder Cardoso Cruz, Dr. Maria Leonor Godinho, Dr. Daniela Seixas, Dra. Sónia Margarida Dourado Instituição/*Institution*: IBMC – Instituto de Biologia Molecular e Celular, Porto (Portugal) Duração/*Duration*: 2009/03 - 2013/10

Objectives: This research project aims at understanding the alterations that occur following the onset of prolonged and stressful pain conditions, in the connectivity of brain areas that process rewarding and aversive stimuli and in areas critical for learning and memory.

Method: For achieving our goal we use a combination of novel decision-making and working-memory operant tasks together with state-of-the-art multielectrode neurophysiology recordings in awake freely moving animals. In a tipical experiment we chronically implant 16-32 tungsten microwires in up to 4 brain areas.

Results: We obtained results on five distinct topics:

- a) Using multielectrodes implanted in the orbitofrontal cortex of adult rats performing the Rodent Gambling Task, we have shown that the neuronal firing rate was correlated with the probability of choosing a low versus high-risk food reward in each trial.
- b) Using multielectrodes implanted in the hippocampus of rats performing a food-reinforced alternation task, we showed that neuropathic pain induces an increase of the number of place fields encoded in the hippocampal networks.
- c) Using continuous 24-hour recordings in the thalamocortical loop, we showed that chronic pain disrupts sleep patterns, and causes a large decrease in the functional connectivity in the thalamocortical axis.
- d) Using *in vivo* recordings, patch clamp in brain slices, and various behavioral assays, we showed that pain increased neuronal activity in the amygdala that triggered a decrease in prefrontal activation and impaired decision-making.
- e) Using multielectrodes implanted in the hippocampus and in the prefrontal cortex we showed that pain induces a clear impairment of working memory performance that is temporally correlated with a decrease in single neuron activity in the mPFC.
- f) We demonstrated that the lack of pain in the KO mice Prrxl1^{-/-} of congenital hypoalgesia causes a behavioural and neurophysiological pattern of brain activity that is the inverse of what we observe in animals with chronic pain.

Conclusions: Our studies demonstrated that chronic pain causes a wide alteration in the functional connectivity of limbic and somatosensory brain circuits, and raises the hypothesis that therapeutic strategies aimed at reversing these alterations may be a valid tool for prolonged pain relief.

Publications:

1 book chapter, 11 published papers, and 3 papers in revision in international peer-reviewed journals of neuroscience (average impact factor of published papers: 5, 34).

Book chapters:

Galhardo, V. (2013) Dynamics of thalamic responses to noxious stimuli. In: Encyclopedic Reference of Pain, 2nd ed, Willis WD, Schmidt RF (eds), Springer-Verlag.

Full papers:

Dourado M, Cardoso-Cruz H, Monteiro C, Matos M, Galhardo V (2013). Dopaminergic modulation of risk sensitivity encoding by orbitofrontal neurons during a rodent gambling task. The Journal of Neuroscience (in preparation).

Monteiro C, Cardoso-Cruz H, Dourado M, Matos M, Lima D, Galhardo V (2013). No Pain, Big Gain: decreased anxiety and enhanced learning in the Prrxl1 knockout mice model of congenital hypoalgesia. Nature Neuroscience (in second revision).

Cardoso-Cruz H, Dourado M, Monteiro C, Matos M, Lima D, Galhardo V (2013). Modulation of hippocampal dorsoventral field connectivity by dopamine D2/3 receptor activation during spatial working-memory performance in a rat model of neuropathic pain. Proceedings of the National Academy of Sciences USA (submitted).

Cardoso-Cruz H, Sousa M, Vieira JB, Lima D, Galhardo V (2013) Prefrontal cortex and mediodorsal thalamus reduced connectivity is associated with spatial working memory impairment in rats with inflammatory pain. Pain, 154:2397-2406.

Cardoso-Cruz H, Lima D, Galhardo V (2013) Impaired spatial memory performance in a rat model of neuropathic pain is associated with reduced hippocampus-prefrontal cortex connectivity. The Journal of Neuroscience, 33:2465-2480.

Pais-Vieira M, Aguiar P, Lima D, Galhardo V (2012) Inflammatory pain disrupts the orbitofrontal neuronal activity and risk-assessment performance in a rodent decision-making task. Pain, 153:1625-1635.

Oliveira-Maia AJ, de Araujo IE, Monteiro C, Workman V, Galhardo V, Nicolelis MA (2012) The insular cortex controls food preferences independently of taste receptor signaling. Frontiers in Systems Neuroscience, 6:5.

de Visser L, Homberg JR, Mitsogiannis M, Zeeb FD, Rivalan M, Fitoussi A, Galhardo V, van den Bos R, Winstanley CA, Dellu-Hagedorn F (2011) Rodent versions of the iowa gambling task: opportunities and challenges for the understanding of decision-making. Frontiers in Neuroscience, 5:109.

Cardoso-Cruz H, Sameshima K, Lima D, Galhardo V (2011) Dynamics of Circadian Thalamocortical Flow of Information during a Peripheral Neuropathic Pain Condition. Frontiers in Integrative Neuroscience, 5:43

Cardoso-Cruz H, Lima D, Galhardo V (2011) Instability of spatial encoding by CA1 hippocampal place cells after peripheral nerve injury. European Journal of Neuroscience, 33:2255-2264

Seixas D, Sá MJ, Galhardo V, Guimarães J, Lima D (2011) Pain in portuguese patients with multiple sclerosis. Frontiers in Neurology, 2:20.

Monteiro C, Rebelo S, Galhardo V, Reguenga C, Lima D (2011) Postnatal expression of the homeobox gene Prrxl1 (Drg11) is increased in inflammatory but not neuropathic pain. European Journal of Pain, 15:477-481.

Ji G, Sun H, Fu Y, Li Z, Pais-Vieira M, Galhardo V, Neugebauer V (2010) Cognitive impairment in pain through amygdala-driven prefrontal cortical deactivation. Journal of Neuroscience, 30:5451-5464.

Silva A, Cardoso-Cruz H, Silva F, Galhardo V, Antunes L (2010) Comparison of anesthetic depth indexes based on thalamocortical local field potentials in rats. Anesthesiology, 112:355-363.

Keywords: Pain, Memory, Decision-making, Neurophysiology, Prefrontal cortex

135/08 – "Electrophysiological Correlates of Learning New Faces: A study with event-related potentials and skin-conductance responses"

Investigadores/*Researchers*: Dr. Isabel Maria Barbas dos Santos, Dr. Christopher Alexander Longmore, Dr. Jorge Manuel Costa Oliveira

Instituição/*Institution*: Laboratório de Psicologia Experimental e Aplicada (PsyLab) do Centro de Investigação em Educação e Ciências do Comportamento (CIECC), Universidade de Aveiro, Departamento de Ciências da Educação (Portugal)

Duração prevista/Estimated duration: 2009/05 - 2014/04

Objectives: Although people are extremely proficient at recognizing familiar faces, they are remarkably poor at recognising unfamiliar ones. Little research has investigated the mechanisms by which novel faces become familiar. This project aimed to investigate how new faces are learned, using event-related potentials (ERPs) and skin-conductance responses (SCRs) to assess implicit measures of recognition, as well as explicit behavioural measures.

Method: In several studies, we investigated the potential benefit of learning novel faces in more than one viewpoint when recognition from an unseen viewpoint is required and the role of prototype formation in learning new faces. Most of the studies were based on a paradigm where participants underwent an extensive learning procedure where they saw novel faces either in one or two viewpoints (frontal, profile or both) and were tested for recognition in the seen (frontal and profile) and unseen (three-quarter) views.

Results: Behavioural and SCR results did not reveal a global advantage for the faces learned in two viewpoints compared to one for the critical three-quarter view, suggesting that participants extract mostly pictorial/viewpoint dependent codes. Nonetheless, ERP results showed a modulation of the N170 face-related ERP by the number of learning views, whereby faces learnt in a single view elicited more negative amplitudes than faces learnt in two viewpoints, when tested on the three-quarter view. This result is compatible with a facilitation effect of learning two viewpoints when recognition on a previously unseen view is required compared to learning a single viewpoint, indicating some degree of generalisation from full-face and profile views to an unseen three-quarter view. Other studies also provided some evidence that participants extracted both the mean of the two studied images (i.e. the prototype) as well as storing the seen exemplars.

Conclusion: ERPs suggested that some kind of structural information was extracted during learning, which facilitated recognition from novel views, even though this was not apparent in behavioural performance or other indirect measures, like SCRs. However, another set of studies provide support for a face processing system that extracts the mean representation of the face (the prototype) whilst at the same time storing exemplars. These effects will need to be investigated further in future experiments.

Keywords: Face recognition, Unfamiliar faces, ERP, N170, Prototypes

136/08 – "Psychophysiological Markers of Externalizing Personality in Non-Clinical and Criminal Populations"

Investigadores/*Researchers*: Dra. Isabel Maria Barbas dos Santos, Dr. Jorge Manuel Costa Oliveira, Dr. Paula Emanuel Rocha Martins Vagos, Prof. Nick Anthony DeFilippis

Instituição/*Institution*: Laboratório de Psicologia Experimental e Aplicada (PsyLab) do Centro de Investigação em Educação e Ciências do Comportamento (CIECC), Universidade de Aveiro, Departamento de Ciências da Educação (Portugal)

Duração/Duration: 2009/01 - 2014/02

Objectives: This project aimed to identify the psychophysiological markers of externalizing personality within a non-clinical population, during performance on a range of executive, emotional and social tasks. Externalization is a higher-order psychopathology factor that seems to underpin a number of the most frequent conduct disorders, including childhood conduct problems, adult antisocial behaviour, and substance-use disorders, being a high-risk factor for psychopathy. A common behavioural pattern reflected in many manifestations of externalizing is poor impulse control and an apparent failure to learn from experience. This raises the possibility that externalizing may involve a deficit in executive cognitive function. Additionally, and based on evidence that misinterpretation of social and emotional cues can result in the generation of inappropriate social responses, such as violence, it has been hypothesised that high externalizers may have some deficit in emotional and social processing from faces.

Method: The project involved the translation and adaptation to Portugal of the Externalizing Inventory (ESI), which was subsequently applied, together with other measures of personality, anxiety and depression, to a sample of 426 university students. Based on their externalizing scores (high, average and low), a sample of 58 participants was tested in a number of laboratory tasks of executive, emotional and social processing, with the co-registration of EEG/ERP.

Results: The validation studies of the ESI showed good psychometric qualities, consistent with the original structure of the instrument. Participants scoring high and average on the externalizing vulnerability performed significantly worse on the subscale "Loss of Set – Conceptual" of the Halstead Category Test than participants scoring low, and ERP differences were also observed in executive tasks. Results from a speeded emotion categorization task (emotional vs. neutral face) showed significantly slower RTs in the angry and happy conditions for the high externalizers than low externalizers, as well as differences in early and late ERPs.

Conclusions: Present results indicate that a higher externalizing vulnerability is associated with an increased difficulty at the level of abstract concept formation and poor cognitive flexibility. Moreover, there is evidence of an emotion specific deficit for high externalizers.

Keywords: Externalizing, ERP, Executive function, Emotion, Social cognition

141/08 – "Neural and Computational Mechanisms of Conscious and Unconscious Decisions Under Uncertainty"

Investigadores/*Researchers*: Dr. Edward Vul, Prof. Nancy Kanwisher, Prof. Joshua Tenenbaum Instituição/*Institution*: Department of Psychology, University of California, San Diego, CA (USA) Duração/Duration: 2010/11 - 2014/02

Objectives: We quantified contributions of various sources of uncertainty to risky decision-making across domains. We have measured such behavior for conscious and unconscious perception in tasks ranging from intuitive physics in infants and adults, binocular rivalry, and early visual processing.

Method: We ask people to make decisions under risk in scenarios where the environment is uncertain, and compare their behaviour to Bayesian ideal observers. Combining psychophysical experiments with Bayesian computational cognitive modelling, allows us to precisely characterize which sources of uncertainty people consider, and how they are combined to yield decisions.

Results: In visual search, we found that people learn target distributions from the environment, and integrate this learning with uncertain, sparse measurements of the richness of a given scene, to yield near-optimal foraging behavior.

In intuitive physics, we showed that a simple kinematic model can account for infants' surprisal in an object perception experiments, indicating that infants combine uncertainty about object dynamics and with base rates. In adults, most of the uncertainty in these cases arises from stochastic dynamics: our forward physical models are not deterministic, but are themselves uncertain.

Our models of perception, showed that uncertainty in timing of rapid sequences of events can explain repetition blindness, attentional blink, and their error patterns. Moreover, bistability during binocular rivalry reflects optimal inference given uncertainty about the latent causes of visual input, with MCMC inference capturing global and local perceptual dynamics.

Conclusions: Overall, our results suggest a theory in which optimal uncertain reasoning, with approximate inference algorithms, can offer "rational process models" of human cognition.

Publications:

Cain MS., Vul E., Clark K. & Mittroff SR. (2012) A Bayesian optimal foraging model of human visual search. *Psychological Science*,

Teglas E., Vul E., Girotto V., Gonzalez M., Tenenbaum JB. & Bonatti LL. (2011) Pure reasoning in 12month-olds as probabilistic inference. *Science*, *332*(6033), 1054-1059

Gershman S., Vul E. & Tenenbaum JB. (2012) Multistability and perceptual inference. *Neural Computation*, 24(1), 1-24

Reith CA. & Vul E. (2012) Expectations About the Temporal Structure of the World Result in the Attentional Blink and Repetition Blindness, 34th Cog Sci.,

Griffiths TL., Vul E. & Sanborn AN. (2012) Bridging Levels of Analysis for Probabilistic Models of Cognition, *Current Directions in Psychological Science*, 21(4), 263-268

Vul E., Sullivan J. & Barner D. (2013) Slow drift of individuals magnitude-to-number mapping. Proceedings of the 35th Annual Meetings of the Cognitive Science Society,

Smith KA. & Vul E. (2013) Sources of Uncertainty in Intuitive Physics, *Topics in Cognitive Science*, 5(1), 185-199

Smith KA., Huber DE. & Vul E. (2013) Multiply-constrained semantic search in the Remote Associates Test, *Cognition*, *128*, 64-75

Vul E., Lashkari D., Hsieh PJ., Golland P. & Kanwisher N. (2012) Data-driven functional clustering reveals dominance of face, place, and body selectivity in the ventral visual pathway. *Journal of Neurophysiology*.

Keywords: Human reasoning, Bayesian modelling, Uncertainty, Risky decision-making
180/08 – "Emotional influences on psychophysiological indices of focused attention and response anticipation in social anxiety: A combined neuroimaging and electroencephalographic study"

Investigadores/Researchers: Dr. Yoko Nagai, Prof. Hugo Critchley, Dr. Marcus Gray Instituição/Institution: Clinical Imaging Sciences Centre, Brighton and Sussex Medical School, University of Sussex (UK)

Duração prevista/Estimated duration: 2009/10 - 2014/04

Objective: Social anxiety disorder (SAD) is a common psychiatric condition affecting 3 -13 % of population. The characteristics of SAD includes heightened arousal, inability to focus and blocking of productive behaviour accompanying subjective fear or loss of control triggered by the presence or anticipation of social challenge. Novel insights into the mechanisms through which emotional processes interfere with basic cognitive and behavioural processes may shape future approaches to the management of social anxiety.

Method: In the current study, we examined the impact of emotional distraction (emotional face stimuli presented in the interval of the forewarned reaction time task) on the Contingent Negative Variation (CNV) and related brain activity. CNV refers to anticipation related slow cortical potential indicate cortical excitation. 15 healthy and 5 patients with social anxiety disorder went through combined neuroimaging (fMRI) with simultaneous EEG to index neural activity associated with focused attention during response anticipation.

Results: The basic CNV task replicated findings reported in our previous study regarding cortical excitability and attentional deployment (Nagai et al., 2004). Here the anticipatory motor preparation during the forewarned reaction time was associated with enhanced neural activity within, bilateral thalamus, midcingulate, SMA, motor and accessory motor regions (associated with button press response). Brief presentation of different emotional faces during CNV task (between warning and imperative tones) modulated neural activation related to CNV task. Specific neural activation related to face presentation relative to scrambled face stimuli was identified within bilateral fusiform gyri. Comparison of negative emotional faces (angry, disgust and fear) versus other face stimuli (neutral, happy and scrambled) robustly engaged amygdale bilaterally and enhanced fusiform and inferotemporal cortices. Contrary to our initial hypothesis regarding the suppression of CNV-related activity during processing of 'anxiogenic' negative emotional stimuli, activation of thalamus and cingulate cortices was positively correlated with CNV task related neural activation within these regions.

Conclusion: The neural substrates of supporting anticipatory attentional engagement during the CNV forewarned reaction time task are modulated by the 'attention grab' of negative emotional faces. However our neuroimaging evidence suggests enhanced augmentation of shared distributed attention related activity suggesting compensatory recruitment of midline attentional systems alongside the dedicated engagements of face and emotion-related substrates. Importantly our findings predict a mechanisms non-linear load-dependent decompensation and suggest targets for modifying the impact of social anxiety on task performance.

Keywords: Social anxiety disorder, Contingent Negative Variation (CNV), Attention

189/08 – "Exploration of the Effect of Local Geomagnetic Activity and Tibetan Buddhist Meditation on Psychic Awareness"

Investigadores/*Researchers*: Dr. Serena M. Roney-Dougal, Dr. Adrian Ryan Instituição/*Institution*: Psi Research Centre, Glastonbury, Somerset (UK) Duração/*Duration*: 2009/10 - 2013/07

Objectives: Research in parapsychology has found evidence that psychic experiences (psi) are related to fluctuations (termed geomagnetic activity (GMA)) in the Earth's magnetic field. However, in some studies psi is related to higher GMA and in some with lower GMA. It has been suggested that this anomaly may be clarified by studying local measurements of GMA. Therefore, a four-year study was conducted with experienced meditators located close to a geological observatory. Throughout the period of experimentation solar activity, and consequently GMA, was at its lowest level in 100 years.

Method: The experimental design was identical to that used in previous meditation research (Roney-Dougal & Solfvin, 2012): after a 15-minute meditation period, the participant attempted to identify a 'target', which was a pseudo-randomly selected video clip. The computer programme (PreCOG) chose a target set at random from a pool of 25 sets, and a target video clip at random from the four-clip set. Each participant completed a minimum of eight sessions each year. There were 25 participants, all meditators residing at Kagyu Samye Ling Tibetan Centre or in the nearby village, who had practiced meditation for at least ten years. Three questionnaires and one psychological test were completed: the Meditation Attainment Questionnaire (MAQ) is a measure of the level of meditation attainment achieved; the Freiburg mindfulness questionnaire (FMI) assesses the level of mindfulness attained; the Necker cube test is a measure of focus of attention; and the Temporal Lobe Epilepsy (TLE) questionnaire assesses temporal lobe lability, which may indicate both a participant's propensity for psi-type experiences and the degree to which the person is affected by GMA. Geomagnetic field measurements were supplied by the British Geological Survey's Eskdalemuir observatory, which is located two miles from Samye Ling.

Results: The main findings were:

Overall, males scored negatively (mean psi score = -0.15, p = .02, 2-tail), whereas females scored at chance; the difference was significant (p = .03).

Psi scoring was non-significantly lower at high levels of band 3 GMA. The GMA threshold at which scores dropped was close to that observed in a similar study conducted at Lancaster University.

Participants whose psi scoring correlated most strongly with GMA were those with the highest scores on the TLE questionnaire; this effect bordered on significance (p = .06).

The data exhibited seasonal effects somewhat similar to those found by Sturrock & Spottiswoode (2007).

Conclusions: The unusually low-level of GMA during the period of the study made it impossible to fully realize the aims. However, the correlation between psi scoring and band 3 GMA was as hypothesized.

Publications:

Roney-Dougal, S.M., Ryan, A. & Luke, D. (2013). The relationship between local geomagnetic activity, meditation and psi. Part 1: Literature review and theoretical model, *Journal of the Society for Psychical Research*, 77(2), 72-88.

Keywords: GMA, Psi scoring, Meditation.

2010

01/10 – "Neurocognitive Correlates of the Out-of-Body Experience and Kindred Hallucinations of Embodiment and the 'Self'"

Investigador/*Researcher*: Dr. Jason John Braithwaite Instituição/*Institution*: Selective Attention and Awareness Laboratory (SAAL) Behavioural Brain Sciences centre, School of Psychology, University of Birmingham (UK) Duração/*Duration*: 2011/03 - 2013/05

Objectives: The current project investigated neurocognitive biases underlying predisposition to striking out-of-body experiences (OBEs). More specifically, the current project investigated; (i) biases in exocentric perspective-taking that may underlying external perspectives in OBEs; (ii) biases in susceptibility / resistance to the rubber-hand illusion as a function of such anomalous bodily experiences; and (iii) degrees of cortical hyperexcitability in those who report OBEs relative to control participants.

Method: A variety of behavioural and psychophysiological methods were used and devised for the current project, including reaction time behavioural experiments, common methods for the rubber-hand illusion paradigm, and newly devised pattern-glare tasks for measuring cortical hyperexcitability.

Results: OBEers were more efficient at adopting exocentric perspectives in a spatial task relative to participants who did not report such experiences. In addition, OBEers declared the presence of the rubber-hand illusion later than controls and showed distinct profiles in terms of their autonomic emotional responses (electrodermal activity / skin conductance responses) relative to control participants. Furthermore, those reporting OBEs showed signs of elevated cortical hyperexcitability relative to control participants.

Conclusions: Collectively, the present findings suggest that specific neurocognitive biases may predispose certain individuals to have these striking anomalous bodily experiences. These results are generally consistent with a "Dysconnection" account of hallucinatory experience where aberrant connectivity between and within brain regions predispose the individual to anomalous experience and disorders in self consciousness.

Publications:

Braithwaite, J.J., James, K., Dewe, H., Medford, N., Takahashi, C., & Kessler, K (2013). Fractionating the unitary notion of dissociation: Disembodied but not embodied dissociative experiences are associated with exocentric perspective-taking. *Frontiers in Neuroscience*, 7:719. doi:10.3389/fnhum.2013.00719.

Braithwaite, J.J., Broglia, E., Bagshaw, A.P, Wilkins, A.J. (2013) Evidence of elevated cortical hyperexcitability and its association with out-of-body experiences in the non-clinical population: New findings from a Pattern-Glare Task. *Cortex.* 49, 793-805.

Braithwaite, J.J., & Broglia, E (2012). Exploring embodiment and perspective-taking in reports of outof-body experiences in the non-clinical population. *Cognitive Processing*, *13*, Springer-Heidelberg. (Published proceedings of "Bodily awareness and embodied mental transformations of egocentric space" *symposium of the 5th International Conference on Spatial Cognition (ICSC), Rome, Italy*, September, 2012).

Braithwaite, J.J., Broglia, E., & Watson, D.G. (2014 / in press). Autonomic emotional responses to the induction of the rubber-hand illusion in those that report anomalous bodily experiences: Evidence for specific psychophysiological components associated with illusory body representations. *Journal of Experimental Psychology: Human Perception & Performance*.

Keywords: Out-of-body experiences, Perspective-taking, Embodiment, Dissociation, Cortical hyperexcitability

08/10 – "Hallucination Experience and Psi (Phase II): New Psychological, Psychopathological, Psychophysiological and Transcultural Approach"

Investigadores/Researchers: Dr. Alejandro Enrique Parra, Dr. Romina Ileana Mielgo, Dr. Irma Juana Caputo

Instituição/Institution: Universidad Abierta Interamericana, Facultad de Psicología, Buenos Aires (Argentina)

Duração/Duration: 2011/03 - 2013/01

Objectives: The purpose of the present study is to test whether hallucinatory experiences respond to the dimensionality principle and whether they occur in non-psychotic disorders. Hence, we will try to detect potential differences (if they were so) between a group of "hallucinators" and a group of "non-hallucinators" with regard to personality and psychopathological traits.

Method: Six hundred fifty six undergraduate students, 76% females and 24% males (age range 17-57), completed seven scales, such as the *Hallucination Experiences Scale*, *Paranormal Experiences Questionnaire*, *Creative Experiences Questionnaire*, *Tellegen Absorption Scale*, *Dissociative Experiences Scale*, *Schizotypical Personality Questionnaire*, and *Eysenck Personality Inventory*.

Results: Data for persons seeing apparitions (and having other experiences) were compared with data for those who did not. Experients scored higher on absorption (z = 6.06), dissociation (z = 4.65), fantasy proneness (z = 4.76) and cognitive perceptual schizotypy (z = 8.21) than non-experients. Twentyfour (80%) out of 30 correlations were also significant.

Conclusions: Apparitional and apparition-like experiences are related to higher levels of reports of absorption, dissociation and imaginative-fantasy experiences. Such findings suggest that visions of ghosts may be related to cognitive processes involving fantasy and cognitive perceptual schizotypy proneness, which are correlated with each other. The results showed a higher level of cognitive-perceptual, schizotypy, absorption, dissociation, fantasy and hallucination proneness, and visual imagery in experiencers than in non- experiencers and confirm previous studies. The findings suggest that especially cognitive-perceptual aspects of schizotypy, such as disturbances in sense of self, certainly of self, and self-awareness, are essential features of persons who had paranormal experiencers.

Publications:

Books

(2011). ¿Qué es... Sensibilidad Psíquica? Buenos Aires: Longseller. ISBN: 978-987-582-108-8. Pp. 190. Peer review articles

(2011). Encuesta on-line de experiencias anómalo/paranormales y su impacto emocional: Relación con género, edad, y otras variables. *Persona, 14*, pp.211-228.

(2011). Indicadores de propensión a la esquizotipia en individuos creyentes en lo paranormal: Examinando la intensidad de la imaginería y las experiencias alucinatorias. *Psicología: Teoria e Prática, 12*(3), 78-94.

(2011). Encuesta on-line de experiencias anómalo-paranormales y su impacto emocional: Relación con género, edad y otras variables. En F.E. da Silva (Ed.), *Séptimo Encontro Psi: Pesquisa Psi e Psicología Anomalística* (pp. 99-108). Curitiba, Paraná: Facultades Integradas "Espírita".

(2012). Varieties of clinical practices with exceptional experiences. Third International Expert Meeting on Clinical Parapsychology. *MindField*, 4(2), 53-55.

(2012). Relación entre las experiencias paranormales y esquizotipia positiva/negativa. *Acta Psiquiátrica y Psicológica de América Latina*, 58(4), pp. 246-255.

(2012) Experiencias perceptuales inusuales, experiencias anómalo/paranormales y propensión a la esquizotipia. *Universitas Psychologica, 11*, pp.657-666.

(2013). Experiencias paranormales y su relación con el sentido de la vida. *Liberabit*, *19*(2), pp. 33-44. <u>Symposiums</u>

(2011). Variedades de la experiencia alucinatoria y la experiencia psi. En F.E. da Silva (Ed.), *Séptimo Encontro Psi: Pesquisa Psi e Psicología Anomalística* (p. 211). Curitiba, Paraná: Facultades Integradas "Espírita".

Keywords: Hallucination experience, Cognitive-perceptual schizotypy, Absorption, Dissociation, Fantasy proneness

21/10 – "Effects of intentionally enhanced tea on mood"

Investigadores/*Researchers*: Prof. Yung-Jong Shiah, Dr. Dean Radin Instituição/*Institution*: Psychology Department of Kaohsuing Medical University, Kaohsuing, (Taiwan) Duração/*Duration*: 2011/04 - 2012/11

Objective: This study explored whether drinking tea "treated" with good intentions would enhance mood more than drinking ordinary tea, under double-blind, randomized conditions.

Method: Stratified random sampling was used to assign 189 adults into two groups matched by age, gender, the psychological trait of neuroticism, and the amount of tea consumed on average per day. All participants were Taiwanese and lived in Kaohsiung, Taiwan, and the test was conducted over the course of one week to reduce mood fluctuations due to changes in local weather and other common influences. Each evening for 7 days in a row volunteers recorded their mood using the Profile of Mood States questionnaire. On days 3, 4 and 5 of the test each participant drank 600 cc of oolong tea in the morning and again in the afternoon. One randomly assigned group blindly received tea that had been intentionally treated by three Buddhist monks; the other group blindly received untreated tea from the same source. On the last day of the test each person indicated what type of tea they believed they had been drinking.

Results: Those who drank treated tea showed a greater increase in mood than those who drank untreated tea (Cohen's d = 0.65, p = 0.02, two-tailed). Change in mood in those who believed that they were drinking treated tea was much better than those who did not believe (Cohen's d = 1.45, p = 0.00002, two-tailed).

Conclusion: Tea treated with good intentions improved mood more than ordinary tea derived from the same source. Belief that one was drinking treated tea produced a large improvement in mood, but only if one was actually drinking the treated tea, indicating that belief and intentional enhancement interact. This also suggests that the aesthetic and intentional qualities associated with the traditional tea ceremony may have subtle influences that extend beyond the ritual itself.

Publication: The study was accepted for publication by the Explore-The Journal of Science and Healing.

Keywords: Intention, Tea, Mood, Mind-matter interaction

32/10 – "Facilitating healthy ageing: Investigating neuroprotective effects of mindfulness" Investigadores/*Researchers*: Dr. Peter Malinowski, Prof. Thomas Gruber, Dr. Cathy Montgomery Instituição/*Institution*: Liverpool John Moores University, School of Natural Sciences and Psychology Byrom Street, Liverpool (UK)

Duração/Duration: 2011/04 - 2013/05

Background: The demographics of most Western countries are changing towards a larger proportion of older people and the health of this ageing population is of major concern. The decline of memory functions and attentional control mechanisms as for instance the ability to ignore or suppress potentially interfering information or to switch flexibly between tasks constitutes a significant challenge. In recent years clear evidence for neural plasticity of functional relevance in older people has accumulated and there is indirect indication that mindfulness practices may serve neuroprotective functions. We thus argue that mindfulness training may have utility for increasing cognitive reserve, a potential mechanism by which age-related declines in cognitive functions may be mitigated.

Objectives: We investigated whether regular engagement with a simple and brief mindfulness practice would result in improvements in the self-regulation of attention and foster changes in neuronal activity related to attentional control.

Method: A longitudinal randomised active control group study was conducted to compare the effects of mindfulness training exercises (MT) to simple brain training exercises (BT) in a sample of 56 aged participants (mean age 64.5 years). At baseline and after 7 to 8 weeks of MT or BT, the participants completed various tasks that assess attentional control processes, while their brain activity was recorded with EEG.

Results: In line with improvements in behavioural performance, event-related potential (ERP) analysis demonstrated that MT resulted in significant changes in ERP components (N2 and P3a) indicative of improved focal attention and response inhibition; BT did not.

Conclusions: This is the first longitudinal study confirming that mindfulness practice is causally effective in improving cognitive performance in older participants. The observed improvement of neurophysiological markers of attentional functions (N2, P3a) is encouraging in light of previous research into cognitive ageing and neurodegenerative diseases which has shown that N2 and P3a mean amplitudes are diminished in the aged, with the former often absent and the latter linked to mild cognitive impairment and Alzheimer's disease. Our findings suggest that MT alters the efficiency of allocating cognitive resources, leading to improved self regulation of attention in older individuals. They indicate that a mindfulness-based approach may contribute to achieving better cognitive health.

Keywords: Mindfulness, Attention, Cognitive ageing, Randomised active controlled trial, EEG

37/10 – "Psychophysiological mechanisms of hierarchical novelty detection in the human auditory brain"

Investigadores/*Researchers*: Prof. Carles Escera, Dr. Sabine Grimm, Dr. Marc Recasens Instituição/*Institution*: Research Institute for Brain, Cognition and Behavior (IR3C) and Department of Psychiatry and Clinical Psychobiology, Faculty of Psychology, University of Barcelona (Spain) Duração/*Duration*: 2011/04 - 2013/03

Objectives: The present project aimed at demonstrating that novelty detection is a basic principle of the functional organization of the auditory system, expanding from lower levels along the auditory pathway in the brainstem up to higher-order areas of the cerebral cortex. Traditionally, auditory novelty detection has been studied by means of the mismatch negativity (MMN) evoked potential, generated in the auditory cortex with a latency of about 100-150 ms.

Method: Auditory Evoked Potentials in the Middle Latency Response (MLR) were recorded in human healthy participants to sequences of sounds feature two types of stimuli: A frequently repeated one ("standard") and low probability, rare one ("deviant"). In different experiments, "deviants" differed from the "standards" in intensity (Althen et al., 2011) or spatial origin (location; Grimm et al., 2012).

Results: Auditory stimuli differing in intensity or in location from the preceding acoustic regularity established by the repetition of the standards, not only elicited the MMN but much earlier deviance-related correlates, by the Na for location and by the Na-Pa transition for intensity changes, respectively. These effects occurred only at 20-30 ms from change onset, revealing that deviance detection is a pervasive property of the auditory system. Moreover, as the experiments were appropriately controlled, so that deviant stimuli were compared to identical low probability stimuli but occurring on a context random stimuli, the present results support deviance detection based on regularity encoding.

Conclusions: Together with related results from other studies in our group, the results of the present project support that deviance detection based on regularity encoding is a pervasive property of the auditory system. Furthermore, we proposed a model where much more complex types of regularity would be encoded higher up in the auditory hierarchy yielding change-related effects only by the latency window of the MMN (Grimm & Escera, 2012).

Publications:

Althen H, Grimm S, Escera C. (2011). Fast detection of unexpected sound intensity decrements as revealed by human evoked potentials. *PLoS ONE*, 6(12):e28522.

Grimm S, Recasens M, Althen H, Escera C. (2012). Ultrafast tracking of sound location changes as revealed by human auditory evoked potentials. *Biol Psychol*, 89:232-239.

Grimm S, Escera C. (2012). Auditory deviance detection revisited: Evidence for a hierarchical novelty system. *Int J Psychophysiol*, 85:88-92.

Keywords: Auditory perception, Sound detection, Regularity encoding, Involuntary attention, Sensory memory

39/10 – "Paranormal Belief, Evaluation of Paranormal Experiences, Schizoptypy and Reality Testing"

Investigadores/Researchers: Dr. Neil Andrew Dagnall, Dr. Gary Munley, Dr. Andrew Parker, Dr. Kenneth Drinkwater

Instituição/*Institution*: The Manchester Metropolitan University, Research Institute of Health and Social Change, Faculty of Health, Psychology and Social Care, Dep. of Psychology, Manchester (UK) Duração/*Duration*: 2011/09 – 2013/11

Objectives: The present study examined the relationship between performance on probabilistic reasoning tasks and belief in the paranormal. Of particular interest was the degree to which misperception of chance and conjunction fallacy were associated with belief in the paranormal.

Method: An opportunity sample of 305 participants (64 male & 241 female) took part in the study. Mean age 22.97, SD = 8.19). Each participant completed a booklet containing paranormal scales (Revised Paranormal belief scale, Australian Sheep Goat Scale and the Manchester Metropolitan University New Scale), a reality testing measure and probabilistic reasoning tasks (perception of randomness; base rate; conjunction fallacy, standard vs. paranormal context; & probability). Scale order was counter-balanced across participants.

Results: Findings were consistent across paranormal belief measures. Reasoning performance correlated negatively with belief in the paranormal; as belief in the paranormal increased the number of problems solved decreased. No association was found between overall reasoning performance and reality testing. Regression revealed the best predictor of paranormal belief to be perception of randomness. Comparisons (below vs. above the median) supported the regressional analysis. Participants below the median solved more perception of randomness problems. A similar result was observed for reality testing. No consistent effects were found for conjunction fallacy. Interestingly, a difference was observed between conjunction types (standard vs. paranormal). Although, participants produced more correct responses when problems were framed in a paranormal context, framing effected low and high belief groups differently; participants above the median solved fewer paranormal conjunction problems than those below. Significant negative correlations were found between the number of paranormal conjunctions solved and paranormal measures. Similarly, a negative correlation was found between reality testing and conjunction solved.

Conclusion: The findings support the notion that paranormal believers demonstrate greater misappreciation of probability when faced with perception of randomness tasks. However, there was no evidence to support the notion that conjunction fallacy is a major factor associated with the development and maintenance of paranormal belief.

Publications: Project findings are currently being prepared for publication in peer reviewed academic journals.

Keywords: Reasoning, Paranormal Belief, Reality Testing

42/10 - "Conscious Induction of Theta EEG Patterns by a Healing Procedure"

Investigadores/*Researchers*: Dr. Stefan Schmidt, Dr. Thilo Hinterberger Instituição/*Institution*: Center for Mindfulness, Meditation and Neuroscience Research, Institute of Environmental Health Sciences, University Medical Center Freiburg (Germany) Duração/ *Duration*: 2011/11 – 2013/03

Objectives: A new healing procedure termed ThetaHealing is making extraordinary claims regarding healing effects and healing mechanism. The method is propagating quickly but so far no scientific evaluation has been conducted. One of the basic claims of ThetaHealing is that the experienced theta healer enters via a special meditation in a so-called 'theta state'. According to ThetaHealing alleged healing effects are taking place in this special state which is also induced in the patient by the healer.

Method: The name ThetaHealing originates from the fact that this 'theta state' is correlated with strong theta rhythmic activity patterns (4-7Hz) in the respective EEG of healer and patient. In this study we assessed this claim in a dual EEG study where we have recorded simultaneously EEG from 10 experienced ThetaHealers and 10 naïve patients. Our hypotheses were that (i) the healers taught in this method will elicit theta rhythmic activity at will in their EEG. (ii) there will be an increase of theta rhythm brain activity in the patient once the ThetaHealer tried to connect to his/her state to the patient and (iii) there will be significant more correlational patterns between the healer's and the patient's EEG once both are in the so called theta state compared to a control condition.

Results: We found no changes in theta activity for different healing phases and comparisons in the clients. We furthermore found either no changes or even significant decreases of theta-activity in the healers. Over the course of the whole session theta-activity decreased significantly in healers. With respect to correlation patterns between the power spectra of healers and clients of the same session we found either none or only moderate correlations. There was no excess of significant correlations compared to baseline measures.

Conclusion: Overall it is concluded that none of the claims of ThetaHealing could be supported by the data of our study. Our study had good internal validity and moderate to good external validity. Thus we consider our results as valid. Our study has not assessed any aspects of the claim to heal clients by this methods and no conclusion can be made with regard to this claim.

Publications:

von Haugwitz, A.-C. (in preparation) "Grundlagenforschung zur Induktion eines Theta-Rhythmus durch ein Heilverfahren", Medical Dissertation, Medical Faculty of the University of Freiburg.

Keywords: ThetaHealing, EEG, Spectral analysis, Simultaneous EEG measurement

50/10 - "Trance: Cortical Representations" - only abstract available

Investigadores/*Researchers*: Dr. Alessandra Ghinato Mainieri, Dr. Julio Fernando Prieto Peres, Prof. Alexander Moreira de Almeida, Prof. Ute Habel, Dr. Nils Kohn

Instituição/Institution: Department of Psychiatry and Psychotherapy, RWTH Aachen University, Aachen (Germany)

Duração/Duration: 2011/03 - 2013/05

Objectives: Evidence has shown that there are high levels of psychotic experiences in the general population, often not related to mental disorders. We investigated the neural correlates of psychotic experiences in healthy spiritual mediums.

Method: A fMRI study was developed with 8 healthy mediums and 6 controls. The mediums entered in mediumistic trance state using a standardized manner; in a control condition they were instructed to reenact the same mediumistic experience that they had during trance condition but in a non-trance state. Both groups took part in a resting state session. The data was analysed using model-based (GLM) and model-free analysis (ICA).

Results: Vivid mediumistic state and deep level of spiritual connection reported by the mediums during trance were associated with stronger activation areas related to sensory and attentional networks compared to re-enaction and rest: lateral occipital cortex, posterior cingulate cortex, temporal pole, middle temporal gyrus and orbitofrontal cortex. We also observed increased functional connectivity within the regions of sensory and auditory resting state networks for mediumistic state compared to control condition. The default mode network (DMN) was identified in all conditions and groups. However, we did not find any change in connectivity within the regions of DMN (between conditions or groups).

Conclusions: Increased activation in cortical sensory and attentional areas during mediumistic state and preserved functional connectivity within the DMN regions might reflect an expression of the non-pathological nature of psychotic experiences in mediums. Our results are not conclusive but point out to a possible heterogeneity between the populations who present hallucinatory experiences. Further investigations comparing mediumistic states to pathological and drug induced delusions and hallucinatory states would provide more evidences on the neural correlates underlying hallucinatory states in nonclinical populations especially interactions between the DMN and neural correlates of pathological and non-pathological dissociative and hallucinatory states.

Publications: The preliminare results of the study were presented as poster in the DGPPN (Deutsche Geselschaft für Psychiatrie, Psychotherapie und Neurologie) in Berlin in 2012. The original paper is under submission.

Keywords: fMRI, Spiritual and anomalous experiences, Psychotic experiences

55/10 – "The developmental and psychophysiological emergence of dreams and nightmares: statedependent and state-independent fronto-cortical disconnectivity"

Investigadores/*Researchers*: Dr. Róbert Bódizs, Dr. Peter Daniel Simor, Dr. Piroska Sándor, Dr. Szilvia Csóka, Klára Horváth

Instituição/Institution: Institute of Behavioural Sciences, Semmelweis University, Budapest (Hungary) Duração/Duration: 2011/03 - 2014/02

Objectives: Our aim is to characterize sleep and to test the frontal dysfunction hypothesis of subjects with frequent nightmares, as well as to bridge the relationship between the ontogeny of frontal-executive and emotion regulation functions with age-related peculiarities of dreams and nightmares.

Method: Computer testing of frontal-executive functions as well as two-night polysomnographic investigations of young adult nightmare sufferers and controls was performed. A similar investigation of 4–8 years old children was implemented. The latter studies were paralleled by the development and execution of a home dream collection method adapted to the specific psychological features of children between the ages of 4–8 years. Reports on children dreams were subjected to a content analysis procedure.

Results: Nightmare sufferers are characterized by performance decreases in several executive tasks including the Emotional Go/NoGo, the Emotional Stroop, and the Verbal Fluency tasks. Moreover, alterations in the macrostructure of sleep (decreases: sleep efficiency and slow wave sleep; increases: wakefulness, nocturnal awakenings, REM sleep), microstructure of sleep (increases in A2-type microarousals of the cyclic alternating pattern), and sleep EEG spectra (increased REM sleep high alpha power and phase synchronization), paralleled by a more pronounced first-night effect were also revealed. Children were characterized by the lack of a significant age-effect in polygraphic sleep measures, by the positive correlations of dream report length and performance in the Emotional Stroop test as well as by an inverse relationship between the developmental level of executive functioning and dream recall frequency. Neither IQ nor the scores on the subtests of the intelligence test battery correlated significantly with dream report length or quality.

Conclusions: Our results suggest that individuals with frequent nightmares are characterized by impairments in executive tasks involving the suppression of task-irrelevant semantic representations. Moreover, nightmare-related alterations in sleep architecture and microstructure are characterized by wakefulness (-like) intrusions disturbing the neuro-cognitive organization of sleep, as well as by emotion-related increases in REM propensity. Children's dreams should be collected by novel methods, involving their parents. Children's dreams depend on the maturation of emotion regulation and executive functions.

Publications:

Simor P, Pajkossy P, Horváth K, Bódizs R. Impaired executive functions in subjects with frequent nightmares as reflected by performance in different neuropsychological tasks. *Brain Cogn* 2012;78(3):274–283.

Simor P, Horváth K, Gombos F, Takács KP, Bódizs R. Disturbed dreaming and sleep quality: altered sleep architecture in subjects with frequent nightmares. *Eur Arch Psychiatry Clin Neurosci* 2012;262(8):687–696.

Simor P, Bódizs R, Horváth K, Ferri R. Disturbed dreaming and the instability of sleep: altered nonrapid eye movement sleep microstructure in individuals with frequent nightmares as revealed by the cyclic alternating pattern. *Sleep* 2013;36(3):413–419.

Simor P, Horváth K, Ujma PP, Gombos F, Bódizs R. Fluctuations between sleep and wakefulness: Wakelike features indicated by increased EEG alpha power during different sleep stages in nightmare disorder. *Biol Psychol* 2013; doi: 10.1016/j.biopsycho.2013.05.022.

Kis A, Szakadát S, Simor P, Gombos F, Horváth K, Bódizs R. Objective and subjective components of the first-night effect in young nightmare sufferers and healthy subjects. *Behav Sleep Med* 2013 (accepted for publication)

Keywords: Nightmares, Sleep, Dreaming, Children

58/10 – "Somatic Psi vs. Survival Psi: A Quantitative Investigation of Mediums' Phenomenology comparing Psychic Readings and Ostensible Communication with the Deceased" – only abstract available

Investigadores/Researchers: Dr. Julie Beischel, Dr. Adam J. Rock, Dr. Mark Boccuzzi, Dr. Michael Biuso

Instituição/Institution: The Windbridge Institute for Applied Research in Human Potential, Tucson (USA)

Duração/Duration: 2011/03 - 2013/02

Objectives: Previous research has demonstrated that skilled mediums can report accurate and specific information about the deceased loved ones (termed discarnates) of living people (termed sitters) using anomalous information reception (AIR); that is, without any prior knowledge about the discarnates or sitters, in the absence of any sensory feedback, and without using deceptive means. The source of the information obtained using AIR, however, has not been established. The body of proof-focused data collected to date cannot differentiate between the (1) super-psi and (2) psychic reservoir models (collectively "somatic psi") in which mediums use clairvoyance, precognition, and/or telepathy with the living to acquire information about discarnates and (3) the survival of consciousness hypothesis in which mediums use "survival psi" to communicate telepathically with discarnates. Recent qualitative research, however, indicates that mediums' subjective experiences during mediumship readings for the deceased are distinguishable from their experiences during psychic readings for the living.

Method: In order to further investigate these findings, this study employed the Phenomenology of Consciousness Inventory (PCI), a standard retrospective phenomenological analysis tool that quantitatively measures 26 phenomenological dimensions, to assess the experiences of 10 Windbridge Certified Research Mediums (WCRMs) during readings for living targets and readings for deceased targets. During each reading, the medium was given the first name of a target and then asked specific questions about the target (e.g., physical and personality descriptions, hobbies/interests). Both the WCRMs and the experimenter interacting with them were blinded to which targets were living and which were deceased. After each reading, the medium completed the PCI.

Results: During 19 of the 20 readings, the WCRM stated her impressions regarding the status of the named target (living or deceased). In 14 of those cases, the WCRM's impressions accurately reflected the status (74%, binomial probability, one-tailed, p = 0.032). In addition, six of the WCRMs were able to accurately determine the status of the targets in both of their readings. It should be noted that the WCRMs were instructed that the target for each reading could be living or deceased and *not* that they would be reading one of each type of target. A significant difference was seen between the living target condition and the deceased target condition for the dimension Love with higher scores in the deceased reading condition (living target: 2.65 ± 1.11 vs. deceased target: 3.55 ± 0.55 , p < 0.05). In the subset of six WCRMs who accurately determined the status of the targets, significantly higher intensity values were seen for readings for deceased targets (vs. readings for living targets) for the dimensions Positive affect, Joy, and Love (all p < 0.05).

Conclusions: These quantitative data collected under blinded conditions reflect the WCRMs' qualitative descriptions of the differences between communication with the deceased and acquisition of psychic information and provide further evidence distinguishing between survival psi and somatic psi.

Publications:

The research described in this abstract was presented at the 2013 meeting of the Society for Scientific Exploration.

Beischel, J., Rock, A., Boccuzzi, M., & Biuso, M. (2013, June). The source of mediums' information: A quantitative phenomenological analysis. Presented at the 32nd Annual Meeting of the Society for Scientific Exploration, Dearborn, Michigan.

Keywords: Mediums, Anomalous information reception, Source of psi, Phenomenology

63/10 – "Mindful ageing. Avoiding age related cognitive decline"

Investigadores/*Researchers*: Prof. Isabel Pavão Martins, Prof. Nuno Lunet, Dr. Carolina Maruta, Dr. Clara Loureiro, Dr. Vanda Freitas, Dr. Joana Morgado, Dr. Sofia Reimão, Dr. Joana Tavares

Instituição/Institution: Laboratório de Estudos de Linguagem, Unidade Neurologica de Investigação Clínica, Faculdade de Medicina de Lisboa e Instituto de Medicina Molecular, Universidade de Lisboa (Portugal)

Duração prevista/Estimated duration: 2011/04 - 2014/04

Objectives: Cognitive aging is a heterogeneous process both among individuals and across cognitive domains. An early identification of subjects at risk of decline is a requirement to prevent dementia. We assessed whether baseline cognitive functioning could predict cognitive impairment in a cohort of 479 community dwelling individuals aged \geq 55 years, who had undertaken a neuropsychological evaluation five years before, as part of a previous project.

Method: After ethics committee and health authorities' approval, subjects were invited for a cognitive re-evaluation and brain MRI, being classified as normal or impaired according to age/education adjusted cognitive scores plus panel consensus. MRIs were analyzed visually and by automatic parcellation for regional volumes.

Results: So far 234 subjects (70 \pm 8.2 years old, 151 females, with 7.4 \pm 4.2 years of education) have been evaluated (130 with MRI). The majority (88%) presented a normal performance, 20 a significant (<-1.5 SD) cognitive impairment and 8 dementia. Individuals with decline/dementia were older (p=.03), less educated (p=.003) and had a more severe general cortical atrophy (p=.035) than those remaining normal. They also presented lower executive functioning (p<.001) and more cognitive complaints at incepts and at re-evaluation (but not significantly). GPs could only identify as impaired those with more severe decline.

Their baseline performance on a combined measure of executive tests (processing speed, attention and inhibitory control), was the single best variable to predict cognitive outcome. It also correlated with Fazekas score for white matter changes (p=.02), and with cortical (p=.03) and subcortical atrophy (p=.04), 5 years later. Among subjects that remained well, there was a tendency for a raw score decline (compared to first assessment) in verbal learning, free delayed recall and in processing speed that was most evident in the eldest.

Conclusion: In a primary care setting, executive functioning may predict the likelihood of pathologic cognitive aging and structural brain abnormalities five years later, showing that decline begins earlier. Despite their close contact with patients and families, primary care doctors are more likely to detect patients in more advanced stages of decline, which stresses the need of simple cognitive assessment tools. Literacy and cognitive stimulation are related to cognitive outcome and may be viewed as potential modifiers of decline.

Keywords: Aging, Cognitive aging, Cognitive decline, Risk factors for dementia

64/10 – "A psychophysiological investigation of semantic contributions to episodic memory" – only abstract available

Investigadores/Researchers: Dr. Andrea Greve, Prof. Edward Wilding

Instituição/Institution: Cardiff University Brain Research Imaging Centre (CUBRIC), School of Psychology, Cardiff University (UK) Duração/Duration: 2011/05 - 2013/12

Objectives: The objective of this study was to test the hypothesis that stimulus-driven semantic relations promote subsequent familiarity, while task-driven semantic manipulations promote recollection. This investigation builds upon previous experiments which suggest that two kinds of semantic processes have distinct effects on retrieval. We tested two classes of material – words and pictures – with a view to determining whether the same relationships hold for different stimulus formats, as there is evidence that memory is sensitive to different types of stimuli.

Method: We assessed this question by investigating how established event-related potential (ERP) indices of Familiarity (providing a sense of previous encounter, indexed by the early frontal old/new effect, occurring at 300-500ms post stimulus) and Recollection (retrieval of detailed contextual information, indexed by a later parietal old/new effect, occurring at 500-800ms post stimulus) varied with semantic relations between stimuli and type of semantic encoding subjects employed to process the stimuli.

Results: Experiment 1 revealed that stimulus-driven semantic manipulations have a particularly strong impact on episodic retrieval via familiarity-driven processes. Reliable differences in ERP indices occurred at anterior scalp locations from 300-500ms (early frontal old/new effect) for related vs. unrelated items. Experiment 2 was able to investigate the basis of this impact in more detail and demonstrated that the familiarity-driven memory effect is linked to semantic feature overlaps between stimuli, but less so to the kind of semantic processing employed. Our data revealed modulations in early frontal old/new effects that were linked to changes in semantic relatedness between stimuli. The level of strategic semantic processing employed at encoding, however, did not modulate early frontal old/new effects.

Conclusion: Our overall findings allow us to establish a more detailed account by which semantic information is able to influence episodic retrieval. Our data suggest that stimulus driven semantic processes modulate familiarity based memory judgements. These findings have important implication for how semantic information can be used to structure learning environments to become more memorable.

Publication:

Abstracts publication at Cognitive Neuroscience Society, Chicago, April 2012 Peer Review Paper (in preparation).

Keywords: Episodic memory, Semantic memory, ERP, Familiarity, Recollection

66/10 – "The Spiritual Brain: neuropsychological and neurophysiologic investigations of Self-transcendence and Spirituality"

Investigadores/*Researchers*: Dr. Salvatore Maria Aglioti, Prof. Cosimo Urgesi, Dr. Franco Fabbro, Dr. Matteo Candidi, Dr. Fabio Campanella

Instituição/*Institution*: Department of Psychology, University of Rome "La Sapienza", Rome (Italy) Duração/*Duration*: 2011/04 - 2013/02

Objectives: Religiousness and spirituality (RS) are two ubiquitous aspects of human experience typically considered impervious to scientific investigation. Nevertheless, associations between RS and frontoparietal neural activity have been recently reported. However, much less is known about whether such activity is causally involved in modulating RS or just epiphenomenal to them.

Method: Here we combined two-pulse (10Hz) transcranial magnetic stimulation (TMS) with a novel, adhoc developed RS-related, Implicit Association Test (IAT) to investigate whether implicit RS representations, although supposedly rather stable, can be rapidly modified by a virtual lesion of inferior parietal lobe (IPL) and dorsolateral prefrontal cortex (DLPFC). A self-esteem (SE) IAT, focused on selfconcepts nonrelated to RS representations, was developed as control.

Results and Conclusions: A specific increase of RS followed inhibition of IPL demonstrating its causative role in inducing fast plastic changes of religiousness/spirituality. In contrast, DLPFC inhibition had more widespread effects probably reflecting a general role in the acquisition or maintenance of task-rules or in controlling the expression of self-related representations not specific to RS. Furthermore, converging evidence on the importance of the parietal cortex in RS come also from a sample of 12 patients with lesion to either parietal or frontal brain regions.

Publications:

Crescentini, C., Aglioti, SM., Fabbro, F., & Urgesi, C. Virtual lesions of the inferior parietal cortex induce fast changes of implicit religiousness/spirituality (under review after revision) *Cortex*. Crescentini, C., Urgesi, C, Fabbro, F., Eleopra, R., & Aglioti SM. Contribution of the parietal cortex to implicit religiousness/spirituality: evidence from patients with focal lesions (in preparation).

Keywords: Religiousness-Spirituality, Inferior parietal lobe, Dorsolateral prefrontal cortex, TMS, IAT

72/10 – "Neurocognitive mechanisms supporting the influence of memory on visual attention in healthy and disease"

Investigadores/Researchers: Dr. José Miguel Pinto Cardoso de Bourbon Teles, Dr. David Soto, Dr. Paul Bentley

Instituição/Institution: Centre for Neuroscience, Faculty of Medicine, Department of Neuroscience and Mental Health, Imperial College London (UK)

Duração/Duration: 2011/04 - 2013/10

Objective: The functional contribution of the thalamus to higher-level cognitive functions like attention, working memory, rule-based learning remains poorly understood, especially in comparison to cortical frontoparietal networks, which have been thoroughly investigated in this regard. Recent functional MRI (fMRI) research suggests that guidance of attention from the contents of working memory (WM) engages a complex network including frontal areas in dorsolateral prefrontal cortex (DLPFC), superior frontal gyrus (SFG), thalamic nuclei and occipital visual cortex. However, evidence from fMRI is only correlational and therefore it is difficult to determine which of the identified brain regions are necessary and causally involved in WM guidance of attention. We addressed this issue by systematically characterizing the functional role of the thalamus in linking memory and attention in visual processing, first exploiting the power of lesion studies to infer causal relationships between brain structure and function, and subsequently using functional MRI in healthy volunteers to test predictions derived from the lesion data.

Method: Several stroke patients were tested. Patients were required to perform a memory task and a verbal cueing task for a target object presented amongst distracters. The memory task assessed the capacity of patients to keep the cues in memory for a later recognition test. The verbal cueing task was divided in three different conditions: in the valid condition the colour of the sought after target was precued by a verbal cue presented prior to the search display. On neutral trials, patients did not receive any cue prior to search. On invalid trials, the verbal memory cue specified the colour of a search distracter. Subsequently, we conducted two fMRI experiments with healthy participants. The first experiment involved learning of abstract stimulus-stimulus associations to optimize attentional selection in visual search. Participants were exposed to a learning paradigm that required forming associations between Japanese hiragana cues and the colors of the circles surrounding the search target. There were four hiragana cues that were predictive: namely, each of them was associated with a particular color surrounding the search target. As a baseline condition, there were 4 different hiragana cues, which were not associated with any color information surrounding the search target. During scanning, participants were encouraged to learn the association between the hiragana cues and the color surrounding the search target, in order to boost search performance. In the second fMRI experiment, we conducted a similar verbal cueing task as previously applied to thalamic patients, with main exception that performance in valid trials was compared with neutral trials (no invalid trials included).

Results: Analysis of search performance revealed that patients with focal thalamic lesions showed no memory cueing effect of search despite having intact memory performance in a control memory task. Search performances were faster in invalid trials relative to neutral and valid trials. In contrast, the control groups of patients with damage outside the thalamus and age-match controls displayed the normal effect of memory-capture of attention, as indexed by faster reaction times in valid relative to neutral and invalid trials. Analysis in the subsequent fMRI experiments with healthy participants revealed that for the learning experiment, search performance became increasingly faster in predictive relative to non-predictive trials as training developed, consistent with the acquisition of abstract stimulus-stimulus associations. Critically, we found that responses in the left thalamus tracked the predictiveness of the hiragana cues across the training phase, consistent with both linear and exponential learning trends. The behavioral data for the second fMRI experiment, namely, the verbal cueing task, showed that participants used the predictable color word cues to guide attention towards search target as indexed by faster search responses in valid relative to neutral trials. The response profile of the left thalamus was enhanced for valid relative to neutral cues.

Conclusion: The results from the lesion studies showed that focal thalamic lesions lead to impaired guidance of visual attention by abstract information held in memory. Thalamic patients displayed reduced memory-cueing effects relative to age-match controls and patients with damage outside the thalamus. Neuroimaging evidence from healthy participants corroborated that the thalamus mediates the biasing of

attention by abstract (verbal) cues but more critically it further illustrated that the response profile of the thalamus tracks the learning of stimulus-stimulus associations that are used to optimize attentional selection in visual search. The currents findings highlight the thalamus as a key substrate for top-down guidance of visual attention through 'online' memory and experience-dependent learning, hence stressing the importance of understanding the role of subcortical nuclei beyond cortico-cortical (e.g. parietofrontal) mechanisms of attentional control.

Publications:

de Bourbon Teles, J., Bentley, P., Koshino, S., Malhotra, P., Egner, T., Masud Husain & David Soto. Thalamic control of human attention driven by memory and learning. Nat Neurosci (under consideration). Soto, D., Humphreys, G.W. & Rotshtein, P. Dissociating the neural mechanisms of memory-based guidance of visual selection. Proc Natl Acad Sci U S A 104, 17186-17191 (2007).

Corbetta, M. & Shulman, G.L. Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci 3, 201-215 (2002).

Keywords: Thalamus, Lesion, Working memory, Attention, fMRI.

74/10 – "The Psychobiological Effects of Yoga/Meditation in a Prison Population"

Investigadores/*Researchers*: Dr. Miguel Farias, Dr. Amy Bilderbeck Instituição/*Institution*: Department of Experimental Psychology, University of Oxford (UK) Duração prevista/*Estimated duration*: 2012/02 – 2014/04

Objectives: Yoga and meditation have been shown to be effective in alleviating symptoms of depression and anxiety in healthy volunteers and psychiatric populations. Recent work has also indicated that yoga can improve cognitive-behavioural performance and control. Although there have been no controlled studies of the effects of yoga in a prison population, we reasoned that yoga could have beneficial effects in a setting where psychosocial functioning is often low, and the frequency of impulsive behaviours is high.

Method: Participants were recruited from 7 British prisons, and randomly allocated to either a 10-week yoga programme (yoga group; 1 class per week; N=45) or a control group (N=55). Self-report measures of mood, stress, and psychological distress were collected before and after the intervention period. Participants completed a cognitive-behavioural task (Go/No-Go) at the end of the study, which assessed behavioural response inhibition and sustained attention.

Results: Participants in the yoga group showed increased self-reported positive affect, and reduced stress and psychological distress, compared to participants in the control group. Participants who completed the yoga course also showed better performance in the cognitive-behavioural task, making significantly fewer errors of omission in Go trials and fewer errors of commission on No-Go trials, compared to control participants.

Conclusions: Yoga may be effective in improving subjective wellbeing, mental health, and executive functioning within prison populations. This is an important consideration given the consistently high rates of psychological morbidity in this group and the need for effective and economical intervention programmes.

Publications:

Bilderbeck, A.*, Farias, M.*, Brazil, I., Jacobowitz, S., & Wikholm, C. (2013) (*shared first authorship). Participation in a 10-week course of yoga improves behavioural control and decreases psychological distress in a prison population. *Journal of Psychiatric Research*, *47*, 1438-1445.

Keywords: Yoga, Prison, Behavioural control, Stress, Mood

85/10 – "Importance of cognitive coping in facilitation of hypno-relaxation in stressed students and in anxious patients: holistic psycho-neuroendocrino-immunological analysis (Building telepathic contact with the inner adviser)"

Investigadores/*Researchers*: Prof. Margit Keresztes, Prof. Tibor Rudisch, Dr. Zoltán Kovács, Prof. János Tajti, Dr. János Gardi, Dr. Gyöngyi Serfőző

Instituição/*Institution*: Dept. Biochemistry, Medical Faculty, University of Szeged, Szeged (Hungary) Duração/*Duration*: 2011/03 - 2012/10

Objective: Our goal was to study whether there could be any differences between the impact of a cognitive coping-type hypnorelaxation and standard imagery ones on the psycho-neuroendocrino-immune state of healthy stressed students (before-during examination term) and chronic anxious patients.

Method: Students (n=16-20) and patients (n=24-30) participated in 3 hypnorelaxations (one/week): the first and the third ones were standard sessions (with pleasant field imaginations), while the second, cognitive coping-type session included suggestions to contact and to ask help from the inner adviser. Perceived stress and coping (Rahe), depression (BDI), hypnotizability (Harvard), trait and state anxiety (Spielberger) psychotests were employed. Biosamples were collected before and after hypnorelaxations. ACTH and cortisol were assayed by chemiluminescence, special immunological markers (LL-37, lactoferrin, sICAM-1, IL-6, galectin-3) were tested by ELISA in blood plasma. Tensions of 7 muscle pairs (on head, neck, shoulder) were measured by computer-assisted surface EMG.

Results: State anxiety score was reduced significantly (p<0.05) after each hypnorelaxation in patients; no changes were seen in students. Plasma ACTH decreased significantly (p<0.05) following each session in students; standard sessions appeared to be more effective to downregulate cortisol concentration (p<0.01) than cognitive hypnorelaxation. In patients, cortisol level decreased both after the second (p<0.001) and the third (p<0.01) hypnorelaxations. Onset of the examination term enhanced muscle tension dramatically in students (about 8-10-fold, p<0.0001); no alterations were observed after standard hypnorelaxations, and cognitive coping-type session resulted in increased muscle tension (p<0.05) on the left side. In patients, the first hypnorelaxation led to decreased muscle tension (p<0.001); the second session was followed by elevated muscle tension also in them, especially on the left side (p<0.001). No significant changes were seen in the plasma immunological markers.

Conclusions: Comparing the two types of hypnorelaxations, a main neurophysiological difference emerged: the cognitive coping-type session appeared to lead to elevated muscle tension, primarily on the left side, that could be due to excitation in the motor area of the stress-responsive muscles, especially on the right side of the brain.

Keywords: Hypnorelaxation, Cognitive coping, Stress, Muscle tension

86/10 – "The different faces of one's self: Neural correlates of changes in selfidentity" Investigadores/*Researchers*: Dr. Ana Tajadura-Jiménez, Dr. Emmanouil (Manos) Tsakiris Instituição/*Institution*: Department of Psychology, Royal Holloway University of London (UK) Duração/*Duration*: 2011/09 - 2012/10

Objectives: Mirror self-recognition is considered as an index of self-awareness. Neuroimaging studies have identified a neural circuit specialized for the recognition of one's own current facial appearance. However, faces changes considerably over a lifespan, highlighting the necessity for representations of one's face to continually be updated. This research project aimed at understanding the neural processes that underpin the cognitive capacity for self-face recognition by investigating two important dimensions: aging-related changes and sensory-driven changes in self-face identification.

Method: Two experiments were designed to address separately these two questions using functional magnetic resonance imaging (fMRI). In Experiment 1 participants viewed images of either their own face as it currently looks morphed with the face of a familiar other or their childhood face morphed with the childhood face of the familiar other. In Experiment 2 participants experienced tactile stimulation delivered to their face, whilst observing either temporally synchronous or asynchronous tactile stimulation delivered to another person's face on either a congruent or incongruent location.

Results: Experiment 1 showed that activity in areas that have a generalised selectivity for faces, including the inferior occipital gyrus, the superior parietal lobule and the inferior temporal gyrus, varied with the amount of current self in an image. Importantly, activity in areas involved in memory encoding and retrieval, including the hippocampus and the posterior cingulate gyrus, and areas involved in creating a sense of body ownership, including the temporo-parietal junction and the inferior parietal lobule, varied with the amount of childhood self in an image.

Experiment 2 showed an effect of synchronous, congruent stimulation in the activity in a network of multisensory areas, including the right temporo-parietal Junction (rTPJ) and middle frontal gyrus, the bilateral anterior insula and intraparietal sulcus. Activity in the rTPJ was scaled with the extent to which the participants' felt identification with the observed face during stimulation.

Conclusions: These results suggest that distinct neural structures encode changes in self-identity across time, and provide a functional basis for the neural plasticity of the self-recognition network.

Publications:

Published peer-reviewed papers:

Apps, M.A.J., Tajadura-Jiménez, A., Turley, G., & Tsakiris, M. The different faces of one's self: an fMRI study into the recognition of current and past self-facial appearances. Neuroimage 2012, 63, 1720–1729.

Apps, M.A.J., Tajadura-Jiménez, A., Sereno, M., Blanke, O., & Tsakiris, M. Plasticity in Unimodal and Multimodal Brain Areas Reflects Multisensory Changes in Self-Face Identification. Cerebral Cortex, doi: 10.1093/cercor/bht199.

Abstracts (proceedings and meetings):

Apps, M.A.J., Tajadura-Jiménez, A., Turley, G., & Tsakiris, M. The different faces of one's self: an fMRI study into the recognition of current and past self-facial appearances. 2012 Bial Foundation Symposium "Sleep and Dreams", Casa do Médico, Porto, Portugal, March 28-31 2012.

Apps, M.A.J., Tajadura-Jiménez, A., Turley, G., & Tsakiris, M. The different faces of one's self: an fMRI study into the recognition of current and past self-facial appearances. UK Synaesthesia Association annual conference, Oxford, UK, April 14-15, 2012.

Apps, M.A.J., Tajadura-Jiménez, A., Turley, G., & Tsakiris, M. The different faces of one's self: an fMRI study into the recognition of current and past self-facial appearances. International Multisensory Research Forum, Oxford, UK, June 19-22, 2012.

Apps, M.A.J., Tajadura-Jiménez, A., Turley, G., & Tsakiris, M. The different faces of one's self: an fMRI study into the recognition of current and past self-facial appearances. Annual meeting of the Association for the Scientific Study of Consciousness, Brighton, UK, July 2-6, 2012.

Tajadura-Jiménez, A., Apps, M.A.J., Sereno, M., Blanke, O., & Tsakiris, M. Multisensory brain areas reflect changes in self-face recognition. The British Neuroscience Association's Festival of Neuroscience, April 7th-11th, 2013.

Apps, M.A.J., Tajadura-Jiménez, A., Sereno, M., Blanke, O., & Tsakiris, M. Unimodal and Multimodal plasticity reflects multisensory driven changes in self-recognition. 19th Annual meeting of the organization for Human Brain Mapping, June 16th-20th, 2013.

Tajadura-Jiménez, A., Apps, M.A.J., Sereno, M., Blanke, O., & Tsakiris, M. Plasticity in Unimodal and Multimodal brain areas reflects multisensory changes in self-face identification Multisense Japan meeting, NTT, November 21st-22nd, 2013.

Keywords: Self-identity, Self-recognition, Face, Multisensory, fMRI

94/10 – "Cortical and autonomic responses associated with accurate intuition" – only abstract available Investigadores/*Researchers*: Prof. Paul J. Mills, Dr. Arnaud Delorme, Dr. Julie Beischel, Dr. Dean Radin, Dr. Rael Cahn Instituição/*Institution*: Institute of Noetic Sciences, California (USA) Duração/*Duration*: 2011/10 - 2013/04

Objectives: During advanced meditative practices, unusual perceptions can arise including the sense of receiving information about unknown people who are deceased (i.e., discarnates). As with meditation, this mental state of mental communication with the deceased involves calming mental chatter and becoming receptive to subtle feelings and sensations. The present study investigated six professional mental mediums to explore two research questions: First, we examined correlations between the accuracy of mediums' statements and their electrocortical activity; and second, we studied differences in mediums' brain activity when they intentionally evoked four subjective states: perception, recollection, fabrication, and communication.

Method: Psychometric and brain electrophysiology data were collected from six individuals who had previously reported accurate information about discarnates under double-blind conditions. Each experimental participant performed two tasks with eyes closed. In the first task, the participant was given only the first name of a discarnate and asked 25 questions. After each question, the participant was asked to silently perceive information relevant to the question for 20 seconds and then respond verbally. Responses were then transcribed and scored by individuals who knew the discarnates. In the second task, participants were asked to experience four mental states for one minute each. Each mental state was repeated three times. Mental states were: (1) Thinking about a known living person, (2) Listening to a biography, (3) Thinking about an imaginary person, and (4) Interacting mentally with a known discarnate.

Results: In the first task, of the six participants, two could not be evaluated, and the four other participants scored higher than chance level (p < 0.03 for 3 of the 4 participants). The correlation between accuracy and brain activity during the 20-second of silent mediumship communication was significant in frontal theta for one participant (p < 0.01). In the second task, statistically significant differences in electrocortical activity among the four conditions were obtained in all six participants, primarily at the gamma band.

Conclusion: Differences observed suggest that the impression of communicating with the deceased may be a distinct mental state distinct from ordinary thinking or imagination.

Publication:

Delorme, A., Beischel, J., Michel, L., Boccuzzi, M., Radin, D., Mills, P.J. (2013) Electrocortical activity associated with subjective communication with the deceased. Frontiers in psychology, in press http://www.frontiersin.org/Journal/10.3389/fpsyg.2013.00834/abstract

Keywords: Mediums, EEG, Intuition, Mental states, Transcendence

96/10 – "The psychophysiology of positive psychology"

Investigadores/*Researchers*: Prof. Angela Clow, Dr. Lisa Thorn, Dr. Nina Smyth, Prof. Frank Hucklebridge Instituição/*Institution*: Psychophysiology and Stress Research Group, Department of Psychology, University of Westminster, London (UK)

Duração/Duration: 2011/06 - 2013/10

Objectives: Psychology has typically focused on the study of ill-being (e.g. stress, depression), demonstrating relationships with insecure attachment styles and poor health. In recent years, the field of Positive Psychology has directed more attention to the study and pormotion of well-being (e.g. meaning in life, happiness, life satisfaction). The link between well-being and better health demonstrates the need for designing and evaluating effective interventions to enhance well-being. But first we must understand the behavioural and physiological pathways by which well-being impacts on health. This bursary aimed to assess both well-being and ill-being in relation to the diurnal cortisol pattern in healthy individuals to better understand the physiological pathways underpinning the relationship between well-being and health.

Method: *Study 1:* young healthy females completed measures of trait well-being and ill-being and attachment style. Over four days state well-being and ill-being was assessed by aggregated mood ratings. To measure the diurnal pattern of cortisol on the four days participants collected six saliva samples (0, 15, 30, 45 min and 3 and 12 hr post-awakening). Sampling timings were objectively measured which is crucial for accurate measurement of cortisol. *Study 2:* younger and older healthy females completed trait measures of well-being, ill-being and attachment style. A hair segment was collected which provided a measure of cortisol secretion over the last three months.

Results: *Study 1:* Securely attached people exhibited better well-being. However neither well-being, illbeing nor attachment style were associated with the diurnal cortisol pattern. Objectively determined sampling delay impacted on measurment of the diurnal cortisol pattern. *Study 2:* well-being or ill-being was not associated with hair cortisol, except in the older females in which higher well-being was associated with higher hair cortisol.

Conclusions: These findings provide evidence for the neurotoxicity hypothesis of cortisol secretion: well-being did not relate to cortisol secretion in early adulthood with effects emerging in late adulthood. The older females had higher hair cortisol than the healthy young, which is interpreted as a consequence of aging. Surprisingly we found that older females with higher HC had higher levels of well-being. This finding suggests that cortisol acts as an 'energiser' in healthy older females.

Publications:

Peer-reviewed papers

Smyth, N., Clow, A., Thorn, L., Hucklebridge, F., & Evans, P. (2013). Delays of 5-15min between awakening and the start of saliva sampling matter in assessment of the cortisol awakening response. Psychoneuroendocrinology, 38(9), 1476-1483.

Smyth, N., Hucklebridge, F., Thorn, L., Evans, P., & Clow, A. (2013). Salivary cortisol as a biomarker in social science research. *Social and Personality Psychology Compass*, 7(9), 605-625. <u>Oral presentations</u>

Smyth N, Thorn L, Evans P, Hucklebridge F, Clow A. Patterns of Salivary Cortisol Secretion in High and Low Well-being Students. Psychobiology British Psychological Society Annual Conference, Lake District, Sept 2011.

Smyth N, Oskis A, Clow A. The Relationship between Trait and State Well-being and Attachment Style in Students. Selected and presented for a data blitz session at the American Psychosomatic Society Annual Conference, Athens, March 2012.

Smyth N, Evans P, Thorn L, Hucklebridge F, Clow A. Impact of saliva sampling delay on assessment of the cortisol awakening response (CAR) in a healthy student sample. Psychobiology British Psychological Society Annual Conference, Lake District, Sept 2012.

Smyth, N., Clow, A., Thorn, L., Hucklebridge, F., Evans, P. The CAR: impact of short delays and associations with trait and state well-being. Cortisol Network meeting, Imperial College, January 2013. Evans P, Smyth, N, Thorn L, Hucklebridge F, Clow, A. Delays of 5-15 minutes between awakening and

the start of saliva sampling matter in assessment of the cortisol awakening response. American Psychosomatic Society Annual Conference, Miami, March 2013.

Poster presentations

Smyth N, Thorn L, Evans P, Hucklebridge F, Clow A. Discrepancies between self-reported and objective sampling delay for the cortisol awakening response. American Psychosomatic Society Annual Conference, Athens, March 2012.

Smyth N, Evans P, Thorn L Hucklebridge F, Clow A. State Well-being or Ill-being does not predict cortisol patterns in a young healthy sample. American Psychosomatic Society Annual Conference, Miami, March 2013.

Smyth N, Evans P, Thorn L Hucklebridge F, Clow A. Trait Hedonic and Eudemonic Well-being/Ill-being and Diurnal Cortisol Patterns. American Psychosomatic Society Annual Conference, Miami, March 2013.

Smyth N, Evans P, Thorn L Hucklebridge F, Clow A. State Well-being or Ill-being does not predict cortisol patterns in a young healthy sample. American Psychosomatic Society Annual Conference, Miami, March 2013.

Papers in preparation

Plan to submit papers to *Psychoneuroendocrinology* the end of August 2013 with the following authors Smyth, N., Hucklebridge, F., Thorn, L., Evans, P., Clow, A.

In salivary cortisol a good biomarker in healthy females?

Exploring relationships between hair cortisol and well-being/ill-being in young and old females.

Keywords: Salivary cortisol, Hair cortisol, Well-being, Ill-being, Attachment style

100/10 – "Replicating von Lucadou's Psycho-Physical Correlation Matrices" Investigadores/*Researchers*: Prof. Harald Walach, Dr. Nikolaus von Stillfried Instituição/*Institution*: Institute for Transcultural Health Sciences (INTRAG), European University Viadrina, Frankfurt Oder (Germany) Duração prevista/*Estimated duration*: 2011/11 – 2014/03

Background and Method: Psychokinesis (PK)-Experiments are beset by the problem of replicability. This became clear, when the largest replication of micro-PK failed (Jahn et al. 2000), driving the otherwise significant total PK-database towards a null effect (Bösch, Steinkamp & Boller 2006). In such experiments an operator is asked to change a true random process purely by intention. Von Lucadou has been arguing that PK effects are of a correlational nature, and hence will not be replicable if treated as a causal signal. To overcome this problem, he has advocated an indirect design. Thereby, the target outcome is not the mean-shift of the random-sequence as in classical PK-experiments, but a correlationmatrix. To create such a matrix, the PK-experimental set-up is slightly changed. The display of the random-sequence, in this case a fractal spiral that moves to the left or the right, can only be progressed if any out of three different buttons is pressed. The button press, however, has nothing to do with the direction into which the spiral moves. But the participants in the experiments will of course quickly generate hypotheses as to the meaning of the three different buttons. Apart from that the experiments comes with three, randomly sequenced, instructions to change the spiral's direction towards the left, the right, or keep it stable. Out of all potential psychological and physical variables a matrix of 45x45 cells is created of variables that can be correlated with the mean-shift in deviation from randomness. In previous experiments von Lucadou could show that he could replicate the fact that more significant correlations were produced than expected by chance. While the exact positioning of the correlations within the matrix changed over different experimental replications, the fact that the total number of correlations was always higher than expected by chance remained unaltered. Hence we started a large independent replication.

Results: The experimental database was closed on the 31st of January 2014. We collected 398 runs. Currently the data are being evaluated and the results will be presented.

Keywords: Psychokinesis, Experimental study, Replicability

102/10 – "The Importance of the Rapid Eye Movement Sleep Stage for Creativity and for Creative Problem Solving"

Investigadores/*Researchers*: Prof. Ingegerd Carlsson, Per Davidson, Dr. Una Gustafsson, Dr. Markus Jansson-Frõjmark, Prof. Sara Mednick, Dr. Marianne Ors Instituição/*Institution*: Department of Psychology, Lund University, Lund (Sweden)

Duração/Duration: 2011/07 – 2013/11

Objectives: REM sleep is important for cognition and memory, and has high associative brain functioning, as has creative cognition. The project investigated relations between REM, creative problem solving and creativity.

Hypotheses: Building on Cai et al.(2009) *hypothesis 1* assumed a relation between REM and creative problem solving (Remote Associates Test RAT) taken after nap. It was tested in a priming design, i.e. the answers to a Primed RAT were implicitly primed before nap. *Hypothesis 2* was as in Cai et al. that sleep alone would not contribute to improvement on a Baseline RAT repeated after nap, i.e. with no implicit primes. *Hypothesis 3* assumed a relation between REM and creativity. Creativity may contribute to REM, thus affecting sleep processing of the primes, and to RAT. Creativity was tested by Alternate Uses and Creative Functioning Test. *Hypothesis 4* predicted a positive relation between RAT and creativity.

Participants: The RAT was constructed in USA, so participants had English as native tongue. Most were from USA (n=42) and the rest (n=26) from other countries. For nap condition, n=52, for resting condition n=16.

Results: *Hypothesis 1* was not supported. For *hypothesis 2*, contrary to prediction, in the US group the sleep group improved more than the rest group on the repeated Baseline RAT. This was not found in the Non-US group. For *hypotheses 3* and *4* there was no significant result.

Discussion: Research has shown that sleep is important for memory, supporting the result on hypothesis 2 in the US group. The RAT, constructed in USA, may contain culture specific items. In the non-US group, sleep processing of the baseline RAT would be of little use for the repeated RAT, if culture specific knowledge does not exist in memory.

The present high-REM group had similar time in REM sleep as the High-REM group in Cai et al. The present investigation controlled for confounds anxiety and depression, but not for memory. Future studies of hypotheses 3 and 4 should measure an entire night's sleep with participants evenly balanced on creativity.

Publication: The forthcoming article will be submitted to an international journal.

Keywords: REM sleep, Creative problem solving

105/10 – "Analgesic Properties of Computer Games"

Investigadores/*Researchers*: Dr. Stephen Fairclough, Dr. Helen Poole Instituição/*Institution*: School of Natural Sciences and Psychology, Liverpool John Moores University, Liverpool (UK) Duração/*Duration*: 2011/09 – 2013/02

Objectives: The aim of this work was to study the concept of immersion during computer game play using ERP measures. Immersion was defined with respect to selective attention, specifically the ability of a person to attend to sensory stimuli in his or her physical environment whilst playing a computer game. A methodology was developed wherein the participant engaged with a computer game using two versions of an ERP paradigm. The first involved exposing participants to auditory oddball stimuli during game play and measuring the amplitude of the ERP (particularly late positive components) as an index of immersion. For the second study, participants were exposed to thermal pain stimuli whilst playing the game and ERP responses to pain were recorded as a measure of immersion.

Method: The first study involved 20 participants who played a racing game (WipeOut) under three conditions of difficulty (easy, hard, impossible). The participants were divided into two groups: one played the game on a large TV screen and the other via a Head-Mounted Display (HMD). The second study (N=20) used the same manipulation of task difficulty but sensory immersion was manipulated by increasing the size of a projected display (small vs. large visual field of view). An auditory oddball task was used for the first study whereas a MEDOC system was used to deliver thermal pain stimuli during the second study. In both cases, ERP data were recorded from 32-channel EEG system.

Results: The first study revealed that game difficulty exerted a greater influence on immersion compared to the characteristics of the display. This hypothesis was supported by the ERP data, amplitude of late positive components influenced by the game demand, not display characteristics. The second study was inconclusive and ERP responses to pain stimuli were not sensitive to manipulations of immersion.

Conclusions: The majority of research has focused on technological properties of visual and auditory displays, this work has indicated that the cognitive demand associated with game play could exert a stronger influence on immersion.

Keywords: Immersion, Computer Games, Attention, Pain, ERPs

106/10 – "Mapping the Psychophysiology of Anxiety Responses Using Virtual Reality" – only abstract available Investigadores/*Researchers*: Dr. Simon Dymond, Dr. Philip M. Newton, Dr. Bryan Roche Instituição/*Institution*: Department of Psychology, Wales Institute of Cognitive Neuroscience, Swansea University, Swansea (UK) Duracão/*Duration*: 2011/07 - 2014/01

Objectives: To model the development and generalization of anxiety-related behaviours in humans using the conditioned suppression paradigm.

Method: A multi-stage conditioning and testing format was implemented within a first-person shooter virtual reality task. Participants first underwent operant training in which they learned to shoot at crates to find hidden gold bars worth 100 points. Next, fear conditioning occurred in which a background colour conditioned stimulus (CS+) was paired with an instructed unconditioned stimulus (US), such as the screen shaking and a loss of accumulated points. Another background colour was not paired with the US (CS-). Conditioned suppression was then tested with presentations of the CSs while participants were searching for gold. Suppression ratios were calculated for multiple topographies of response (shots, hits, breaks, and accuracy). Generalized suppression was investigated via acquired equivalence, symmetry and equivalence derived relations.

Results: Significant suppression and generalized suppression was found for all response measures and for a post-experimental measure of CS-US awareness. Suppression generalized to cues indirectly related to the trained CS via acquired equivalence, symmetry and stimulus equivalence.

Conclusions: The present findings demonstrate, for the first time, unequivocal evidence of conditioned and generalized suppression in humans using a novel virtual reality task.

Publications:

Greville, W.J., Dymond, S., Newton, P.M., & Roche, B. (in press). Acquired equivalence and generalized suppression in a virtual reality environment. *Learning & Behavior*. Greville, W.J.S., Newton, P.M., Roche, B., & Dymond, S. (2013). Conditioned suppression in a virtual environment. *Computers in Human Behavior*, 29, 552–558.

Keywords: Conditioned suppression, Virtual reality, Generalization, Acquired equivalence, Symmetry, Stimulus equivalence, Anxiety

141/10 – "Pattern Classification of Emotion-Induced Physiological Changes" – only abstract available

Investigadores/Researchers: Dr. Julia Mossbridge, Dr. David Little

Instituição/Institution: Northwestern University Visual Perception, Cognition, and Neuroscience Laboratory, Evanston (USA)

Duração prevista/Estimated duration: 2011/04 - 2014/03

Objective: To further examine whether pattern classification can be used to predict seemingly unpredictable future events based on physiological activity before these events.

Method: In the previous symposium's abstract, we presented our electroencephalographic (EEG) study of auditory and visual attention that allowed us to obtain data on which we could train a pattern classifier to predict upcoming events. Here we present data from an attempted replication of that study.

As in the original experiment, each of 20 undergraduates were fitted with 64 EEG electrodes. Participants used their right hand to press the left mouse button as soon as they saw a "1" or heard a low tone, and the right button if they saw a "2" or heard a high tone. All stimuli were randomized. Raw EEG was current-source density transformed and artifacts were removed before analysis. The dependent variables were the phase of the mean (across-trial) peak alpha (7.5-12 Hz) frequency for each person at each electrode relative to 550 ms preceding the onset of the upcoming stimulus presentation (left vs. right), and the pre-stimulus event-related potential (ERP) obtained from each type of stimulus presentation (left vs. right).

A random forest algorithm was used. For statistical analysis, the classifier was executed using the actual data versus a randomized version of the same data. The analysis of these data was pre-registered at the Koestler Parapsychology Registry.

Results: In 100 runs of the classification algorithm, it was able to significantly predict the upcoming stimulus presentation based on this new data set (p<0.05, two-tailed), but after 1000 runs this significance level fell to borderline (p<0.10, two-tailed, d=2.23).

In an exploratory effort (not part of the registered analysis), we combined the two data sets (N=40) to determine whether there remained a statistically significant ability to predict the upcoming stimulus. Based on these data, the prediction was at 74% accuracy (p<0.05, d=2.94 by the distribution tail test). Further, when all 40 participants were classified independently, 30 of the 40 participants had significant classifications.

Taken together, these data suggest that brain alpha phase preceding upcoming stimuli may predict the content of those stimuli or the correct response to those stimuli.

Conclusions: Pattern classification of EEG signals suggests that physiological prediction of seemingly unpredictable future events is possible.

Publications:

Dalkvist J, Mossbridge JA and Westerlund J. (2013). How to handle expectation bias in presentiment experiments. *To be presented at the 56th Annual Convention of the Parapsychological Association*.

Mossbridge JA, Utts J, and Tressoldi P. (2012). Predictive anticipatory activity preceding seemingly unpredictable stimuli: A meta-analysis. *Frontiers in Psychology*: 3:390.

Mossbridge JA. (In Press). Physiological activity that seems to anticipate future events. To appear in *The Evidence for Psi*, edited by Ben Goertzel and Damien Broderick.

Keywords: Psychophysiology, Temporal processing, Pre-stimulus physiological measures, Anticipatory responses, Pattern classification

155/10 – "Memory for personal experience and the parietal cortex" Investigadores/*Researchers*: Dr. Charlotte Russell, Dr. Paresh Malhotra, Dr. Adrian Williams Instituição/*Institution*: Centre for Cognition and Neuroimaging, Department of Psychology, Brunel University, Uxbridge (UK) Duração prevista/*Estimated duration*: 2011/07 - 2014/03

Objectives: Although there is a great deal of support from functional imaging studies for parietal lobe involvement in episodic memory, until now there has been little experimental evidence from neuropsychological studies with patients suffering from focal parietal damage to suggest that parietal integrity is necessary for episodic memory function. Given the key role of frontoparietal networks in visuospatial representation, we hypothesised that the parietal lobe may play a crucial role in episodic memory with respect to the recollection of details from an egocentric perspective.

Method: We tested 3 experimental groups: patients with stroke affecting right parietal cortex; patients with right hemisphere stroke not affecting parietal cortex; neurologically healthy control subjects. We designed a novel experimental task utilising a head-mounted camera to record images from the participants' perspective. This enabled us to directly evaluate the integrity of memory from the individuals' own personal point of view. All participants also carried out standard episodic memory tasks.

Results: We found that parietal patients were able to recall information as accurately as both control groups when they were asked to recollect what particular items had been present in an array or where items had been presented in relation to each other. They were also equivalently accurate in all standard tests of episodic memory. However, these patients were severely impaired when attempting to judge from which perspective they had viewed the scenes. This specific impairment was striking and in contrast to the relative ease of this condition for the control groups.

Conclusions: These results provide the first evidence for a specific deficit in episodic memory in patients with parietal damage, and highlight the importance of the original spatial context in this type of memory.

Keywords: Episodic memory, Parietal cortex, Stroke, Neuropsychology

157/10 – "Control of cognitive and emotional processing of faces by the frontal theta Rhythm" Investigadores/*Researchers*: Dr. Alberto João Rodrigues Leal, Dr. Ricardo Jorge de Pina Ramos Machado Lopes, Dr. Patrícia Arriaga, Prof. Francisco Gomes Esteves Instituição/*Institution*: Centro de Investigação e Intervenção Social, ISCTE-IUL, Lisboa (Portugal) Duração prevista/*Estimated duration*: 2011/04 - 2014/04

Introduction: The ability to process multiple visual domains of the human face is a well-developed capability in man, contributing significantly to social interaction. The extraction of emotional content out of facial features is one such domain, and it involves well-known brain structures, whose detailed contribution is nevertheless poorly characterized.

Objectives: Our emphasis is on detection and functional characterization of the brain areas involved in emotional processing of faces, with particular focus on contribution of frontal lobes. As a validation test we applied the protocols to patients with focal epilepsies undergoing surgery of epilepsy near the areas of interest.

Method: Mapping neurovascular (BOLD) responses to facial emotional content was obtained through 1.5T functional Magnetic Resonance (fMRI) while volunteers (N=17) were presented with pictures of human faces taken from the Karolinska Directed Emotional Faces database. The functional connectivity analysis between frontal and occipital lobes was performed using high-resolution EEG recordings (124 channels), while subjects viewed the same collection of pictures presented in the fMRI. Epilepsy patients were enlisted from a Surgery for Epilepsy project and the fMRI studies performed complemented the clinical imaging evaluation.

Results: A group of 17 subjects underwent the fMRI protocol and were the base for the construction of a quantitative database including the following brain structures: Fusyform Gyrus, Insula, Amigdala, Cingulate Gyrus, Fronto-orbital cortex. The frontal lobe responses were very consistent, providing a good background the EEG-based functional analysis. Responses in patients revealed abnomalities consistent with the location of the epileptogenic area.

The analysis of the fronta-occipital functional connectivity put in evidence a functional link between these structures, mainly in the theta range of frequencies. Ongoing work is concentrated on the association of the technique of Transcranial Magnetic Stimulation (TMS) with EEG to uncover the causal relationship in this connectivity.

Conclusions: We quantified responses to facial emotional content of a number of critical brain structures. Validation of the protocol in patients with focal epilepsies revealed promising clinical results. The EEG analysis put in evidence a strong functional conectivity between the frontal and occipital lobes in the theta range, in which current work using TMS will uncover causal relationships.

Publications: A paper is in preparation.

Keywords: Emotion, Faces, Functional connectivity, fMRI

170/10 – "The role of fusion of multisensory percepts in dynamic facial/body expressions: an fMRI study"

Investigadores/*Researchers*: Dr. Gina Maria Costa Caetano, Prof. Miguel Castelo-Branco, Prof. Beatrice de Gelder, Eng. Gregor Philipak

Instituição/Institution: Instituto Biomédico de Investigação de Luz e Imagem - IBILI-, Faculdade de Medicina, Universidade de Coimbra (Portugal)

Duração/Duration: 2011/04 - 2013/11

Objectives: The role of subcortical structures in processing sensory information conveying emotional content is still highly debated. It is known that the amygdala is the gateway to sensory processing of emotions, although its functional role at the interface between emotion and cognition remains to be clarified. Similarly, the role of other subcortical structures in affective processing is under debate. This study aimed at identifying the neural correlates of emotion detection and recognition, irrespective of sensory modality, focusing on the role of subcortical structures (colliculus, amygdala, and basal ganglia).

Method: To achieve this objective we studied recognition and categorization of deviant emotional content (happy, angry, afraid) embedded in fast dynamic neutral displays (unimodal or bimodal). Sixteen healthy male participants underwent fMRI measurements in three separate sessions (pseudo-randomized: visual/auditory; and audiovisual), respectively, in which dynamic displays were presented in 4 s miniblocks, interleaved by 12–16 s rest periods, followed by an emotion categorization task.

Results: Our findings confirm amygdala's active role in attributing value to sensory information, as amygdala response increased once the emotionally loaded deviant stimulus was presented. Importantly, the superior colliculus and thalamic nuclei showed increased response prior to display of emotional content, whereas bilateral putaminal activation was observed once emotion content is present and thereafter.

Conclusions: These results suggest a differential role of subcortical structures in the dynamics of emotion processing: the superior colliculus in anticipatory evaluation of sensorial input, the amydgala in explicit emotional content processing, and the basal ganglia in the integration of this information towards goal-oriented action selection.

Keywords: Emotion, Recognition, fMRI, Subcortical.

Aknowledgements: We warmly thank **Beatrice de Gelder** for all the support and input towards the success of this work.

180/10 – "Neuronal mechanisms underlying sex hormone-dependent switching of sexual receptivity"

Investigadores/*Researchers*: Dr. Kensaku Nomoto, Dr. Susana Lima Instituição/*Institution*: Champalimaud Foundation, Lisboa (Portugal) Duração/*Duration*: 2011/05 - 2013/07

Objectives: Female behavior is heavily influenced by the reproductive cycle. In mice, females show different behaviors in response to a male across the estrous cycle (i.e., having copulation or rejecting a male), although they start social interactions in a similar manner. Previous studies have elucidated important brain areas which control female sexual behavior. However, it is not known how these brain areas respond during initial social interactions in which there is not clear behavioral difference. Our objective is to clarify this issue by recording neuronal activity with the electrophysiological technique in freely behaving animals.

Method: We targeted the ventrolateral part of the ventromedial hypothalamus (VMHvl) as the recording site because it is known to be involved in the control of female sexual behavior. In our behavioral paradigm, the test animal was allowed to interact freely with the stimulus animal (either male or female), while neuronal activity was recorded.

Results: In our paradigm, we did not find clear behavioral difference across the estrous cycle. These results were consistent with the idea that females behaved similarly at the beginning of social interactions independent of the estrous cycle.

As for neural activity, we found VMHvl neurons that significantly responded with increased or decreased activity during social investigation compared to the activity during the control period. Furthermore, we found that the proportion of male-responsive neurons during the sexually receptive phase was higher than those during the other phases.

Conclusions: Our results suggest that, although female mice show similar behavior at the beginning of social interactions, the VMHvl neurons are already more responsive to males during the sexually receptive phase. Given that a majority of VMHvl neurons is glutamatergic, our results suggest that increased male-responsive VMHvl neurons facilitate transmission of male information during the sexually receptive phase, which might result in increased sexual receptivity.

Publications:

Nomoto, K. and Lima, S.Q. Social signals in the ventromedial hypothalamus of female mice: influence of the reproductive cycle. (*in preparation*)

Keywords: Electrophysiology, Hypothalamus, Social behavior, Rodent

186/10 - "Brain Mechanisms of Placebo Analgesia"

Investigadores/*Researchers*: Prof. Magne Arve Flaten, Prof. Per M. Aslaksen, Prof. Torgil R. Vangberg, Dr. Odd Petter Eldevik, Prof. Jan Bergdahl, Dr. Sara Vambheim, Dr. Just C. Thoner Instituição/*Institution*: University of Tromsø and University Hospital of North Norway, Tromso (Norway)

Duração/Duration: 2011/03 - 2014/02

Objectives: To investigate the role of negative emotions (fear, anxiety, nervousness) for the often observed pain reduction after administration of placebo (placebo analgesia).

Method: Expectations of reduced pain were induced by verbal information. Pain was induced by contact heat or laser in healthy volunteers in several experiments. Pain reactions were recorded verbally, by event-related potentials and by heart-rate variability.

Results: Expectations reduced pain (placebo analgesia). This effect was mediated partly via a reduction in negative emotions. If information did not reduce negative emotions, pain was not reduced. Induced fear abolished placebo analgesia.

Conclusions: Reduction in negative emotions due to information explains part of the placebo effect.

Publications:

Journal articles:

Aslaksen PM et al. (2011) Gender differences in placebo analgesia... Psychosom Med 73, 193-199.

Bjørkedal E & Flaten MA (2011) Interaction between expectancies and drug effects:... *Psychopharmacol* 215, 537-548.

Flaten MA et al. (2011) The relation of emotions to placebo responses. *Phil Trans Royal Soc – Sect B* 366, 1818-1827.

Lyby PS et al. (2011) Variability in placebo analgesia and the role of fear of pain ... *Pain*152, 2405-2412. Meissner K et al. (2011) The placebo effect: ... *J Neurosci* 31, 16117-16124.

Lyby PS et al. (2012) Induced fear reduces the effectiveness of *Pain* 153, 1114-1121.

Bjørkedal E & Flaten MA (2012) Expectations of increased or decreased pain... *J Pain Res* 5, 289-300. Books/book chapters:

Flaten MA & Al'Absi M (2012) Placebo and placebo effect. Encyclopedia of Behavioral Medicine. Springer 1497-1499.

Flaten MA (2012) Nocebo and nocebo effect. Encyclopedia of Behavioral Medicine. Springer 1340-1341.

Colloca L, Flaten MA, & Meissner K (2013) Placebo and Pain. From Bench to Bedside. Elsevier (312 p). Flaten MA et al. (2013) The role of positive and negative emotions In Colloca L et al. Placebo and Pain. Elsevier, 73-81.

Flaten MA (2013) Antagonistic responses, homeostasis, and... In Colloca L et al. Placebo and Pain. Elsevier, 103-113.

Flaten MA et al. (2013) Methodological issues in...In Colloca L et al. Placebo and Pain. Elsevier, 149-157.

Keywords: Placebo effect, Nocebo effect, Negative emotions.

190/10 – "The Sharefeld: A new standard for free response ESP research"

Investigadores/Researchers: Dr. Mario Varvoglis, Dr. Peter Bancel, Dr. Djohar Si Ahmed, Eng. Jean-Paul Bailly

Instituição/*Institution*: Institut Metapsychique International, Paris (France) Duração/*Duration*: 2011/04 - 2013/09

Objectives: 1. Develop and perfect a novel automated testing framework that combines forced-choice protocols with subject-optimization procedures, so as to obtain a flexible and powerful psi-research tool. 2. Conduct a telepathy experiment based on this testing approach, to assess its viability and determine improvements. Three hypotheses were assessed:

a) The trial effect size for the Optimized-Session (OS) will be significant

b) The OS trial effect size will be superior to that obtained in the Non-Optimized Session (NOS)

c) The OS session effect size would be superior to that established for the Ganzfeld

Method: Following development of the software and hardware, a formal experiment was defined with 25 participant-pairs. Participants went through a 10-minute training session (the Non-Optimized session, or NOS) involving 12 ESP trials, followed by a 40-minute Optimized Session (OS) with 20 trials. For both NOS and OS, the two subjects were situated in separate rooms and alternated roles, on a trial-by-trial basis, as Sender (who observed a randomly selected target) and Receiver (who had to decide which of two possibilities was the target for that trial). In the OS, subjects were also taken through audiovisual optimization procedures, and experienced the entire session (including the psi tasks), through an immersive head-mounted display system.

Results: None of the hypotheses was confirmed. However, post-hoc analyses showed abnormally high scoring variability in the OS condition (p=0.012), suggesting that the null results may have been due to a combination of psi-hitting / psi-missing, rather than the absence of psi. By contrast, NOS scoring variability was normal.

Conclusion: While the hypotheses were not confirmed, the post-hoc analyses did provide some evidence that the protocol elicited psi functioning, albeit in an unstable manner. Debriefings suggest that trial-by-trial feedback may have been discouraging for participants and that the head-mounted display was a source of considerable discomfort and distraction. Nevertheless, participants found the Sharefield experience to be very positive, and were motivated to continue with new sessions. More generally, we are encouraged by the successful integration of optimization procedures in an automated multiple-trial protocol, and are now working on improvements for the next experiment.

Publication: Proceedings of the 56th Annual Convention of the Parapsychological Association

Keywords: Subject-optimization, Telepathy, Forced-choice

191/10 – "Lucid dream induction by transcranial cortex stimulation: A test of the prefrontal hypothesis of lucid dreaming"

Investigadores/*Researchers*: Prof. Michael Schredl, Dr. Claudia Schilling, Dr. Ahmed Karim, Dr. Daniel Erlacher, Birgit Schütz

Instituição/*Institution*: Central Institute of Mental Health, Mannheim (Germany) Duração/*Duration*: 2011/08 – 2012/10

Objectives: Recent studies suggest that lucid dreaming (awareness of dreaming while dreaming) might be associated with increased brain activity over frontal regions during rapid eye movement (REM) sleep. By applying transcranial direct current stimulation (tDCS), we aimed to manipulate the activation of the dorsolateral prefrontal cortex (DLPFC) during REM sleep to increase dream lucidity.

Method: 19 participants spent 3 consecutive nights in a sleep laboratory. The first night served as an adaptation night, while the second and third nights were experimental nights: On one night (in a randomized order) the participants received 1 mA anodal tDCS for 10 min over the bilateral DLPFC (positions F3 and F4 according to the Ten-Twenty system) and on the other night they received sham stimulation. The stimulation was delivered during each REM period starting with the second one. One minute after the stimulation, the participants were awakened and asked for dream reports and additional questions about their experiences during the dream. Dream reports were transcribed, permutated and scored for lucidity and bizarreness by an external judge.

Results: In total, 109 REM awakenings were made. Stimulation had disruptive effects on REM sleep - in many cases participants awakened when tDCS was applied (for 3 participants no awakenings were possible during the tDCS night). According to the participants' self-ratings, tDCS over the DLPFC during REM sleep increased lucidity in dreams. The effects, however, were not strong and found only in frequent lucid dreamers. The judge rated dreams from tDCS nights as more lucid and more bizarre, but the differences disappeared when controlled for the dream report length. Additional analysis of microarousals showed that lucidity cannot be explained by increased arousal due to tDCS.

Conclusions: This study provides preliminary support for the involvement of the DLPFC in lucid dreaming, however further research, controlling for indirect effects of stimulation and including other brain regions, is needed. Due to small effects, tDCS might not be a promising tool for lucid dream induction on a practical level.

Publications:

Stumbrys, T., Erlacher, D., & Schredl, M. (2013). Testing the involvement of the prefrontal cortex in lucid dreaming: A tDCS study. *Consciousness and Cognition*, 22(4), 1214–1222. doi:10.1016/j.concog.2013.08.005

Keywords: Lucid dreaming, Dorsolateral prefrontal cortex, REM sleep, Transcranial direct current stimulation
199/10 – "Psychophysiology of Spiritual Transmission"

Investigadores/*Researchers*: Dr. Cassandra Vieten, Dr. Dean Radin, Dr. Marilyn Schlitz, Dr. Arnaud Delorme Instituição/*Institution*: Institute of Noetic Sciences, California (USA)

Duração/Duration: 2011/09 - 2013/06

Objectives: Practitioners from a variety of spiritual traditions occasionally report strong psychophysiological reactions when a spiritual teacher or *guru* who has achieved some level of mastery directs his or her attention toward the practitioner. In the Hindu tradition, this energy is called *shaktipat*, a Sanskrit term that roughly translates as "energy putting" (shakti - pat) or more simply as "sending energy." The objectives of this exploratory project were to investigate the psychophysiological correlates of the experience of spiritual transmission, and to develop methods to objectively measure them in both senders and recipients under controlled laboratory conditions.

Method: We first conducted a survey of people who reported having experienced this phenomenon. We analyzed these data to better describe the lived experience of receiving such a transmission, and to inform selection of subjective and objective measures for laboratory experiments. Then, to study the phenomenon under controlled conditions, we recruited an internationally recognised medical doctor and intuitive from Spain (the sender) who claims that he can "send energy" at a distance and has many patients who support his claim. We asked the sender to periodically send energy remotely to six recipients, one at a time, while they were isolated in our lab's electromagnetically shielded chamber some 50 meters away. We recorded the recipients' EEG (32 channels) and several autonomic measures throughout the testing period. None of the recipients knew the sender, and all were blind to when he was sending energy.

Results: Analysis of the resulting data suggested that in some recipients, significant changes in physiology were observed during the sending periods as compared with the rest periods. We also found differences in the physiological reactions of some participants when they were in the presence of the experienced sender vs. a "sham guru," i.e., an actor playing the part of a guru.

Conclusions: This preliminary investigation indicates that it is possible to investigate spiritual transmission using psychophysiological methods under controlled conditions, and that the reported effects of *shaktipat* or other forms of spiritual transmission may be objectively measurable. We are currently using this protocol to investigate additional sender/recipient pairs, and are preparing a manuscript reporting our protocol and results for publication in a peer-reviewed academic journal.

Publications: manuscript in preparation.

Keywords: Spiritual transmission, Electro-encephalography, Shaktipat, Remote influence

201/10 – "The effects of audience size and audience rating on field random number generator output: A case study of Japanese professional baseball"

Investigadores/*Researchers*: Dr. Takeshi Shimizu, Prof. Masato Ishikawa, Dr. Tatsu Hirukawa Instituição/*Institution*: Science Communicatoin Laboratory, Meiji University, Tokyo (Japan) Duração/*Duration*: 2011/03 - 2012/10

Objectives: This study examined the association between the outputs of a true random number generator (RNG) and audience size during Japanese professional baseball games. We regarded an RNG as a signal detector of field consciousness and hypothesized that the number of signal sources might increase the ability of an RNG to detect signals.

Method: Experimenters and assistants voluntarily obtained 76 samples from a total of 78 baseball games during the 2010–2011 baseball seasons. The effects of audience size at the stadium (M = 38970 ± 6058 SD, N = 78) and TV audience ratings (M = 7.07 ± 2.32 SD, N = 23) were examined in relation to the measurements of multiple Random Streamer and Psyleron RNG devices. RNGs set at remote locations ran simultaneously during the games.

Results: Our results show a positive correlation between accumulated chi-squared statistics by Random Streamer and audience size at the stadium.

Conclusions/Discussion: Unexpectedly, identical RNGs showed strong negative correlations between different machines, which suggests that their outputs cancelled each other out. Finally, some future tasks are discussed.

Publications:

Shimizu, T. & Ishikawa, M. (2012) Feld-RNG-Experimente mit Kurzfilmen: Eine Untersuchung zur Hypothese der fokussierten Aufmerksamkeit und zur Emotionshypothese. Zeitschrift fur Anomalistik, 12(1), in Press.

Shimizu, T. & Ishikawa, M. (2012) Audience Size Effects in Field RNG Experiments: The Case of Japanese Professional Baseball Games. Journal of Scientific Exploration, 26(3), 67-83.

Shimizu, T. & Ishikawa, M. (2012) Reliability of Outputs of Field Random Number Generator Movie Experiments. Neuro Quantology, 10(3), 389-393.

Shimizu, T. & Ishikawa, M. (2012) Examination of Retroactive Effects in a Field RNG Experiment Using Prerecorded Files. Journal of the International Society of Life Information Science, 30, 5-16.

Shimizu, T. & Ishikawa, M. (2012) Field RNG Experiments Using Short Movies: An Examination of the Focused-attention and Emotion Hypotheses. Journal of the International Society of Life Information Science, 30, 17-30.

Keywords: Baseball Stadium, MMI, Rpg102, and multiple RNG

206/10 – "Extrasensory Perception, Dissociation, and Motor Automatisms" Investigadores/*Researchers*: Dr. John Palmer, Dr. Christine Simmonds-Moore Instituição/*Institution*: Rhine Research Center, North Carolina (USA) Duração/*Duration*: 2011/03 - 2012/10

Objectives: The objective of the study was to test the association of state and trait dissociation with performance on an ESP task modelled after the Ouija Board.

Method: Onto the board (a computer writing tablet) was affixed a 16-square grid dividable into four quadrants, with a number 1 to 4 in each square. The three target designations were: square (p = 1/16), quadrant (p = 1/4), and number (p = 1/4). The main dependent variable was "location hits," an unweighted composite of square and quadrant hits. For each of 36 trials, 80 participants explored the surface of the grid with the computer pen, indicating their responses by stopping for 1 sec. Beforehand, they completed at home Watson's Dissociative Processes Scale, which has three subscales: Obliviousness, Imagination, and Detachment. They were randomly assigned to four cells. Independent variables were hand used to move the pen [R vs. L] and additional procedures applied during the ESP task to facilitate dissociation. For one of these (Eyes-closed: E), participants were instructed to keep their eyes closed and blank the mind as much as possible. For the other (Quotations: Q), the intent was to distract the conscious mind by having participants read quotations that appeared in succession on a computer screen.

Results: A 2x2 ANOVA yielded a significant Method by Hand interaction, with significant psi-hitting in the combined ER, EL, and QR conditions (EQR). Significant psi-missing in the QL condition was attributed to frustration due to high task difficulty in this condition. Participants who reported experiencing their hand being moved by an outside force during the ESP task scored significantly higher than other participants. Positive responses to the outside-force question were predicted by DPS Detachment. Significant positive correlations were found between ESP and DPS Imagination and Detachment. The above results apply to location hits in the EQR condition. All DPS subscales positively predicted number hits in the QL condition.

Conclusion: The data were interpreted as reflecting the operation of two distinct processes mediating different trials in the ESP run: (a) a (primarily) motor process restricted to location hits the EQR condition and (b) a (purely) cognition process operative for location and number hits across all conditions.

Publications:

Abstract published in *Proceedings of the Parapsychological Association* 56th Annual Convention, p. 25.

Keywords: ESP, Dissociation, Motor

215/10 - "Vestibular contributions to self-awareness"

Investigadores/*Researchers*: Prof. Patrick Haggard, Dr. Elisa Raffaela Ferre Instituição/*Institution*: Institute of Cognitive Neuroscience, University College London (UK) Duração/*Duration*: 2011/10 - 2013/04

Objectives: Vestibular inputs do not produce conscious perceptions of their own, yet correct processing of these signals is essential for our interactions with the external environment. For instance, the ability to acquire a sense of direction and orientation in external space depends on the capacity of our brain to integrate vestibular inputs arising from the otolith organs and semicircular canals with other sensory signals. Here we demonstrated that vestibular system contributes to *self-world* interaction at least in three different ways: modulating bodily sensations, affecting the representation of the body as a spatially extended object, influencing the mechanisms for maintaining the self-world differentiation.

Method: In a series of psychophysical and electrophysiological experiments, the vestibular organs of healthy volunteers were non-invasively stimulated either thermally (Caloric Vestibular Stimulation, CVS) or electrically (Galvanic Vestibular Stimulation, GVS). Participants made judgements about the body and its relation to the environment both under vestibular stimulation, and under control conditions.

Results: Both CVS and GVS modulated somatosensory processing, increasing the sensitivity for touch, but decreasing sensitivity for pain [1,2]. Accordingly, vestibular stimulation influenced somatosensory brain evoked potentials [3], suggesting a role of the vestibular system in influencing bodily sensations. Further, GVS altered the localisation of stimuli on body surface [4]. Blindfold participants were touched at one of several different locations on the hand, and immediately attempted to point to the location where they had been touched. During GVS, touches on the hand were perceived as shifted toward the wrist [4]. The shift was systematically in a distal-proximal direction, thus directed towards the centre of the body, indicating a vestibular-induced shrink of the representation of the body. Finally, the spatial relation between body and environment was investigated by judging the distance between one's own body and an external stimulus. Both visual and auditory stimuli were presented. In both cases, GVS caused overestimation of distance, particularly for objects located farther away. These results suggest that the vestibular system maintains the normal spatial relation between the body and external objects.

Conclusions: Vestibular organs are activated by head movements. However, every movement of the head implies a new relation between the self and the world. Our findings revealed that the vestibular system directs a form of sensory signal management, balancing bodily sensations and behaviours in relation with the external environment changes [5].

Publications:

- 1. Ferrè, E. R., Bottini, G., Iannetti, G. D., & Haggard, P. (2012). The balance of feelings: Vestibular modulation of bodily sensations. Cortex. 49(3):748-58. doi: 10.1016/j.cortex.2012.01.012.
- 2. Ferrè, E.R., Day, B.L., Bottini, G. & Haggard, P. (2013) How the vestibular system interacts with somatosensory perception: a sham-controlled study with galvanic vestibular stimulation. Neuroscience Letter. 550:35-40. doi: 10.1016/j.neulet.2013.06.046.
- 3. Ferrè, E. R., Bottini, G., & Haggard, P. (2012). Vestibular inputs modulate somatosensory cortical processing. Brain Structure and Function, 217(4), 859-864.
- 4. Ferrè, E. R., Vagnoni, E., & Haggard, P. (2013). Vestibular contributions to bodily awareness. Neuropsychologia. 51(8):1445-52. doi: 10.1016/j.neuropsychologia.2013.04.006.
- 5. Ferrè, E.R., Vagnoni, E., & Haggard, P. (2013) Galvanic vestibular stimulation influences randomness of number generation. Experimental Brain Research. 224(2):233-41. doi: 10.1007/s00221-012-3302-6.

Keywords: Bodily Awareness, Vestibular system, Self-world relation

223/10 – "Exploring the relationship between the synaesthesias and anomalous experiences" Investigadores/*Researchers*: Dr. Christine Simmonds-Moore, Dr. Carlos Alvarado, Dr. Nancy Zingrone, Ferrell Carpenter Instituição/*Institution*: University of West Georgia (USA) Duração/*Duration*: 2011/09 - 2013/05

Objectives: Incidence and distribution of the synaesthesias and their relationship to anomalous experiences, schizotypy and well-being. Comparing synaesthetes and matched controls on psi performance and memory.

Method: An online survey included the Synaesthesia Experience Questionnaire (SEQ) the Oxford Liverpool Inventory for Feelings and experiences (OLIFE), Deiner's Life Satisfaction Questionnaire, the Anomalous Experiences Inventory (AEI) and 5 items tapping parapsychological experiences. Twenty-seven synesthetes and 27 matched controls completed the TimeStyleTM inventory, the synesthesia subscale of the TAS, Bem's precognitive memory task and a Mental time travel task. Synesthetes completed a Synaesthetic Characteristics Questionnaire. Interviews were conducted.

Results: Different types of synaesthesia varied in incidence. The SEQ was not normally distributed but was reliable and loaded onto one factor. SEQ scores correlated with scores on the AEI and positive schizotypy. Traditional paranormal experiences were associated with scoring higher on the SEQ. SEQ scores did not relate to well-being. This relationship appears to be mediated by schizotypy cluster membership. There was no evidence for ESP in the combined group, the controls or the synaesthetes and differences between groups was not significant. SEQ scoring did not correlate with ESP. Associators scored higher on the psi task than projectors (post hoc). Future thinking correlated with SEQ scores but not ESP. Past thinking correlated with ESP. Mental time travel did not relate to ESP but some variables were stronger in synaesthetes. An IPA suggested that ability to represent has a role in synaesthesia and anomalous experiences.

Conclusions: There is an overlap between the tendency to experience synaesthesia and anomalous experiences which may include ESP performance in some types of synaesthesia.

Publications:

Simmonds-Moore, C. (2012). Exploring the Synesthesias and anomalous experience. Paper presented at the synesthesia pre-conference workshop at Toward a Science of Consciousness. Simmonds-Moore, C.A., Alvarado, C., & Zingrone, N. (2012). The relationship between the synesthesias and anomalous experiences. Poster presented at the 2012 Annual Convention of the PA.

Keywords: Synaesthesia, Schizotypy, Wellbeing, Anomalous experience, ESP

231/10 – "Toward understanding visual awareness: An intracranial EEG study on transient suppression phenomena of conscious visual perception"

Investigadores/Researchers: Dr. Tonio Ball, Prof. Andreas Schulze-Bonhage, Prof. Ad Aertsen, Dr. Jörn Rickert, Markus Kern

Instituição/*Institution*: Epilepsy Center, University Hospital, Freiburg (Germany) Duração prevista/*Estimated duration*: 2011/08 - 2014/04

Objectives: To date, little is known about the neural mechanisms of blink and saccadic suppression, i.e., the transient suppression of conscious visual perception during blinks and saccades. We hypothesized that, in addition to the classically investigated early visual areas, associative brain regions could provide new important insights into the neural mechanisms of conscious visual perception. Thus, we tested whether blinks and saccades are preceded by suppression of activity in local neural networks, both in occipital visual areas and associative areas located in the prefrontal cortex. Furthermore, we analysed in which way the long-range communication between these areas was modulated in the time period preceding the blinks and saccades.

Method: In this study we used intracranial EEG (iEEG) recordings with high spatial- and temporal resolution high signal to noise ratio. Since variations of activity in local neural networks are closely associated with spectral power changes, we used established methods for time-frequency analysis to detect these changes. To investigate possible modulations in the communication pathway between the aforementioned areas, we used established methods for assessing long-range phase-synchrony. As a prerequisite for these studies, we characterized the influence of physiological noise on phase-synchrony statistics in iEEG recordings.

Results: Our results obtained within this project strongly support our assumption that saccades are preceded by a suppression of local activity in primary visual area V1. This basic finding indicates that a top-down visual suppression mechanism exists that effectively shuts down local neuronal communication in early visual areas and thereby generates the transient visual sensitivity loss during saccades and blinks. Such a top-down signal could originate from dorsolateral prefrontal cortex, a region involved in the processing of fluctuations in the contents of visual consciousness.

Conclusion: By using a template-based correction algorithm to remove pulse-related physiological noise, analyses of blink- and saccade-related modulations of long-range phase synchrony within the cortical network of regions involved in visual perception are now underway.

Publications:

Kern, M. et al., 2013. Heart cycle-related effects on event-related potentials, spectral power changes, and connectivity patterns in the human ECoG. *NeuroImage*, 81, pp.178–190. 2)

Kern, M. et al., revision in review. Gamma band responses in human visual areas V1-V3 during blinks and saccades: an ECoG study (submitted)

Keywords: Visual suppression, Gamma band, Electrocorticogram

238/10 – "Effect of the comprehensive Art of Living yogic breathing programme on brain function in correlation with physiological and psychological well-being"

Investigadores/*Researchers*: Dr. Sanja Kostrun, Dr. Irena Svenda, Dr. Kresimir Jergovic, Dr. Drazen Durch, Prof. Jagoda Doko Jelinic, Prof. Fahri Saatvcioglu, Dr. Alen Pticar, Dr. Sanja Kordic Instituição/*Institution*: Art of Living Croatia, Zagreb (Croatia) Duração prevista/*Estimated duration*: 2011/11 - 2014/04

Objectives: Objective of this study was to investigate effects of yoga and breathing techniques on brain function in correlation with physiological and psychological well-being. The comprehensive yogic program of The Art of Living Foundation consisting of asanas (postures), pranayama (breathing exercises), Sudarshan Kriya (unique rhythmic breathing exercise), relaxation techniques, stress management, group processes and team work, was applied on new volunteers and were compared to the age long practitioners.

Method: Main parameters measured were: psychological parameters encompassing general health status, satisfaction with life, quality of life, self-esteem, emotional status, anxiety, neuroiticism, social distance, spirituality and religion tolerance and smoking habits, diet (eating) habits and alcohol consumption; physiological parameters encompassing metabolic status, blood pressure and lung capacity and EEG analysis of brain function.

The study included pre-post test design with age long practitioners and new volunteers who consist the control group before completing AOL program. After that new practitioners become intervention group, participated in the initial 6 day course and were evaluated immediately after the workshop.

Results & Conclusions: Preliminary results have indicated that long-term practice of AOL program has a positive effect on all investigated psychological parameters. Effects are significantly more pronounced for the age long practitioners than for the new practitioners. Influence of the applied treatment on the physiological parameters was not statistically significant. This is probably due to the stringent inclusion criteria we used in order to select study participants of a very good health. We expect that effects would be more pronounced in the homogeneous group of certain chronic diseases which will be the next step in our research efforts. Preliminary results of EEG analysis are in line with previous findings showing enhanced brain function through increased mental focus and heightened awareness.

Keywords: Breathing techniques, Yoga, Meditation, Sudarshan kriya

2012

41/12 – "The Body beyond the body"

Investigador/Researcher: Prof. Marcello Costantini, Dr. Francesca Ferri Instituição/Institution: Department of Neuroscience and Imaging, University "G. d'Annunzio", Chieti (Italy)

Duração prevista/Estimated duration: 2013/03 - 2014/03

Objectives: More than 100 papers have been published on the rubber hand illusion since its discovery 14 years ago. The illusion has been proposed as a demonstration that the body is distinguished from other objects by its participation in specific forms of intermodal perceptual correlation. Here, we radically challenge this view by claiming that perceptual correlation is not necessary to produce the experience of this body as mine.

Method: Each of 15 participants was seated with his/her right arm resting upon a table just below another smaller table. Thus, the real hand was hidden from the participant's view and a life-sized rubber model of a right hand was placed on the small table in front of the participant. The participant observed the experimenter's hand while approaching - without touching - the rubber hand. Phenomenology of the illusion was measured by means of skin conductance response and questionnaire.

Results: Both measures indicated that participants experienced the illusion that the experimenter's hand was about to touch their hidden hand rather than the rubber hand, as if the latter replaced their own hand. This did not occur when the rubber hand was rotated by 180° or replaced by a piece of wood.

Conclusions: This illusion indicates that our brain does not build a sense of self in a merely reactive way, via perceptual correlations; rather it generates predictions on what may or may not belong to itself.

Publications:

Ferri F, Chiarelli AM, Merla A, Gallese V, Costantini M. The body beyond the body: expectation of a sensory event is enough to induce ownership over a fake hand. Proc Biol Sci. 2013 Jun 26;280(1765):20131140. doi: 10.1098/rspb.2013.1140.

Keywords: Body ownership, Rubber hand illusion, Expectation, Bodily self

46/12 – "Motivational Intensity in the Prefrontal Cortex"

Investigador/Researcher: Prof. Stephen Fairclough, Dr. Christopher Burns Instituição/Institution: School of Natural Sciences and Psychology, Liverpool John Moores University (UK)

Duração prevista/Estimated duration: 2013/03 - 2014/03

Objectives: The aim of this work was to investigate the motivational intensity model (MIM) using measures of brain activation. The MIM has been extensively explored using cardiovascular psychophysiology, however the activation of the prefrontal cortex has not been explored in this particular paradigm. The aim of this study was to investigate how cognitive demand in response to working memory load affected activation of the rostral prefrontal cortex (rPFC) under two conditions: (a) control (no reward) and (b) financial reward. It was hypothesised that the presence of reward would enhance rPFC activation but only when cognitive demand was high.

Method: 40 participants (20 males) volunteered for the mixed-design study where reward group served as a between-participants factor. Cognitive demand was varied by exposing participants to a working memory task (nback) at five levels of difficulty, e.g. 0-back, 1-back, 3-back, 5-back, 7-back. Demand was estimated to be easy (0-back, 1-back), hard (3-back, 5-back) or impossible (7-back). All participants were paid £10 for taking part in the study, but half of the participants were offered an additional monetary reward of £10 that was linked to their performance on the task. Blood oxygenation in the rPFC was captured using a functional near-infrared spectrography (fNIRS) device that covered the forehead region of the participant and monitored BA10.

Results: The results of the study indicated that blood oxygenation in the rPFC was generally higher in the presence of reward. It was also apparent that activation of the rPFC peaked at the 3-back task for participants in the control group, whereas this peak was observed at the 5-back for participants in the reward group.

Conclusions: The rPFC responded to both cognitive demand and the presence of a reward. This effect was consistent with the MIM where the level of effort invested into a task is influenced by the likelihood of success and the presence of an extrinsic reward.

Keywords: Motivation, Working memory, Prefrontal cortex, fNIRS

54/12 – "A Rasch Scaling Validation of a Core "Near-Death Experience (NDE)" A Critical Replication and Extension"

Investigador/*Researcher*: Dr. Rense Lange

Instituição/*Institution*: Integrated Knowledge Systems, Inc., Illinois (USA) Duração prevista/*Estimated duration*: 2013/02 - 2014/03

Objectives: We used Latent Semantic analysis to analyze textual (i.e., typed) accounts of near-death experiences (NDEs) to determine if (i) this is a viable method to study free-response data and (ii) if "true-NDEs" as defined by Greyson's NDE Scale can be differentiated from other clinical accounts whereby perceptions are likely not parapsychological in nature. We are not aware of LSI applications for this purpose, and hence it is necessary to first establish the basic validity of this approach.

Method: Professor Bruce Greyson provided a collection of about 700 NDE accounts, all combined in single MS Word file with a total of 1423 pages with over 700,000 word tokens. The accounts were marked with a classification provided by Greyson (four categories are True positive/negative and False positive/negative). The precipitant for the close brush with death was surgery or childbirth for 36%, illness for 28%, accident for 14%, and "other" (including attempted suicide, criminal assault, and combat) for 23%. Loss of vital signs was reported by 37%, and an additional 37% reported that their condition had been a serious life-threat without loss of vital signs; 26% reported that, in retrospect, they did not consider their condition life-threatening, although it had appeared to be so at the time of the event. Data were first "cleaned" before being transformed into textual units (or, tokens). Specifically, spelling errors were corrected, contractions were uniquely identified as single words by replacing any intervening spaces and dashes by "xxx" (thus, "well-being" and "well --- being" both become "wellxxxbeing"), low information words were omitted ("a", "the", "as", ...). As well, very infrequent (n < 2) or very short words (with fewer than 3 letters) were removed. Next, all words were "stemmed" - which is an algorithmic procedure to remove all prefixes and suffices and grammatical alterations so as to identify the common root of different word forms. For instance, the words "informative" and "information" have a common root, the exact form of which is irrelevant (here) and it is denoted by the token "informati". This step relied on the well-known Porter stemmer. Finally, end-of-sentence markers and bigrams (i.e., contractions of adjacent words) were added. Thus, a segment like "a low information text" yields the following tokens "#|low", "low|informati", "informati|text", 'text|#". In both cases, a vocabulary of about 2000 tokens was obtained. The respective vector spaces were simplified by applying Singular Value Decomposition methods, yielding a space of 200 latent topics (factors).

Results: Percipients' loadings on each of the 200 semantic factors was computed, and the 60 most important factors were used to perform classification analyses. Throughout the following, the procedure was to fit a model on one or more subsets of the data (the training sets), and this model was then applied to the remaining data (the validation set). Reported are the results for the validation set as these reflect the extent to which the predictions can be generalized. The findings indicated that it was possible to distinguish True-NDErs form the other respondent groups with acceptable level of generalizability (60% precision). The distinctions between the other categories was less clear.

Conclusions: The results validate the Support Vector Machine approach, a prediction method that has received increasing attention in Artificial Intelligence. However, additional analyses are planned using different methods and it seems very likely that additional patterns will be discovered. Further, consistent with previous work based on Rasch scaling, True-NDEs again stand out from Greyson's other classifications of NDE accounts. This reaffirms that there seems to be a fundamental NDE experience that is reliably differentiated from other forms of clinical experience close to death.

Keywords: Latent semantic analysis, Near-death experiences (NDEs), Spontaneous cases, Clinical parapsychology

127/12 – "An Investigation of the I Ching Using the Q-Sort Method and a PK-RNG Design"

Investigador/Researcher: Dr. Lance Storm

Instituição/*Institution*: Brain and Cognition Centre, School of Psychology, University of Adelaide and Australian Institute of Parapsychological Research, Incorporated, Gladesville (Australia) Duração prevista/*Estimated duration*: 2013/03 - 2014/03

Objectives: The *I Ching* may involve a paranormal process (Storm, 2008). Given the work by Roe, Martin, and Drennan (2010) using the *I Ching* and the Q-Sort method, it was considered possible to emulate a paranormal (i.e., synchronistic) event artificially by constructing a representation of <u>inner</u> mental (cognitive/emotional) states using the Q-Sort Grid in which 64 *I Ching* descriptor-pairs were thoughtfully placed, followed by the creation of an <u>outer</u> event using a Random Number Generator to generate an *I Ching* hexagram with an associated reading. There were two hypothesized psi-predictors: (i) paranormal belief, measured on the Australian Sheep-Goat Scale (ASGS; Thalbourne, 1995); and (ii) Reactance, measured on the Hong Psychological Reactance Scale (HPRS; Hong & Faedda, 1996)—reactance (a resistance to compliance) is hypothesized to be detrimental to psi effects.

Method: Participants completed the ASGS and the HPRS. Using the Q-Sort Grid, participants gave a rating of +7 to the descriptor-pair that <u>most</u> described their feeling states — it is hypothesized that the <u>strongest</u> feeling state correlates with the outer event (i.e., generating an *I Ching* reading). Q-scores range from +7 to -7 (expected mean = 0.00). Before the PK-RNG task of generating six random numbers for the *I Ching* Hexagram, all participants read a communication (Silvia, 2005) surreptitiously presented as basic information about participating in a psi study. Randomly-selected participants in the treatment condition read the same opinion piece plus a threatening elements to elicit a reactance effect.

Results: Interim results (N = 55; planned: N = 120). <u>RNG score</u> was above MCE, marginally significant, z = 1.48, p = .06. <u>Q-Sort hitting</u> was in a non-significant <u>negative</u> direction, and <u>direct hitting</u> ($P_{MCE} = 1/64 \approx .016$), though there were two direct hits (i.e., above MCE), was not significant. Two sheep-goat effects in the hypothesized direction, but neither was significant: <u>RNG score</u>—mean hit rate for sheep (3.79) was higher than goats (1.04), and <u>Yang lines</u>—mean hit rate for sheep (3.25) was higher than goats (2.96). Two reactance effects in the hypothesized direction, but neither was significant: <u>Direct hits</u>—mean hit rate for reactants (0.03) was lower than controls (0.05), and <u>Yang lines</u>—mean hit rate for reactants (3.09) was lower than controls (3.15). The RNG task was computer timed. Instead of relaxing as was instructed, goats tended to rush the task and RNG scores were lower, whereas sheep took their time and scored higher than goats.

Conclusion: Outcomes were non-significant because the small sample lacked power at this mid-way stage of the study, but the findings bode reasonably well for the hypotheses, and the innovative nature of the experimental design.

Keywords: ESP, PK, RNG, Reactance, Psi, Sheep-goat effect

266/12 – "One ear is better than two; but why and when?"

Investigador/*Researcher*: Prof. Veena Kumari, Dr. Elena Antonova Instituição/*Institution*: Institute of Psychiatry (IoP), King's College London (UK) Duração prevista/*Estimated duration*: 2013/03 - 2014/03

Objectives: The magnitude of the human eye blink reflex to a strong startle-eliciting sensory stimulus, the pulse, is reduced if this is preceded shortly by a weak prestimulus, the prepulse. This effect is known as prepulse inhibition (PPI) and considered to index sensorimotor gating function. PPI is stronger with monaural, than binaural, acoustic prestimuli. It is presently unknown why monaural prepulses produce more PPI than binaural prepulses. The main objective of this research is to investigate the possibility that monaural prepulses are experienced as more salient or attention-capturing (unambiguous to locate and hence engage bottom-up orienting attention network) than binaural prepulses and, if so, this would be expected to result in stronger PPI.

Method: The effect of verbal and visuospatial attention manipulations on monaural and binaural PPI was tested in a group of healthy people from the general population, as well as a healthy group of experienced mindfulness practitioners who are considered to have a stronger information processing capacity and to be more efficient in allocating attentional and information processing resources.

Results: Preliminary analysis of the data in the meditation-naïve group has revealed lower monaural PPI under attention manipulation conditions. Data collection in meditators is ongoing at present and will be used to examine whether they, in line with our hypothesis, show little or no effect of attention manipulations in binaural or monaural PPI.

Conclusions: The fndings of this research, when available in full (by end of March 2014), will help us understand the conditions influencing attention-specific component of PPI phenomenon as well as the effect of mind training (mindfulness practice) on these conditions.

Keywords: Human sensorimotor gating, Startle, Attention, Mindfulness

10º Simpósio da Fundação മ്രീപ്പേവി

A Fundação BIAL tem como missão incentivar o conhecimento científico do Ser Humano, tanto do ponto de vista físico como espiritual.

Instituição sem fins lucrativos, considerada de utilidade pública pelo Governo português, a Fundação foi constituída em 1994 pelos Laboratórios BIAL e pelo Conselho de Reitores das Universidades Portuguesas e conta com os altos patrocínios do Senhor Presidente da República e da Ordem dos Médicos.

A atividade desta instituição desenvolve-se através da atribuição do Prémio BIAL, um dos maiores galardões na área da saúde em toda a Europa, e do lançamento de Bolsas de Investigação na área das Neurociências. Bianualmente, a Fundação BIAL organiza os simpósios Aquém e Além do Cérebro, um espaço de debate onde reúne os seus bolseiros e alguns dos mais prestigiados especialistas mundiais nas áreas da Psicofisiologia e da Parapsicologia.

O ano de 2014 assinalou os 20 anos desde a criação da Fundação BIAL e, simultaneamente, os 30 anos do Prémio BIAL. Para assinalar esta data, a Fundação criou um Centro de Documentação e uma Base de Dados. O primeiro pretende constituir um repositório documental da Fundação, integrando as diversas publicações editadas. A Base de Dados inclui informação relativa aos projetos nas áreas da Parapsicologia e da Psicofisiologia apoiados até à atualidade. Estes dois serviços estão disponíveis *online* em: www.fundacaobial.com

O livro de atas que agora se publica é uma compilação dos textos das palestras apresentadas durante o 10° Simpósio da Fundação BIAL dedicado ao tema "Interações Mente--Matéria".

The BIAL Foundation's mission is to foster the scientific study of the Human Being from both the physical and spiritual perspectives.

The BIAL Foundation is a non-profit-making institution, considered as a public utility by the Portuguese Government and established in 1994 by the BIAL Laboratories and the Council of Rectors of the Portuguese Universities. The Foundation includes among its patrons the President of Portugal and the Portuguese Medical Association.

The activity of this institution involves the BIAL Award, one of the most important awards in the field of health in Europe, and the BIAL Fellowship Programme in the area of Neurosciences. Every two years the BIAL Foundation organizes the "Behind and beyond the brain" symposia – a discussion forum that brings together bursary-holders and several world-renowned experts in the fields of Psychophysiology and Parapsychology.

The year 2014 marked 20 years since the establishment of the BIAL Foundation and simultaneously 30 years of the BIAL Award. To mark this date, the Foundation created a Documentation Center and a Database. The first was designed to be the Foundation's document repository, integrating several publications. The database includes information regarding projects in the fields of Parapsychology and Psychophysiology supported to present. These two services are available online at: www.fundacaoBial.com

The Proceedings that are now being published include the texts of the lectures presented during the 10th Symposium "Behind and Beyond the Brain" dedicated to the theme "Mind-Matter Interactions".



Instituição de utilidade pública Institution of public utility