12º Simpósio da Fundação Bial

Aquém e Além do Cérebro

Behind and Beyond the Brain

Casa do Médico - Porto • 4 a 7 de abril de 2018

FUNDAÇÃO Bial

Instituição de utilidade pública

Institution of public utility

Potenciar a mente

Enhancing the mind

O livro "Aquém e Além do Cérebro" contém as atas do 12º Simpósio da Fundação Bial, realizado na Casa do Médico, de 4 a 7 de abril de 2018, tendo como membros da Comissão Organizadora os Senhores Professores Axel Cleeremans, Etzel Cardeña, Miguel Castelo-Branco, Rui Costa, Rainer Goebel, Mário Simões e Caroline Watt.
Os textos estão disponíveis em www.fundacaobial.com.

The book "Behind and Beyond the Brain" includes the texts of the Bial Foundation's 12th Symposium, held at Casa do Médico, from April 4th to 7th 2018, having as members of its Organizing Committee the following Professors: Axel Cleeremans, Etzel Cardeña, Miguel Castelo-Branco, Rui Costa, Rainer Goebel, Mário Simões e Caroline Watt.
The texts are available at www. fundacaobial.com.

Foi publicado em 1ª edição pela Fundação Bial com uma tiragem de 2.250 exemplares.

It was published as 1st edition by Fundação Bial with a print run of 2.250 copies.

Execução Gráfica / *Printed by*:
Rebelo - Artes Gráficas,Lda.
Depósito Legal Nº 459244/19
ISBN 978-972-99286-8-0

ÍNDICE
INDEX

SESSÃO DE ABERTURA / *OPENING SESSION*

CONFERÊNCIA INAUGURAL / *OPENING CONFERENCE*

PALESTRAS / *LECTURES*

Textos disponíveis em www.fundacaobial.com *Texts availabe at www.fundacaobial.com*

SESSÃO DE ABERTURA
OPENING SESSION

DISCURSO DO PRESIDENTE DA FUNDAÇÃO BIAL

Luís Portela

Boa noite. É para nós um gosto recebê-los nesta XII edição do Simpósio Aquém e Além do Cérebro, desta vez dedicado ao tema "Potenciar a mente". Sejam bem-vindos.

Uma palavra especial de agradecimento pela presença do Senhor Ministro da Ciência, Tecnologia e Ensino Superior, Prof. Manuel Heitor, a quem admiramos, pelo longo e bem conseguido percurso que tem feito ao serviço da Ciência em Portugal, seguindo de perto o exemplo daquele que foi o principal obreiro do desenvolvimento do setor, o Prof. José Mariano Gago, que algumas vezes aqui também esteve connosco.

Muito obrigado pela presença do Senhor Secretário de Estado Adjunto e da Saúde, Prof. Fernando Araújo, a quem estimamos pela forma ponderada e competente como serve a causa pública, na área da Saúde.

Os nossos agradecimentos à Ordem dos Médicos, na pessoa do seu Bastonário, Dr. Miguel Guimarães, e ao Conselho de Reitores das Universidades Portuguesas, na pessoa do seu Vice-Presidente, Prof. Manuel Assunção, por todo o apoio que têm dispensado à Fundação Bial.

O nosso muito obrigado pela presença da Senhora Bastonária da Ordem dos Farmacêuticos, Prof. Ana Paula Martins.

Cumprimento as demais autoridades presentes, os nossos convidados e amigos, os membros da Comissão Organizadora deste simpósio, nomeadamente o seu Presidente, Prof. Axel Cleeremans, os palestrantes, os investigadores por nós apoiados, os representantes dos órgãos de comunicação social e, enfim, todos os presentes.

Esta Fundação é uma instituição sem fins lucrativos, considerada pelo governo português de utilidade pública, criada pelos Laboratórios Bial e pelo Conselho de Reitores das Universidades Portuguesas em 1994 e gerida por representantes destas duas instituições. Tem tido como três grandes atividades a gestão de um prémio de investigação em Saúde criado em 1984 - o Prémio Bial -, um sistema de apoio à investigação

científica em Psicofisiologia e em Parapsicologia e a realização, de dois em dois anos, destes simpósios sob o tema geral "Aquém e Além do Cérebro". Permitam-me um breve balanço.

Nos seus 34 anos de existência, o Prémio Bial distinguiu 266 profissionais de Saúde, contando-se entre eles algumas das mais destacadas figuras da área em Portugal e, também, alguns investigadores de grande craveira internacional. Foram editadas 38 obras premiadas, distribuídas gratuitamente a profissionais de Saúde.

No ano passado, decidimos alterar significativamente as características do Prémio Bial. Manteremos nos anos pares o Prémio Bial de Medicina Clínica, que distingue de entre as obras que se candidatem, trabalhos originais, de índole médica, com tema livre e dirigidas à prática clínica. Tem o valor de €100.000. Neste momento estão abertas candidaturas a este prémio, cujo júri é constituído por representantes das diferentes escolas médicas portuguesas e presidido pelo Prof. Manuel Sobrinho Simões.

Para além disso, criámos um novo prémio, a ter lugar nos anos ímpares, a que chamamos *Bial Award in Biomedicine*. O *Bial Award in Biomedicine* passa a distinguir as obras publicadas de índole biomédica, com tema livre, que representem um trabalho com resultados de grande qualidade e relevância científica. São candidatas as obras propostas pelos membros do Júri e por outras instituições, a indicar oportunamente. A primeira edição deste novo prémio terá lugar em 2019, sendo as obras avaliadas por um júri internacional, presidido pelo Prof. Fernando Lopes da Silva, que também preside ao nosso Conselho Científico. Tem o valor de €300.000.

O nosso sistema de apoio à investigação científica beneficiou, desde 1994 até agora, 614 projetos - que representam 28% do total das candidaturas -, envolvendo 1.351 investigadores de 25 países. Cerca de metade dos apoios foram atribuídos na área da Psicofisiologia e a outra metade à Parapsicologia ou a projetos conjuntos, envolvendo as duas áreas.

Dos projetos apoiados pela Fundação Bial resultaram até agora 910 artigos em revistas indexadas, dos quais 749 em revistas com um fator de impacto médio de 3.5 e 130 em revistas com um fator de impacto superior a 5. Até março de 2018 foi contabilizado um número substancial de citações (12.737), sendo que 171 publicações foram citadas mais de 20 vezes.

Assim, tendo em atenção estes resultados, é com satisfação que lhes anuncio que vamos abrir este ano um novo concurso para apoio a projetos de investigação científica nas áreas da Psicofisiologia e da Parapsicologia, com características semelhantes aos anteriores. O regulamento e a documentação para concurso estarão disponíveis a partir de amanhã no nosso espaço www.fundacaobial.com e o prazo de entrega das candidaturas terminará em 31 de agosto próximo. Sublinho que continuaremos a não apoiar projetos de patologia ou de terapêutica, por desejarmos separar claramente a atividade mecenática da Fundação, da investigação realizada pelos Laboratórios Bial, essa sim focada na terapêutica farmacológica.

Desde 1996 que realizamos, de dois em dois anos, os nossos simpósios Aquém e Além do Cérebro, nos quais se pretende que os investigadores por nós apoiados façam a apresentação pública dos resultados das suas investigações. Mas, também pretendemos reunir alguns dos melhores investigadores mundiais em Neurociências e em Parapsicologia, incentivando a sua aproximação num diálogo enriquecedor e, mesmo, a organização de projetos conjuntos.

E aqui estão, cerca de 90 investigadores por nós apoiados, que apresentarão 40 posters com resultados definitivos, na galeria ao lado deste salão e, ainda, 40 apresentações orais na tarde de amanhã. A generalidade dos resultados, provisórios ou definitivos, poderão também ser consultados na nossa página na internet. Ao longo do simpósio, e sobretudo nas tardes de quinta e sexta-feira, os investigadores por nós apoiados estarão disponíveis para discutir com todos os participantes os resultados dos seus trabalhos.

Teremos também ao longo destes quatro dias cerca de 20 palestrantes de grande relevo, que nos proporcionarão certamente importantes momentos de aprendizado, em torno de um tema atual e de grande impacto para o futuro. Os nossos agradecimentos a todos os intervenientes e os nossos votos de que usufruam com grande satisfação estes quatro dias.

Para que tudo isto seja uma realidade bonita, foi necessário um trabalho dedicado e competente da Comissão Organizadora, o que muito agradecemos aos Professores Axel Cleeremans, Etzel Cardeña, Miguel Castelo-Branco, Rui Costa, Rainer Goebel, Mário Simões e Caroline Watt. A todos estamos muito gratos, mas permitam-me um

agradecimento especial ao meu amigo Mário Simões, que, a seu pedido, não participará na próxima Comissão.

Ele foi o único dos atuais membros que esteve connosco em todas as 12 Comissões deste Simpósio e, para além disso, que nos ajudou a criar a estrutura com que arrancámos com esta iniciativa. Professor de Psiquiatria na Faculdade de Medicina da Universidade de Lisboa, o Prof. Mário Simões é também Diretor do LIMMIT - Laboratório de Interação Mente Matéria de Intenção Terapêutica - da sua Faculdade. Tem interesses científicos em psicologia e psicofisiologia dos estados alterados de consciência, etnomedicina, experiências excecionais humanas e espiritualidade. Teve quatro projetos de investigação que beneficiaram do apoio da Fundação Bial e é membro do nosso Conselho Científico.

Mário, muito e muito obrigado por tudo. Continuamos a contar contigo. Estamos e estaremos solidariamente contigo. Um grande abraço.

O Prof. Stefan Schmidt, das Universidades de Freiburg e de Frankfurt (Oder), substituirá o Prof. Mário Simões na Comissão Organizadora do XIII Simpósio - a ter lugar em abril de 2020 -, mantendo-se os restantes membros e a presidência do Prof. Axel Cleeremans.

Os nossos votos de que passem agora uns excelentes dias aqui na Casa do Médico, que a discussão seja profícua, que as ideias luminosas despontem, que os saberes se entrecruzem e se complementem de uma forma útil para todos os presentes e, oxalá, para a humanidade.

A nossa gratidão pela vossa presença e o meu obrigado pela vossa atenção.

DISCURSO DO PRESIDENTE DA COMISSÃO ORGANIZADORA
SPEECH OF THE PRESIDENT OF THE ORGANIZING COMMITTEE

Axel Cleeremans

Dear Minister, dear colleagues and friends,

It is an immense pleasure for me to say a few words during this opening session, which marks the onset of the 12th Symposium of the BIAL Foundation, titled, as you know, "Enhancing the mind". Preparing such a symposium is a lot of work that spans about two years. And it begins with identifying an overall theme for the meeting, and continues by finding the best possible scientists and philosophers to speak about it in such a way that is both relevant to you, the audience, but also to scientists and philosophers. And our hope here is to ask many questions, so eliciting dialogue from an interdisciplinary perspective and, perhaps, fostering collaborations between you and other people attending this symposium.

I have the privilege of heading the scientific committee that manages the organisation of the symposium. My name is Axel Cleeremans, and I am a cognitive psychologist from the Université Libre de Bruxelles in Belgium. I am extremely grateful to Dr. Luís Portela, who heads the BIAL Foundation that makes all of this possible - thank you, Luís! But I am also very lucky to be in the excellent company of the outstanding scientists who form the scientific committee. Dr. Portela already mentioned your names. I will do it again: Etzel Cardena, Miguel Castelo-Branco, from Coimbra, Rui Costa, from Lisbon and New York University, Rainer Goebel, from Maastricht in the Netherlands, Mário Simões, from Lisbon, and Caroline Watt, from Edinburgh, in Scotland. Thank you all for the excellent and challenging work you have undertaken to make this 12th symposium possible. Last but not least, I should like to express my gratitude to Paula Guedes from the BIAL Foundation and all the other people associated with the BIAL Foundation who are actually running this Symposium

and managing everything, from printing the programmes to welcoming you tonight. Your unwavering supporters truly instrumental to the overall organisation of the entire endeavour - so thank you, Paula.

So, what are we talking about this time? Well the symposium is, as you know, dedicated to enhancement. And enhancement truly is a beautiful thing. "Enhancing the mind" - the topic of this 12th BIAL symposium - is in fact exactly what education is about. The idea that each of us has a responsibility to enhance ourselves so as to better contribute to society itself, and the idea that society has a like responsibility to organise such enhancement, is an old idea that takes its roots in antiquity, but, perhaps a little close to us, in the works of Charlemagne, in Europe, and, later, in the Enlightenment. It is based on the belief that each of us can improve, and so improve society. But such enhancement comes at a price: We need to work hard to enhance ourselves, we need to make substantial effort to learn something new. And this in turns forms the core of our liberal democracies - the very idea of progress.

But what if I told you that you could be enhanced by drugs? What if I told you that there is a technology that will enhance how your brain works without any effort? How about improving one's athletic skills through doping? Would you think this is ethically OK? If not - why not?

These kinds of questions form the core of the debates that will take place here in Porto over the next few days. But such ethical issues cannot be properly addressed unless we know what is actually possible. The very project of "enhancing the mind" finds a loud echo in the transhumanist movement, but it also raises deeply fascinating questions about the underlying technologies and practices. And neuroscience doesn't yet know what is actually possible in this respect. We know that the brain is a highly plastic organ, and we know that its activity can be influenced in many different ways - from direct stimulation to education, or even speech, simply talking to each other, from drugs to mind-expanding rituals. What works? Why does it work? And how does it work?

To explore these issues, the meeting is organised in three sessions, each taking place on a separate day. Tomorrow, in a session moderated by Prof. Goebel, we will talk about cognitive enhancement - what kinds of technologies enable us to improve human cognition, what sorts of questions does using such technologies raise from an ethical point of view.

That session will close with a keynote lecture by Prof. Torkel Klingberg, from Stockholm.

On Friday, we will explore "amplified states of consciousness", with different speakers addressing the mind-altering effects of drugs or of practices such as meditation to regulate functions such as perception, attention or emotion. The session will be moderated by Prof. Caroline Watt. In contrast to the technologies we will talk about tomorrow, using "wise plants" or ritualistic practices to enhance the mind are old practices, and so this second session will also include an historical look at such methods. This second day will close with a keynote lecture by Prof. Antoine Lutz, from Lyon in France.

Finally, the third session, on Saturday, will be dedicated to collective intelligence. We often forget that enhancing your own mind often involves other minds - those of other people, or that of artificial intelligence. This third session will be moderated by Prof. Rui Costa, from Lisbon and New York University, and will feature a keynote lecture by Prof. Chris Chabris, from the USA.

But this is not all! For a long while now we have been thinking about ways of enhancing the symposium itself, in particular through making it more participatory, and I am very pleased to let you know that we will again have four parallel workshops on Friday afternoon, respectively dedicated to wise plants, meditation, neurostimulation, and artificial intelligence. I am afraid these workshops are now fully booked, even though Paula may have a few tickets left, but I very much hope this will give many of you an opportunity to interact more directly with our speakers.

As you know, the BIAL Foundation also supports the work of many scientists, Dr. Portela mentioned 614 projects, through its grants program. The BIAL Fellows whose work benefits from such support form the core of the BIAL Foundation's activity, and we are very pleased to welcome many of them so that they can let all of us know what they have been doing with the funding they got from the Foundation. Thus, tomorrow afternoon, we will not only have a poster session that showcases this work, but also a poster blitz session during which each grant holder has a chance to present his work in 2 minutes. This exciting session will be moderated by Prof. Simões and will take place at 2:30 here in the main auditorium.

Finally, on Saturday, we will close the symposium with a round-table discussion dedicated to the "ethics of enhancement". And this will feature speakers from each of the three sessions and I will moderate that session.

So there you go - I think we have three very exciting days ahead of us, and I am truly happy to welcome you all once again in beautiful Porto for this 12th symposium of the BIAL Foundation, which I hope will enhance each of us! Thank you.

DISCURSO DO BASTONÁRIO DA ORDEM DOS MÉDICOS

Miguel Guimarães

Boa noite. Boa noite a todos. Permitam-me que faça uma saudação especial aos meus companheiros de mesa, começando por cumprimentar o Senhor Ministro da Ciência, Tecnologia e Ensino Superior e dar-lhe as boas-vindas a esta casa, a casa dos Médicos, a casa da ciência.

Um cumprimento muito especial ao meu querido amigo, Prof. Fernando Araújo, Secretário de Estado Adjunto e da Saúde, a quem quero agradecer o trabalho que tem feito no Ministério da Saúde e quero fazê-lo publicamente.

Um cumprimento amigo, ao meu querido amigo Luís Portela, de quem falarei à frente mais um pouco, Presidente da Fundação BIAL.

Uma pessoa conhecida, no país e fora do país, e que tem dado um contributo de facto inestimável para o desenvolvimento da ciência.

Um cumprimento também ao Senhor Presidente da Comissão Organizadora, Dr. Axel Cleeremans.

Permitam-me também que cumprimente três pessoas que estão aqui na plateia, que eu não posso deixar de o fazer. A primeira, o Dr. António Portela, que é o presidente executivo dos Laboratórios BIAL, a quem agradeço também aqui a presença regular na Ordem dos Médicos, que tem tido ao longo destes tempos; à minha querida amiga Ana Paula Martins, Bastonária da Ordem dos Farmacêuticos, que dá um toque distinto a esta reunião e cuja presença eu não posso deixar de realçar; e um cumprimento obviamente ao meu querido amigo, Presidente do Conselho Regional do Norte, Prof. António Araújo, na pessoa de quem aproveito para cumprimentar toda a plateia e todos os presentes.

E quero em nome dele e em nome da Ordem dos Médicos dar as boas-vindas a todos vocês, cientistas, Homens da ciência, Homens que estão a contribuir, cada um à sua maneira, para o desenvolvimento da medicina, para conseguirmos alcançar resultados cada vez melhores, para se calhar acontecer aquilo que Lev Grossman dizia há uns tempos atrás, e que fez capa da revista Time, em 2011, que é: "2045: o ano em que o

homem atinge a imortalidade". Claro que a imortalidade ele referia-se a que provavelmente qualquer dia nós vamos conseguir controlar a maior parte das doenças, seja tornando-as doenças crónicas, ou seja curando as doenças e isso começa a acontecer, e começa a acontecer muito graças a pessoas como o Luís Portela.

Luís Portela dedicou a sua vida primeiro nos Laboratórios BIAL. Mais recentemente, enfim, nos últimos anos, já tem uns anos também, na Fundação BIAL, e tem dado um apoio a todos aqueles que se interessam pela investigação, a todos aqueles que querem dar o seu contributo para o desenvolvimento da medicina. Tem dado um apoio muito, muito importante. Mas muito importante também naquilo que é a imagem que o nosso país tem fora daqui, fora da cidade do Porto, fora de Portugal.

É muito importante o primeiro medicamento Português, no qual julgo eu - acho que não estou a cometer nenhuma inconfidência, posso dizê-lo -, os laboratórios gastaram cerca de 350 milhões de euros. Um investimento que foi difícil de fazer, um investimento que o estado português possivelmente não o pode fazer; e um investimento que é fundamental que a iniciativa privada possa fazê-lo, para que nós possamos continuar a nossa evolução positiva na medicina e por isso eu quero publicamente fazer-lhe este agradecimento, em nome de todos os médicos portugueses.

Quero também realçar o forte apoio que tem sido dado aos jovens e aqui eu acho que é particularmente e especialmente importante a motivação que nós damos aos nossos jovens, e eu vejo muitos jovens aqui sentados nesta plateia, provavelmente de dezenas de países diferentes (se calhar nem estão a perceber bem aquilo que eu estou a dizer), mas a verdade é que nós dependemos de vocês. Sem os jovens nós perdemos a capacidade de inovação, perdemos a capacidade de ir mais longe, perdemos a capacidade de investigar de forma diferente, e investigar de forma diferente é fundamental para a evolução da ciência.

Por isso meus amigos eu vou terminar pedindo-vos uma grande salva de palmas para o Luís Portela e agradecer-lhe pessoalmente todo o trabalho que ele fez até hoje. Muito obrigado a todos.

DISCURSO DO SECRETÁRIO DE ESTADO ADJUNTO E DA SAÚDE

Fernando Araújo

Muito obrigado, muito boa noite a todos.

Gostava de começar por cumprimentar, o nosso Ministro da Ciência e Tecnologia Superior, Prof. Manuel Heitor, cumprimentar o Dr. Luís Portela, Presidente da Fundação BIAL, cumprimentar o meu Bastonário da Ordem dos Médicos, Dr. Miguel Guimarães, cumprimentar o Presidente da Comissão Organizadora - e seguramente alguém que esteve a trabalhar durante muito tempo neste evento que hoje começa - Prof. Axel Cleeremans.

Aproveitar também para cumprimentar a Bastonária da Ordem dos Farmacêuticos, Prof. Ana Paula Martins. Eu acho até que este exemplo de termos aqui dois Bastonários, é o exemplo claro que cada vez mais a ciência, na área da saúde, ultrapassa muito o contexto específico da medicina. Precisamos cada vez mais de ter equipas multidisciplinares, com vários olhares diferentes sobre o conhecimento para conseguirmos seguramente avanços robustos em termos de saúde.

Cumprimentar o Presidente da ARS Norte, o Pimenta Marinho, o Presidente do Conselho Regional do Norte da Ordem dos Médicos (por acaso estamos aqui hoje nas instalações dele), o Prof. António Araújo, e acima de tudo cumprimentar todos os presentes, como disse o Dr. Miguel Guimarães e é verdade, temos aqui representantes de muitos países, todos unidos por um único objetivo realmente que é discutir ciência e neste caso discutir a neurociência e as minhas últimas palavras são também para o Dr. Luís Portela, a agradecer o amável convite para estar aqui hoje presente, que desde logo aceitei por três ordens de razão.

A primeira pela forma como a BIAL e aqui, enfim, juntando um pouco o que se calhar não faz muito sentido juntar, a Fundação com o laboratório, mas o certo é que ao longo destes anos tem sido um exemplo na saúde e eu acho que aqui é muito importante, e aqui do lado da saúde tem sido um exemplo. Um exemplo por um lado pela forte aposta na

investigação. Quer básica, mais até que translacional e aplicada. Tem sido claramente um caso de sucesso e eu acho que o caso de sucesso deve-se fundamentalmente às equipas, aos cursos, aos investigadores que conseguiu sensibilizar, captar e congregar nos laboratórios. Eu conheço muitos deles ligados ao meio académico, ligado ao Sistema Nacional de Saúde (SNS), que nós temos imenso orgulho em pertencer aos quadros do SNS e realmente é com base nesses recursos, que são recursos de excelência, do melhor que há em todo o mundo, que se consegue fazer essa investigação, que não é fácil e simples, e que se consegue ter esses resultados como os que vocês têm hoje.

Eu acho que isso é algo que é diferente do que nós estamos acostumados aqui em Portugal. Essa aposta no empreendedorismo e na inovação, que é uma aposta que necessita de coragem, desde logo pelos valores que o Dr. Miguel Guimarães focou, mas muito mais que os valores, quer dizer, a forma de olhar para estes projetos. A BIAL sempre olhou, enfim, eu que estou de fora, mas sempre vi a BIAL olhar para os projetos a médio e longo prazo. Apostar na credibilidade, na confiança, acima de tudo apostar no saber e no conhecimento e isso faz toda a diferença. Por vezes demora tempo até termos resultados, mas quando os resultados chegam, são resultados fortes, robustos e que se mantêm, que perduram. E isso é a imagem de marca da BIAL seguramente.

A segunda ordem de razões tem a ver com o evento em si e aqui já muito ligado à Fundação BIAL. É verdade que estes 12 Simpósios correspondem a 24 anos. Vinte e quatro anos significa uma enorme sustentabilidade. Há muitos congressos que nós temos, ligados à saúde, que não duram tanto, que acabam e terminam por razões várias. O facto de este ter esta longevidade significa apenas uma coisa, quer dizer que tem seguramente excelentes, tem tido ao longo destes anos todos, excelentes oradores, excelentes temas, excelente motivação para trazer as pessoas cá e eu acho que isso é fundamental. E ter hoje esta casa aqui cheia é um sinal claro do reconhecimento, da capacidade que vocês tiveram de construir um projeto forte e que consegue congregar as pessoas.

Eu tenho falado com algumas pessoas ligadas às neurociências e todos me dizem a mesma coisa. Que você conseguiu ao longo do tempo encontrar aqui um ponto de encontro. Este evento acaba por ser um ponto de encontro dos melhores investigadores a nível nacional e internacional

e que já marcam nas suas agendas a questão do Simpósio da BIAL como local para poderem estar juntos, discutir projetos, construir pontes e fazer alguma diferença nesse sentido. Eu acho que isso é muito importante. Vocês conseguiram realmente construir aqui um porto de abrigo para que as pessoas das várias áreas, de vários países, possam juntar-se, apresentar os temas e acima de tudo discutir formal e informalmente e construir pontes para o futuro e isso realmente é muito relevante.

E um terceiro grande grupo de razões pelas quais me associei desde logo a esta iniciativa teve a ver com questões mais pessoais. Pela forte aposta e ligação que a BIAL tem ao Porto e ao norte do país e seguramente pelo exemplo que tem sido dado pela liderança, a liderança pelo exemplo, diria eu da família Portela nas várias gerações, pelo qual eu tenho uma enorme admiração e respeito. Eu penso realmente que vocês são um caso de sucesso, mas muito mais que um caso de sucesso, são acima de tudo, um fator emotivo de orgulho para o Sistema Nacional de Saúde e um motivo de orgulho para o país e daí realmente o enorme interesse e prazer em estar aqui hoje presente e desejar-vos a vocês todos, participantes, oradores, enfim, ao evento, as maiores felicidades e seguramente que a Saúde estará convosco neste evento. Muito obrigado.

DISCURSO DO MINISTRO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

Manuel Heitor

Muito obrigado. Eu não quero de forma alguma competir com o nosso cientista convidado e viemos aqui para ouvir ciência, mas não posso deixar de fazer um especial agradecimento à BIAL, à Fundação BIAL e certamente à família Portela e, em particular, ao Dr. Luís Portela pelo convite de aqui estar e também ao Prof. Nuno Sousa que tanto insistiu, uns meses a esta parte, para aqui podermos partilhar estes momentos.

E os momentos são sobretudo de reconhecimento pelo trabalho que tem vindo a ser de uma forma persistente feito ao longo destes 24 anos e que nos devem levar a fazer novas perguntas, não sei se novas perguntas, mas pelo menos uma pergunta: "Porque é que temos só uma BIAL e porque é que não conseguimos ter mais Biais ao longo destes vários anos e como é que podemos fazer crescer mais a BIAL e aparecer empresas deste tipo?". O ambiente que aqui temos, de certamente investigadores nas mais variadas áreas, certamente nas neurociências, mas também em áreas afins: da biomedicina às áreas das ciências básicas, que, juntamente com médicos, tentam, não apenas reconhecer aquilo que pode potenciar as funções cognitivas que levam certamente à atividade humana no nosso dia-a-dia, mas certamente também enriquecer as nossas sociedades com mais conhecimento e com uma atividade certamente associada também à criação de emprego qualificado.

Há 24 anos quando BIAL iniciou estes Simpósios investia-se em Portugal pouco mais de 0.5% da riqueza criada em investigação e desenvolvimento, sendo sobretudo nessa altura investimento público. Era pouco mais de 15% a fração do investimento privado e nessa altura a BIAL era de facto umas das poucas empresas que, desde o princípio, reconheceu a necessidade de fazer o futuro com mais conhecimento.

Hoje temos naturalmente um espectro diferente, passamos um percurso e se podemos pensar o futuro é certamente reconhecendo o trabalho daqueles como o Dr. Luís Portela, nos ajudam a pensar o futuro,

certamente com mais conhecimento e que nos leva certamente a acreditar nas pessoas, cada vez mais nas boas pessoas, que nos podem guiar para termos sobretudo uma forma de darmos mais confiança às futuras gerações e acredito que nesta audiência seja fácil adquirir um consenso, que isso se faz com mais conhecimento e por isso atraindo mais jovens para a educação, levando mais conhecimento à prática hospitalar do dia-a-dia, assim como a todas as funções sociais e económicas e por isso se algo que me levou certamente a aceitar desde o primeiro minuto aqui estar é também para nos ajudar a fazer novas questões, como é que podemos continuar este percurso que teve ziguezagues, certamente, mas que só podemos acreditar que é investir mais, com um esforço coletivo cada vez maior, porque certamente não temos nem investigadores a mais, nem estudantes a mais, nem médicos a mais; temos necessidade de evoluir, sempre comparando com os melhores e mais uma vez este Simpósio e o seu espectro certamente e fortemente internacionalizado é o único ambiente que nos pode suscitar novas questões, atrair novos jovens e pôr cada vez mais questões para, quer a prática médica, quer a prática de investigação, quer no sistema público, quer no sistema privado.

E hoje as encruzilhadas dos tempos em que vivemos e as dificuldades que temos que perceber, o esforço que todos temos que nos envolver para não apenas fazer do conhecimento um bem público, mas também fazer do conhecimento uma forma de criar emprego qualificado para dar confiança aos futuros jovens, leva-nos a uma responsabilidade social e institucional que certamente este Simpósio "Aquém e Além do Cérebro" e da atividade específica das Neurociências nos fazem pensar e por isso um agradecimento à Fundação BIAL e ao Dr. Luís Portela e a todos aqueles que ao longo destes anos têm contribuído para dignificar Portugal, os portugueses e sobretudo a ciência e as neurociências em particular.

Muito obrigado

CONFERÊNCIA INAUGURAL
OPENING CONFERENCE

ENHANCING BRAIN AND COGNITION: A THEORY-DRIVEN APPROACH

Lorenza Colzato [1,2,3]

Abstract

The essence of cognitive enhancement is the use of any (legitimate) means to reach one's personal best. Kurt Lewin's claim that "nothing is as practical as a good theory" is the *leitmotif* of this paper about cognitive enhancement. Whereas in the past the field of cognitive enhancement used mainly effect-driven approaches (that seek to demonstrate that an enhancing intervention can have an effect without explaining how it modulates the targeted function), this paper proposes a mechanistically oriented, theory-driven approach that tries to understand how a particular intervention modulates cognition. First, I will introduce the idea that the administration of the amino acid L-Tyrosine, precursor of dopamine, refills resources required for cognitive-control operations. Second, I will show that transcutaneous vagus nerve stimulation may be a promising novel noninvasive brain stimulation tool in enhancing the recognition of other's emotions. Third, I will illustrate how recently popular sub-perceptual doses of psychedelic substances such as truffles, referred to as "microdosing", allegedly have multiple beneficial effects including creativity and problem-solving performance.

Keywords: Cognitive Enhancement, Tyrosine, Transcutaneous Vagus Nerve Stimulation, Microdosing Psychedelics

[1] Leiden University, Cognitive Psychology Unit & Leiden Institute for Brain and Cognition, Leiden, The Netherlands.

[2] Department of Cognitive Psychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr University Bochum, Bochum, Germany.

[3] Institute for Sports and Sport Science, University of Kassel, Kassel, Germany.

Introduction

Cognitive enhancement is the use of any (legitimate) means (e.g., meditation, smart drugs, brain stimulation, neurofeedback, physical exercise or food supplements) to reach one's personal best. Why has this topic become so relevant in the past few years?

The first reason is economical. The interest in cognitive enhancement is mainly driven by the increasing costs of the welfare system, especially with regard to the increasing age of citizens in Western societies. For instance, cognitive enhancement can help to delay cognitive decline in the elderly, which would extend the time people can live autonomously and, thus, reduce the welfare costs for the time thereafter. Along the same lines, training children could speed up the education of healthy individuals and reduce the risk of behavioral deviance and pathology, again with considerable savings for welfare and education systems.

The second reason is ideological. Both Eastern and Western societies are continuously driven towards more individualism, which emphasizes the existence and often also the importance of individual differences over commonalities and collectivistic values. These tendencies go hand in hand with ideological developments in public opinion and within political parties, which in many countries have gravitated towards more neoliberal, individualism-heavy positions over the last 15 years or so. Among other things, this has involved a rather systematic deconstruction of the welfare system and established the view of the individual as an architect of his or her own life.

Research on cognitive enhancement has benefited from these two reasons. The economic problems of the welfare system have boosted the interest in procedures and activities that make welfare societally more affordable, and the ideological turn towards individualism provides a natural breeding ground for the public interest in procedures and activities that help to express and to further develop individual needs and interests.

Kurt Lewin's claim that "nothing is as practical as a good theory" is the *leitmotif* of this paper about cognitive enhancement. Whereas in the past the field of cognitive enhancement used mainly effect-driven approaches (that seek to demonstrate that an enhancing intervention can have an effect without explaining how it modulates the targeted function

and why some people benefit more than others), this paper proposes a mechanistically oriented, theory-driven approach that tries to understand and explain individual differences to a degree that allows a comprehensive understanding of how a particular intervention modulates cognition.

The present paper aims to present three different means to enhance cognition and to get a better understanding of the underlying mechanism of how those means modulate our behaviour. This paper is divided in three parts. The first is devoted to tyrosine, a neurotransmitter precursor. The focus of the second part is dedicated to a novel noninvasive brain stimulation method called transcutaneous vagus nerve stimulation. Finally, the third part addresses "microdosing", a new popular trend regarding the consumption sub-perceptual doses of psychedelic substances.

Part 1: Precursors as cognitive enhancers: the case of tyrosine

This part focuses on the possibility to use neurotransmitter precursors (such as some amino acids) as cognitive enhancers given that, by their ingestion, it is possible to increase certain neurotransmitters levels (Colzato, 2017).

Tyrosine counteracts neurotransmitter depletion

One of the most investigated amino acid is tyrosine (TYR). TYR is contained in many kind of food, such as for example codfish. From a theoretical point of view, TYR is very interesting because it is the chemical forerunner of the neurotransmitter dopamine. TYR administration can augment dopamine levels in the brain (Cuche et al. 1985; Gibson and Wurtman 1977; Tam et al. 1990). Plasma TYR levels peak between 1 and 2 hours after ingestion and can stay significantly elevated up to 8 hours (Glaeser et al. 1979). Once it has passed the blood-brain barrier and is taken up by the appropriate brain cells, the enzyme tyrosine-hydroxylase (Daubner et al. 2011) converts TYR into L-DOPA, see Figure 1.

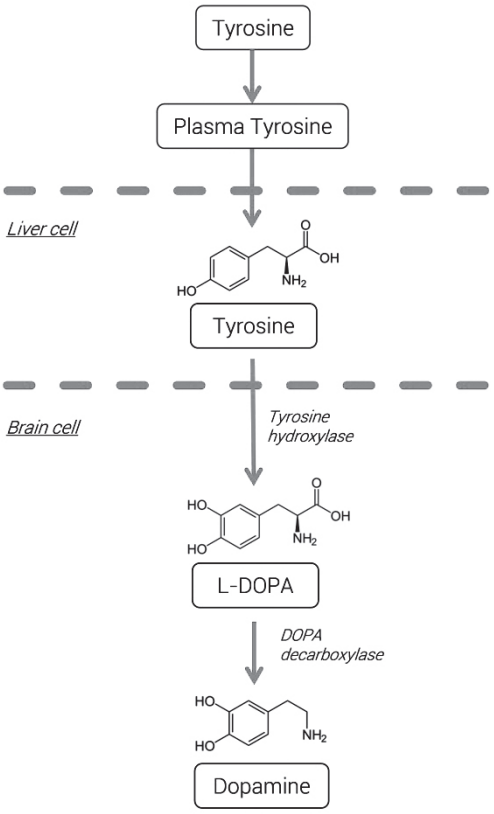

Figure 1. Schematic representation of the effect of acute tyrosine supplementation on tyrosine to dopamine conversion. Once it has passed the blood-brain barrier the enzyme tyrosine-hydroxylase converts tyrosine into L-DOPA. In a second step, L-DOPA is converted, via the enzyme DOPA decarboxylase, into dopamine leading to an elevation in dopamine level

Notably, TYR has been shown to enhance neurotransmitter synthesis only in actively firing neurons (Fernstrom and Fernstrom 2007; Lehnert et al. 1984; Tam et al. 1990). This points to the fact that TYR can *counteract neurotransmitter depletion*, a process in which enhanced brain activity induces decrements in dopamine levels and associated behavioral performance decline. Indeed, when subjected to stress or a cognitively challenging task, dopamine neurons become more active and

their synthesis rate raises (Kvetnansky et al. 2009; Lehnert et al. 1984; Mahoney et al. 2007). As a result, more dopamine is synthesized from TYR in order to meet the situational demands. However, the conversion of TYR into dopamine becomes limited when TYR levels decline. This process is responsible for less dopamine availability and resulting declines in performance (Goldman-Rakic et al. 2000; Muly et al. 1998). In this situation brain function might benefit from TYR administration, which allows dopamine synthesis to carry on and maintain dopamine levels necessary to guarantee optimal performance (Wurtman et al. 1981). This role of TYR as a *depletion counter-actor* seems to take place only in actively firing neurons. Indeed, in rats it has been demonstrated that TYR supplementation only increased dopamine synthesis in the striatum when this region was pharmacologically activated (Tam et al. 1990). That is, TYR administration seems to have a positive effect only in circumstances that encourage neurotransmitter synthesis, i.e., circumstances that are sufficiently stressful or cognitively challenging.

In contrast to dopaminergic agonist drugs, such a s Ritalin, TYR supplementation is very suitable. On the one hand, the fact that the tyrosine-hydroxylase enzyme is already close to saturation under normal circumstances has the advantage to prevent large quantities of TYR be converted. In contrast, the ingestion of Ritalin does not rely on a similar rate-limiting factor, which significantly increase the possibility of leading to "overdosed" dopamine levels that are harmful for performance (Goldman-Rakic et al. 2000; Muly et al. 1998). Taking into account the inverted-U profile of dopamine (Cools and D'Esposito 2011), it is likely for Ritalin supplementation to boost individuals to the lower right end of the curve, while the subtle increment from TYR is unlikely to lead to any "overdose" effect.

Enhancing cognitive demands in healthy humans: the role of individual differences

TYR can promote working memory performance under particularly demanding circumstances. In particular, Thomas et al. (1999) found TYR only enhanced working memory when other tasks were performed at the same time. Moreover, TYR has been found to enhance working memory even in a single-task setting, but only in the task´s more challenging

condition that places a higher load on memory (Colzato et al. 2013). The outcomes of these two studies support the idea that TYR can enhance cognitive performance and emphasize the crucial role of TYR as counteractor in performance-degrading conditions.

In a recent study carried out in my lab for the first time we took into account individual differences (i.e., genetic differences) in base levels of dopamine to explain the effectivity of TYR. Indeed, it is likely that depending on this dopamine baseline levels, some people may benefit more than others from TYR intake (Jongkees et al. 2014). The study showed evidence supporting the idea that TYR supplementation may function as a cognitive enhancer and compensate for unfavorable genetic predisposition (Colzato et al., 2016). TYR were administered to participants, genotyped for the C957T polymorphism at the DRD2 gene (polymorphism related to the striatal dopamine level). Measures of working memory updating and inhibitory control were acquired. T/T homozygotes (i.e., individuals associated with lower striatal dopamine level) showed larger beneficial effects of TYR supplementation than C/C homozygotes (i.e., individuals associated with higher striatal dopamine level). These findings reinforce the idea that genetic predisposition modulates the effect of TYR in its role as cognitive enhancer (Jongkees et al. 2014; Colzato et al. 2016).

TYR in aging: the role of Toxoplasma gondii and immunosenescence

Western (Europe and USA) and Eastern (China and Japan) societies are aging rapidly. In Europe the proportion of people of 65 years and older will rise from 15% in 2009 to 26% in 2039, and the ratio of retired vs. working adults will increase from 25 to 49% (CBS, 2011). Unfortunately, human aging is accompanied by large decrements in cognitive control or executive functions (Vallesi, 2016; Puccioni & Vallesi, 2012; see Jurado & Rosselli 2007, for a review), that is, in cognitive processes that are necessary for goal-directed thought and action, and mental flexibility. Cognitive control is not only particularly relevant for orchestrating adaptive behavior, it is also particularly sensitive and vulnerable: cognitive control functions are the slowest to develop and assumed to be fully functional not much earlier than at 20 years of age, and they are the first to degrade in normal aging (Gazzaniga, Ivry & Mangun, 2008). One

reason for this vulnerability is that cognitive control relies on the integrity of the frontal lobe, which is also known to mature rather late and to begin degenerating only a few years later. A related reason is the general loss of neurochemicals, and the continuous decline of striatal and extrastriatal dopamine - which is driving cognitive control functions - from early to late adulthood and old age (Bäckman et al., 2000, 2006).

Considering the steady increase of elderly populations and the great importance of cognitive control functions for leading an independent, self-fulfilling life, it is crucial to understand how cognitive control can be promoted and, if possible, preserved in old age. In an unpublished study we tested the idea that a useful intervention for this purpose would be the administration of TYR. In a nutshell, our goal was to examine the possibility that TYR, aimed at increasing dopamine levels, is likely to slow down, and (partially) compensate for the cognitive decline associated with the aging-related loss of dopaminergic supplies. In contrast to our expectations, our findings show detrimental effects of TYR on working memory suggesting that, in contrast to young adults (Colzato et al., 2013; Colzato et al., 2014; Steenbergen et al., 2015), the administration of TYR in aging may be counterproductive.

How is it possible for TYR to be beneficial in young adults, but detrimental in old adults? At this point, we can only speculate that TYR administration may be detrimental for performance when the dopamine system is impaired, such as in aging. Very recently it has been pointed out (Beste et al. 2014; Gajewski et al., 2014; Gajewski et al., 2016) that in aging the dopaminergic system is modulated by a number of different factors. One of these factors, that has only been investigated with respect to its possible modulatory role for cognitive functions in elderly individuals in the last few years, is latent *Toxoplasma gondii (T. gondii)* infection. *T. gondii* contains genes coding for tyrosine hydroxylase (Gaskell et al., 2009), which is needed to convert TYR into dopamine in humans (e.g., Fillenz, 1993). As a consequence of the abnormal functioning of the enzyme tyrosine hydroxylase, cells containing bradyzoite cysts of *T. gondii* produce and release more dopamine (Flegr et al., 2013; Martin et al., 2015; McConkey, Martin, Bristow & Webster, 2013). Given the high incidence and prevalence of seropositivity of *T. gondii* (up to 77%) in aging (Wilking et al., 2016), which may impair the function of

tyrosine hydroxylase and lead to abnormal conversion rates of TYR, we hypothesize therefore that TYR may have decreased performance in old adults because of their potential seropositivity of *T. gondii*. That is, it is possible that in seropositive individuals, the abnormal conversion rates of TYR drove our participants beyond optimality (i.e. in the inverted-U-shape function that catecholinergic functions follow) and impaired their working memory performance. This speculative link to explain our results may be supported by two research lines. First, previous studies have shown working memory impairment in *T. gondii* infected older humans (Gajewski et al., 2014; Gajewski et al., 2016). Second, several studies have corroborated the role of *T. gondii* in dopaminergic neural transmission: *T. gondii* is associated to the incidence of schizophrenia (e.g., Webster et al., 2007, 2013) and Parkinson's disease (Miman et al., 2010), two pathologies related to abnormalities in the dopaminergic system. Furthermore, it has been reported that haloperidol, a D2-receptor antagonist, is able to lessen symptoms of acute T. gondii infection (Webster et al., 2006).

Another hypothesis is that TH availability in our sample was affected by increased inflammatory markers, which are known to be augmented in old age. That is, aged-related changes in the immune system, also known as immunosenescence, are associated with increased proinflammatory cytokines (Michaud et al., 2013), which have been found to impact the availability of TH and expression of dopamine transporters, as such dopamine synthesis and release (Felger and Miller, 2012). This could have resulted, again, in pushing individuals over the optimum in the catecholinergic inverted-U-shape function, leading to impaired performance. I advise future studies involving elderly participants to include blood samples in order to test for *T. gondii* specific IgG serum antibodies and for proinflammatory cytokines.

Part 1: Conclusion

TYR, the chemical forerunner of dopamine, has the promising potential to increase dopamine function in the brain in challenging situations. The mechanisms of action of TYR is to help the brain to maintain an elevated rate of dopamine synthesis when the brain needs it the most. At this point, it seems that TYR administration may be beneficial when the dopamine system is intact, such as in healthy young

adults, but it is detrimental for performance when the dopamine system is impaired, such as in aging.

Part 2: Transcutaneous vagus nerve stimulation (tVNS)

This part is devoted to tVNS, a novel brain stimulation technique, by means if which we are able to stimulate the vagus nerve and enhance cognitive functions related to it. In contrast to transcranial magnetic stimulation (see paper by Alexander Sack in this book), tVNS is a bottom-up technique – that is, the propagation of the afferent signal from the vagus nerve travels from peripheral nerves toward the brain stem and from there to higher cortical structures (Colzato and Vonck, 2017).

Charles Darwin and Stephen Porges

In his seminal book "The Expression of Emotions in Man and Animals" (1872/1965), Darwin was the first to propose that emotion expressions are controlled by a bidirectional neural communication between the heart and the brain via the so-called "pneumogastric" nerve. Nowadays known as the vagus nerve, this is the tenth cranial nerve and represents a key component of the parasympathetic nervous system. Notably, the vagus nerve is the longest cranial nerve. Given that it passes via the neck and thorax to the abdomen, the vagus nerve has the broadest distribution in the body. It comprises somatic and visceral afferent fibers, as well as general and special visceral efferent fibers. According to Darwin, emotional facial expressions are evolved and adaptive and serve a crucial communicative function. Unfortunately, at that time, the understanding of the neuroanatomy and phylogeny of the nervous system was limited and Darwin's intuition has been further developed only a century later by Stephen Porges (2001; 2003; 2007) in his influential polyvagal theory. This theory proposes that the vagus nerve is the key phylogenetic substrate that regulates emotional and social behavior. Interestingly, mammals are the only vertebrates characterized by a myelinated vagus that can rapidly regulate the nervous system to foster engagement and disengagement with the environment. According to the polyvagal theory two functionally distinct branches of the vagus fulfil different evolutionary responses in mammals. Whereas, the more primitive branch (The Dorsal

Vagal Complex) is supposed to provoke immobilization behaviors (e.g., feigning death), the more evolved branch (The Ventral Vagal Complex) has been proposed to be related to social communication and self-soothing behaviors (Porges, 2001; 2003; 2007). The polyvagal theory assumes that optimal social interaction, which includes the recognition of emotion in faces, is modulated by the vagus nerve.

tVNS enhances emotion recognition

The aim of our study was to examine, for the first time, the causal involvement of the vagus nerve and the recognition of someone's emotions based on images of the eye region, as indexed by the Reading the Mind in the Eyes Test (RMET). In order to do that, we employed tVNS. tVNS is safe and accompanied only by minor side effects such as tingling or itching sensation under the electrodes. Given the right vagal nerve has efferent fibers to the heart, tVNS is safe to be performed only in the left ear (Kreuzer et al. 2012). tVNS acts via the auricular branch of the vagus nerve (ABVN) which supplies the skin of the concha in the human ear (Peuker and Filler 2002) allowing for a reliable transcutaneous electrical stimulation of the nerve fibers in this area. Following Kraus and colleagues (2007), a clever way to create a sham condition using tVNS is by attaching the stimulation electrodes to the center of the left ear lobe, which is free of cutaneous vagal innervation, see Figure 2. By doing this, the participants perceive the exact same minor side effects of the active stimulation and they are not able to disentangle the active from the sham stimulation.

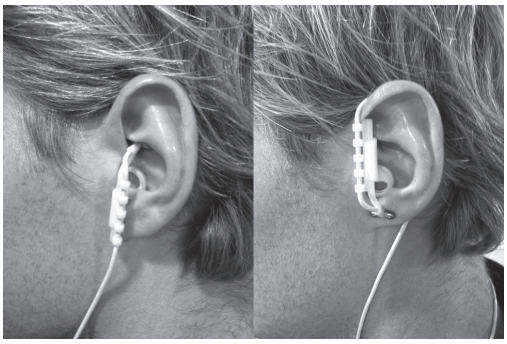

Figure 2. Positioning of the stimulation electrodes in the active (left) and in the sham (right) condition.

In contrast to imaging techniques, which are only correlational, by means of tVNS we are able to infer a causal relation between the stimulated vagus nerve and the related ability to recognize emotions as indexed by performance on the RMET (compare van Leusden, Sellaro and Colzato, 2015). tVNS has been found to reliably activate the vagus nerve. Two functional magnetic resonance imaging (MRI) studies in healthy humans have found that tVNS increased activation in the brainstem region including the locus coeruleus and nucleus of the solitary tract, indicating that tVNS is able to effectively stimulate vagal afferents to the brainstem (Dietrich et al. 2008; Frangos et al. 2015).

The RMET requires participants to assess someone's emotions based on images of the eye region. The test consisted of 36 black-and-white photos of a human's eye region, presented one by one along with four adjectives (one target word and three foil words) arranged around the eye region. On each trial, participants were instructed to choose which of the four words better described what the person in the picture was thinking or feeling, by clicking on it with the mouse. The 36 items were divided in two subsets of easy and difficult items.

In sum, if the vagus nerve is involved in the process of emotion recognition as hypothesized by Darwin (1872/1965) and Porges (2001; 2003; 2007), we would expect that active tVNS, compared to sham stimulation, will enhance performance of the recognition of someone's emotions based on images of the eye region. As predicted, we found that stimulation of the vagus nerve enhances recognition of someone's emotions based on images of the eye region when item difficulty was taken into account (Colzato, Sellaro & Beste, 2017). Indeed, when actively stimulated, participants were better in inferring people's emotional state, but only when confronted with easy items and not when presented with difficult items. This suggests that active tVNS improved the ability to recognize salient social cues, without affecting the recognition of subtler social cues. If one considers that people's fight/flight response strategies are more likely to rely on salient and recognizable social cues, the present findings fit with the proposed role of the vagus nerve to regulate social engagement via emotion recognition (Porges, 2001; 2003; 2007).

Part 2: Conclusion

Our observations provide direct evidence for the idea that the vagus nerve plays a causal role in the recognition of someone's emotions based on images of the eye region. Therefore, these findings may represent an important step in stimulating research to further extend our understanding of the specific role of the vagus nerve in the general processing of emotions. Further, our results support the idea that tVNS is a promising noninvasive brain stimulation technique for enhancing social and affective processes in healthy humans (Colzato and Vonck, 2017).

Part 3: Microdosing psychedelics

This part is dedicated to microdosing psychedelics which act as serotonergic agonists. I will discuss the possibility to use sub-perceptual doses of psychedelic substances, in specific truffles, to enhance creativity.

Microdosing as 'productivity hack'?

Major news outlets throughout the world are reporting on the growing number of professionals using small doses of psychedelics (e.g. magic mushrooms, truffles, or peyote) to boost their productivity and creativity at work. A prominent example is the use of small doses of LSD by employees in Silicon Valley, as a 'productivity hack' (Glatter 2015). This emerging phenomenon is referred to as microdosing, with dosages around one tenth of recreational doses. This is a different phenomenon then the consumption of other psychedelics drugs such as Ayahuasca (see paper by Olga Silva in this book). Yet, despite the low dosages microdosing is still thought to provide a potential boost in cognition according to anecdotal reports (Cooke 2017; Sahakian 2017). Moderate to large doses of psychedelic induce changes in perception, mood and overall consciousness, often described as qualitatively similar to deep meditative or transcendental states (Barrett and Griffiths 2017; Barrett, Johnson and Griffiths 2017), If similar effects apply to microdosing, this would render microdosing a potentially interesting cognitive enhancer in healthy individuals or even the basis of a treatment strategy to tackle various disorders including depression.

Revival of psychedelics

Throughout the 1960's psychedelics were extensively used at recreational doses in experimental research, clinical settings, and in creative and scientific vocations (Sessa 2008), but were made illegal in most countries worldwide as a reaction to the rising counterculture of the 1960's and failure to establish clear efficacy of LSD treatment (Oram 2014). Now, after many decades of disregard, psychedelics have started to reappear as a genuine and promising area of research within experimental and clinical psychology, as well as psychiatry. Moreover, certain psychedelics, such as truffles, have regained a legal status in The Netherlands, offering researchers a particularly interesting opportunity to study its effects in a quantitative manner. This is highly desirable, as previous reports have remained anecdotal (Oberhaus 2017) and qualitative at best, often focusing on experiences of elevated feelings of determination, alertness, and energy, improved pattern recognition, as well as strong reductions of depressive feelings (Fadiman and Krob 2017). Qualitative studies based on self-reports are known to suffer from validity problems due to participants' inaccurate memories, differences in vocabulary and verbal skills, and unintentional or willful distortions of subjective experiences (Schwarz 1999).

Mechanism of action

Classical psychedelics such as psilocybin, the active compound in psychedelic truffels, exert their primary effects by directly binding to serotonin 2A receptors (5-HT2A; Tylš et al. 2014). Interestingly, 5-HT2A agonism has been reported to be associated with enhanced cognitive flexibility (Boulougouris and Robbins 2010), improved associative learning (Harvay 2003) and hippocampal neurogenesis (Catlow 2016) in animals. Additionally, psychedelics have been shown to increase subjective sense of wellbeing, optimism, and openness in humans (Griffiths et al. 2006). Additionally, psychedelics have been shown to increase subjective sense of wellbeing, optimism, and openness in humans (Griffiths et al. 2006). Moreover, multiple clinical trials using moderate to large doses of psychedelics have indicated that psychedelics have anxiolytic, antidepressant (dos Santos et al. 2016; Carhart-Harris et al. 2016; Grob et al. 2011; Griffiths et al. 2016), anti-compulsive (Moreno et al. 2006),

and anti-addictive properties (Bogenschutz et al. 2015, Johnson et al. 2014, dos Santos et al. 2016).

Does microdosing enhance creativity?

The effects of psychedelic substances can be argued to target the serotonergic system and to be beneficial in situations where there is need for mental flexibility, or where one needs to break through rigid patterns of thought. Through the alleged benefits in mental flexibility, a promising behavioral target of psychedelics lies in the area of creativity. Creativity is a multilayered phenomenon, commonly defined as the ability to generate ideas, solutions, or products that are both novel and appropriate (e.g., Amabile 1996; Sternberg and Lubart 1999). Creativity is not a unitary function but consists of two subcomponents: convergent and divergent thinking (Wallas 1926). Convergent thinking, which requires identification of a single solution to a well-defined problem (Mednick 1962). An example of convergent thinking task would be to find the one concept that can be meaningfully combined with three other concepts concepts such as "…man", "…market", and "…bowl" (such as "super"). Divergent thinking requires instead the collection of many possible solutions to a loosely defined problem (Guilford 1967). An example of divergent thinking task would be to list all possible ways in which a brick could be used (for throwing, as a weight, as a weapon, etc.).

We have been offered the unique opportunity to quantitatively study the effects of microdosing truffles during microdosing events of the Psychedelic Society of The Netherlands, a non-laboratory environment. Natural settings like such an event have a number of potential benefits as they are more comparable to situations of real life use than studies in a laboratory environment, see Figure 3.

Figure 3. Picture taken during a microdosing event of the Psychedelic Society of The Netherlands.

The goal of our study was to study the effects of psychedelic truffles on creative thinking. We assessed convergent and divergent thinking separately, by using the Picture Concept Task (PCT; Wechsler 2003) and Guilford's (1967) Alternate Uses Task (AUT), respectively. Given that convergent thinking is correlated with fluid intelligence (e.g., Akbari Chermahini, Hickendorff and Hommel, 2012), we also employed a short 12-item version of Raven's Progressive Matrices Task (Bilker et al. 2012), a standard intelligence test, once before and once during the acute effects of a microdose of truffles. Given the effects of large doses of psychedelics on positive mood, trait openess, and assumed cognitive flexibility reflected by psychosis-like symptoms (Carhart-Hariss et al. 2016), we expected improvements on creativity after microdosing.

The experiment was conducted during a microdosing event organized by the Psychedelic Society of the Netherlands, where we were given the opportunity to ask participants to take part in the experiment. The experiment consisted of a baseline session before participants had consumed any psychedelics and a second session carried out while participants were under the influence of a microdose of psychedelic truffles. We observed an increase in divergent idea generation on the

AUT, as evidenced by a significant increase in fluency, flexibility, and originality scores, as well as an increase in convergent thinking on the PCT after intake of a microdose of magic truffles. Given that fluid intelligence did not change between the two measurement time points suggests a specific effect on creativity performance, but not on general cognition (Prochazkova et al., 2018).

First, our results are in line with Geyer and Vollenweider's (2001) "gating"-theory which posits that psychedelics alter the function of the thalamus that serves as a gate to sensory processing. As a result, the brain fails to selectively filter sensory and interoceptive input, consequently increasing the chance to trigger stored representations. Put differently, the drug-induced disintegration of thalamic gating may increase the availability of novel ideas and possible solutions to a problem. Second, along similar lines, Carhart-Harris (2014) has applied predictive-coding/free-energy theory (Friston et al. 2006) to explain the effects of recreative doses of psychedelics on cognitive flexibility. The theory is based on the idea that the brain continuously attempts to predict consistencies in the environment (Tolman and Brunswik 1935) by creating internal models that minimize the discrepancy between sensory input and prediction of that input (Sokolov 1960). If psychedelics impair the filtering of bottom-up information (Baggott 2015), this could lead to an increase in prediction errors (Carhart-Harris 2014) and futile attempts to reduce them may result in unusual or non-ordinary interpretations of the environment, and promote a brain state of unconstrained cognition (Carhart-Harris et al. 2014).

Part 3: Conclusion

Whereas large doses of psychedelics can introduce a range of undesirable side effects, microdoses of psychedelic substances might prove to be a promising alternative that could eliminate the risks of challenging experiences (sometimes referred to as a ''bad trips") while maintaining the potential benefits of psychedelic substances on human emotion and cognition. The current naturalistic study is the first to quantitatively show that microdosing psychedelics could improve creative performance, possibly by means of enhancing serotonergic levels and inducing a state of unconstrained thought allowing for increased novel idea generation.

Conclusion: moving towards a responsible cognitive enhancement

Most cognitive enhancing programs have a one-size-fits-all design and presuppose that people benefit from the intervention more or less the same way and to more or less the same degree. However, in this paper, I showed evidence suggesting this is not always plausible. I propose that the efficiency of cognitive enhancing interventions will often be modulated by life-span, inter-individual differences, including pre-existing neuro-developmental factors and differences with a genetic basis. Accordingly, only enhancing programs that are tailored to individual abilities, skills, and needs are likely to succeed. Only a theory-driven cognitive enhancement is a responsible cognitive enhancement. Only a mechanistically-oriented, theory-driven approach will allow for the design of individualized cognitive-enhancement interventions required to make such interventions successful for the recipient at an individual level, and to make welfare more affordable at a societal level.

References

Akbari Chermahini S, Hickendorff M, Hommel B (2012) Development and validity of a Dutch version of the Remote Associates Task: An item-response theory approach. *Thinking Skills and Creativity, 7,* 177-186.

Amabile TM (1996) *Creativity in context: Update to the social psychology of creativity*. Westview Press, Boulder, CO

Baggot MJ (2015) Psychedelics and Creativity: A review of the quantitative literature. *PeerJ Preprints, 3*, 1-24

Barrett FS, Griffiths RR (2017) *Classic hallucinogens and mystical experiences: Phenomenology and neural vorrelates.* In: Geyer MA, Ellenbroek BA, Marsden CA, Barnes TRE, L. Andersen S (eds) Current topics in behavioral neurosciences. Springer, Berlin, Heidelberg, pp 1-38.

Barrett FS, Johnson MW, Griffiths RR (2017) Psilocybin in long-term meditators: Effects on default mode network functional connectivity and retrospective ratings of qualitative experience. *Drug and Alcohol Dependence, 171*:e15-e16. doi: 10.1016/j.drugalcdep.2016.08.058

Beste, C., Getzmann, S., Gajewski, P. D., Golka, K., and Falkenstein, M. (2014). Latent Toxoplasma gondii infection leads to deficits in goal-directed behavior in healthy elderly. *Neurobiology of Aging, 35,* 1037-1044.

Bilker WB, Hansen JA, Brensinger CM, Richard J, Gur RE, Gur RC (2012) Development of abbreviated nine-item forms of the Raven's Standard Progressive Matrices Test. *Assessment, 19*, 54-369.

Bogenschutz MP, Forcehimes AA, Pommy JA, Wilcox CE, Barbosa P, Strassman RJ (2015) Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study. *Journal of Psychopharmacology, 29*, 289-299.

Boulougouris V, Glennon JC, Robbins TW (2008) Dissociable effects of selective 5-HT2A and 5-HT2C receptor antagonists on serial spatial reversal learning in rats. *Neuropsychopharmacology, 33,* 2007-2019.

Carhart-Harris RL, Leech R, Hellyer PJ, Shanahan M, Feilding A, Tagliazucchi E, Chialvo DR, Nutt D, Axmacher N, Brooks SJ, Maclean K, Hopkins J (2014) The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience, 8*:20.

Carhart-Harris RL, Bolstridge M, Rucker J, Day CMJ, Erritzoe D, Kaelen M, Bloomfield M, Rickard JA, Forbes B, Feilding A, Taylor D, Pilling S, Curran VH, Nutt DJ (2016) Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *The Lancet Psychiatry, 3*, 619-627.

Catlow BJ, Jalloh A, Sanchez-Ramos J (2016) Hippocampal neurogenesis: Effects of psychedelic drugs. In: *Neuropathology of drug addictions and substance misuse*. Elsevier, pp 821-831.

Centraal Bureau voor de Statistiek (CBS). (2011). *Bevolkingsprognose 2010–2060: sterkere vergrijzing, langere levensduur.* http://www.cbs.nl/NR/rdonlyres/389D62E2-7205-42C3-956F-33E17CFE6433/0/2011k1b15p16art.pdf

Colzato, L.S. (2017). Tyrosine. In: L.S. Colzato (ed.), *Theory-driven approaches to cognitive enhancement*. New York: Springer.

Colzato, L. S., Jongkees, B., Sellaro, R. & Hommel B (2013). Working memory reloaded: Tyrosine repletes updating in the N-Back task. *Frontiers in Behavioral Neuroscience 7*, 200.

Colzato, L. S., Jongkees, B. J., Sellaro, R., van den Wildenberg, W., and Hommel, B. (2014). Eating to stop: Tyrosine supplementation enhances inhibitory control but not response execution. *Neuropsychologia, 62*, 398-402.

Colzato, L. S., Sellaro, R., & Beste, C. (2017). Darwin revisited: The vagus nerve is a causal element in controlling recognition of other's emotions. *Cortex, 92*, 95-102.

Colzato, L. S., Steenbergen, L., Sellaro, R., Stock, A. K., Arning, L., & Beste, C. (2016). Effects of L-Tyrosine on working memory and inhibitory control are determined by DRD2 genotypes: A randomized controlled trial. *Cortex, 82*, 217-224.

Colzato, L.S. & Vonck, K. (2017). Transcutaneous vagus and trigeminal nerve stimulation. In: L.S. Colzato (ed.), *Theory-driven approaches to cognitive enhancement*. New York: Springer.

Cooke R (2017) How dropping acid saved my life. The Guardian. https://www.theguardian.com/global/2017/jan/08/how-dropping-acid-saved-my-life-ayelet-waldman-books-depression. Accessed 25 Dec 2017.

Cools, R., & D'Esposito, M. (2011). Inverted-U-shaped dopamine actions on human working memory and cognitive control. *Biological Psychiatry, 69*, 113-125.

Cuche, J.L., Prinseau, J., Selz, F., Ruget, G., Tual, J.L., Reingeissen, L. et al. (1985). Oral load of tyrosine or l-dopa and plasma levels of free and sulfoconjugated catecholamines in healthy men. *Hypertension 7*, 81-89.

Darwin, C. (1872/1965). *The expression of emotions in man and animals* (Vol. 526). (University of Chicago press).

Daubner, S. C., Le, T., and Wang, S. Z. (2011). Tyrosine hydroxylase and regulation of dopamine synthesis. *Archives of Biochemistry and Biophysics, 508,* 1-12.

Dietrich, S., Smith, J., Scherzinger, C., Hofmann-Preiß, K., Freitag, T., Eisenkolb, A., & Ringler, R. (2008). A novel transcutaneous vagus nerve stimulation leads to brainstem and cerebral activations measured by functional MRI/Funktionelle Magnetresonanztomographie zeigt Aktivierungen des Hirnstamms und weiterer zerebraler Strukturen unter transkutaner Vagusnervstimulation. *Biomedizinische Technik/Biomedical Engineering, 53(3)*, 104-111.

dos Santos RG, Osório FL, Crippa JAS, Riba J, Zuardi AW, Hallak JEC (2016) Antidepressive, anxiolytic, and antiaddictive effects of ayahuasca, psilocybin and lysergic acid diethylamide (LSD): A systematic review of clinical trials published in the last 25 years. *Therapeutic Advances in Psychopharmacology, 6*, 193-213.

Fadiman J, Krob S (2017) Microdosing: The phenomenon, research results, and startling surprises. Lecture presented at the Psychedelic Science 2017 conference, Oakland, CA.

Felger J. C. and Miller, A. H. (2012). Cytokine Effects on the Basal Ganglia and Dopamine Function: the Subcortical Source of Inflammatory Malaise. *Frontiers in Neuroendocrinology, 33*, 315-327.

Fernstrom, J.D., & Fernstrom, M.H. (2007). Tyrosine, phenylalanine, and catecholamine synthesis and function in the brain. *Journal of Nutrition, 137*, 1539S-1547S.

Fillenz, M. (1993). Short-term control of transmitter synthesis in central catecholaminergic neurones. *Progress in Biophysics and Molecular Biology, 60*, 29e46.

Flegr, J. (2013). Influence of latent Toxoplasma infection on human personality, physiology and morphology: pros and cons of the Toxoplasma-human model. *Journal of Experimental Biology, 216,* 127-133.

Frangos, E., Ellrich, J., & Komisaruk, B. R. (2015). Non-invasive access to the vagus nerve central projections via electrical stimulation of the external ear: fMRI evidence in humans. *Brain Stimulation, 8(3)*, 624-636.

Friston, K., Kilner, J., & Harrison, L. (2006). A free energy principle for the brain. *Journal of Physiology-Paris, 100*, 70-87.

Gajewski, P. D., Falkenstein, M., Hengstler, J. G., and Golka, K. (2014). Toxoplasma gondii impairs memory in infected seniors. *Brain Behavior and Immunity, 36*,193-199.

Gajewski, P. D., Falkenstein, M., Hengstler, J. G., and Golka, K. (2016). Reduced ERPs and theta oscillations underlie working memory deficits in Toxoplasma gondii infected seniors. *Biological Psychology, 120,* 35-45.

Gaskell, E.A., Smith, J.E., Pinney, J.W.,Westhead, D.R., and McConkey, G.A. (2009). A unique dual activity amino acid hydroxylase in Toxoplasma gondii. *PLOS One, 4,* e4801.

Gazzaniga, M.S., Ivry, R.B., and Mangun, G.R. (2008). *Cognitive Neuroscience: The Biology of the Mind (3rd edition).* New York: Norton & Company.

Geyer MA, Vollenweider FX (2008) Serotonin research: Contributions to understanding psychoses. *Trends in Pharmacological Science, 29*, 445-453.

Gibson, C.J. & Wurtman, R.J. (1977). Physiological control of brain catechol synthesis by brain tyrosine concentration. *Biochemical Pharmacology, 26,* 1137-1142.

Glaeser, B. S., Melamed, E., Growdon, J. H., & Wurtman, R. J. (1979). Elevation of plasma tyrosine after a single oral dose of L-tyrosine. *Life Sciences, 25,* 265-271.

Glatter R (2015) LSD microdosing: The new job enhancer in Silicon Valley. Forbes. https://www.forbes.com/sites/robertglatter/2015/11/27/lsd-microdosing-the-new-job-enhancer-in-silicon-valley-and-beyond/#109a749b188a. Accessed 25 Dec 2017.

Goldman-Rakic, P.S., Muly, E.C. & Williams, G.V. (2000). D1 receptors in prefrontal cells and circuits. *Brain Research Review, 31*, 295-301.

Griffiths RR, Richards WA, McCann U, Jesse R (2006) Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology, 187,* 268-283.

Grob CS, Danforth AL, Chopra GS, Hagerty M, McKay CR, Halberstad AL, Greer GR (2011) Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archive of General Psychiatry, 68*, 71-78.

Guilford JP (1967) *The nature of human intelligence.* McGraw-Hill, NY

Harvey JA (2003) Role of the serotonin 5-HT2A receptor in learning. *Learning and Memory, 10,* 355-362.

Jongkees, B. J., Hommel, B., & Colzato, L. S. (2014). People are different: Tyrosine's modulating effect on cognitive control may depend on individual differences related to dopamine function. *Frontiers in Psychology, 5*:1101.

Johnson MW, Garcia-Romeu A, Cosimano MP, Griffiths RR (2014) Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. *Journal of Psychopharmacology, 28*, 983-992.

Jurado, M. B., and Rosselli, M. (2007). The elusive nature of executive functions: a review of our current understanding. *Neuropsychology Review, 17*, 213-233.

Kraus, T., Hösl, K., Kiess, O., Schanze, A., Kornhuber, J., & Forster, C. (2007). BOLD fMRI deactivation of limbic and temporal brain structures and mood enhancing effect by transcutaneous vagus nerve stimulation. *Journal of Neural Transmission, 114(11)*, 1485-1493.

Kreuzer, P.M., Landgrebe, M., Husser, O., Resch, M., Schecklmann, M., Geisreiter, F., et al. (2012). Transcutaneous vagus nerve stimulation: retrospective assessment of cardiac safety in a pilot study. *Frontiers in Psychiatry, 3*:70.

Kvetnansky, R., Sabban, E.L. & Palkovits, M. (2009). Catecholaminergic systems in stress: structural and molecular genetic approaches. *Physiological Reviews, 89*, 535-606.

Lehnert, H., Reinstein, D.K., Strowbridge, B.W. & Wurtman, R.J. (1984). Neurochemical and behavioral consequences of acute uncontrollable stress: effects of dietary tyrosine. *Brain Research, 303*, 215-223.

Mahoney, C.R., Castellani, J., Kramer, F.M., Young, A., & Lieberman, H.R., (2007). Tyrosine supplementation mitigates memory decrements during cold exposure. *Physiology & Behavior, 92*, 575-582.

Martin, H. L., Alsaady, I., Howell, G., Prandovszky, E., Peers, C., Robinson, P., and McConkey, G. A. (2015). Effect of parasitic infection on dopamine biosynthesis in dopaminergic cells. *Neuroscience, 306*, 50-62.

McConkey, G. A., Martin, H. L., Bristow, G. C., and Webster, J. P. (2013). Toxoplasmagondii infection and behaviour: Location, location, location? *Journal of Experimental Biology, 216*, 113–119.

Mednick S (1962) The associative basis of the creative process. *Psychological Review, 69,* 220–232.

Michaud, M., Balardy, L., Moulis, G., Gaudin, C., Peyrot, C., Vellas, B., ... & Nourhashemi, F. (2013). Proinflammatory cytokines, aging, and age-related diseases. *Journal of the American Medical Directors Association, 14(12)*, 877-882.

Miman, O., Kusbeci, O.Y., Aktepe, O.C., and Cetinkaya, Z. (2010). The probable relation between Toxoplasma gondii and Parkinson's disease. *Neuroscience Letters, 475*, 129-131.

Moreno FA, Wiegand CB, Taitano EK, Delgado PL (2006) Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder. *Journal of Clinical Psychiatry, 67,* 1735-40.

Muly, E.C. III, Szigeti, K. & Goldman-Rakic, P.S. (1998). D1 receptor in interneurons of macaque prefrontal cortex: distribution and subcellular localization. *Journal of Neuroscience, 18*, 10553-10565.

Oberhaus D (2017) 400 people microdosed LSD for a month in the name of science. Vice Magazine. https://motherboard.vice.com/en_us/article/mgy573/400-people-microdosed-lsd-for-a-month-in-the-name-of-science. Accessed 25 Dec 2017.

Peuker, E. T., & Filler, T. J. (2002). The nerve supply of the human auricle. *Clinical Anatomy, 15*, 35-37.

Porges, S. W. (2001). The polyvagal theory: phylogenetic substrates of a social nervous system. *International Journal of Psychophysiology, 42(2)*, 123-146.

Porges, S. W. (2003). Social engagement and attachment. *Annals of the New York Academy of Sciences, 1008(1)*, 31-47.

Porges, S. W. (2007). The polyvagal perspective. *Biological Psychology, 74(2)*, 116-143.

Prochazkova, L., Lippelt, D.P., Colzato, L.S., Kuchar, M., Sjoerds, Z. & Hommel, B. (2018) Exploring the effect of microdosing psychedelics on creativity in an open-label natural setting. Manuscript under revision.

Puccioni, O., and Vallesi, A. (2012). Conflict resolution and adaptation in normal aging: The role of verbal intelligence and cognitive reserve. *Psychology and Aging, 27*, 1018-1026.

Sahakian B (2017) LSD microdosing is trending in Silicon Valley but can actually make you more creative. IFLScience. http://www.iflscience.com/health-and-medicine/lsd-microdosing-is-trendingin-silicon-valley-but-can-actually-make-you-more-creative/. Accessed 25 Dec 2017.

Schwarz N (1999) Self-reports: How the questions shape the answers. *American Psychologist 54,* 93-105.

Sokolov EN (1960) Neuronal models and the orienting reflex. In: Brazier MAB (ed) *The central nervous system and behavior.* JosiahMacy, Jr. Foundation, NY.

Sternberg RJ, Lubart TI (1999) The concept of creativity: Prospects and paradigms. In: Sternberg RJ (ed) *Handbook of creativity*. Cambridge University Press, London, pp 3-16.

Steenbergen, L., Sellaro, R., Hommel, B., and Colzato, L.S. (2015). Tyrosine promotes cognitive flexibility: evidence from proactive vs. reactive control during task switching performance. *Neuropsychologia, 69*, 50-55.

Tam, S. Y., Elsworth, J. D., Bradberry, C. W., & Roth, R. H. (1990). Mesocortical dopamine neurons: high basal firing frequency predicts tyrosine dependence of dopamine synthesis. *Journal of Neural Transmission, 81*, 97-110.

Thomas, J. R., Lockwood, P. A., Sing, A., & Deuster, P. A. (1999). Tyrosine improves working memory in a multitasking environment. *Pharmacology Biochemistry and Behavior, 64*, 495–500.

Tylš F, Páleníček T, Horáček J (2014) Psilocybin - Summary of knowledge and new perspectives. *European Neuropsychopharmacology, 24*, 342-356.

Tolman EC, Brunswik E (1935) The organism and the causal texture of the environment. *Psychological Review, 42,* 43-77.

Vallesi, A. (2016). Dual-task costs in aging are predicted by formal education. *Aging Clinical and Experimental Research, 28*, 959-964.

Van Leusden, J. W., Sellaro, R., & Colzato, L. S. (2015). Transcutaneous Vagal Nerve Stimulation (tVNS): a new neuromodulation tool in healthy humans?. *Frontiers in Psychology, 6*:102.

Wallas G (1926) *The art of thought.* Harcourt Brace, NY.

Webster, J.P., Kaushik, M., Bristow, G.C., and McConkey, G.A. (2013). Toxoplasma gondii in infection, from predation to schizophrenia: can animal behavior help us understand human behaviour? *Journal of Experimental Biology, 216*, 99-112.

Webster, J.P., Lamberton, P.H., Donnelly, C.A., and Torrey, E.F. (2006). Parasites as causative agents of human affective disorders? The impact of anti-psychotic, mood stabilizer and anti-parasite medication on Toxoplasma gondii's ability to alter host behaviour. *Proceedings Biological Sciences, 273*, 1023-1030.

Wechsler D (2003) *The Wechsler intelligence scale for children*, 4th edn. Pearson, London.

Wilking, H., Thamm, M., Stark, K., Aebischer, T., and Seeber, F. (2016). Prevalence, incidence estimations, and risk factors of Toxoplasma gondii infection in Germany: a representative, cross-sectional, serological study. *Scientific Reports, 6*, 22551.

Wurtman, R.J., Hefti, F. & Melamed, E. (1981). Precursor control of neurotransmitter synthesis. *Pharmacological Reviews, 32,* 315-335.

PALESTRAS
LECTURES

ENHANCING HUMAN COGNITION USING NONINVASIVE BRAIN STIMULATION

***Alexander Sack* ***

Our brain is the source of all our perceptions, our thoughts, emotions, our entire behavior. Understanding the neural mechanism by which the human brain is capable of exerting all of these functions in such dynamic flexibility is paramount for understanding, predicting, and eventually modulating human cognition. In the past 30 years, many noninvasive brain research tools have been developed, enabling us to study the living brain at work. Functional Magnetic Resonance Imaging (fMRI) is one of the most versatile tools to identify which brain areas are active during the execution of a given cognitive task. However, fMRI is limited in revealing whether the observed activity in a given brain region or network is functionally necessary to successfully perform the cognitive function at hand. Also, fMRI is not capable of directly modulating brain activity to change cognitive performances. Therefore, we require a different class of brain research techniques which are referred to as neuromodulation.

Noninvasive neuromodulation allows us to directly stimulate neural activity in a particular brain region with a particular activation rhythm, changing the underlying neural dynamics and subsequently modulating human behavior. One of the most prominent noninvasive neuromodulation techniques is transcranial magnetic brain stimulation (TMS). During TMS, an electromagnetic coil applies strong time-varying magnetic pulses transcranially, i.e through the intact scull, into the brain, inducing electric brain active by means of electromagnetic induction. TMS has immediate effects, leading to depolarization of underlying axons which can either translate into immediate stimulation (evoking motor responses) or causing behavioral disruption in case of stimulating a brain region during task execution with random TMS pulses. Importantly, though, TMS can also be applied in the form of so-

* Department of Cognitive Neuroscience, Faculty of Psychology and Neuroscience, Maastricht University, The Netherlands.

called repetitive TMS (rTMS). rTMS involves the repeated stimulation with many, hundreds, of magnetic pulses for a longer period of time in a given stimulation frequency. We now know, that, depending on the applied stimulation frequency, rTMS can induce neuroplastic changes in the brain, leading to either enhanced or decreased local neural excitability and brain connectivity.

In this sense, one could think about using rTMS to induce longer lasting changes in brain activity which may translate into longer lasting behavioral effects. The question is then, can we use TMS or neuromodulation to enhance our cognitive abilities like attention and/or memory? So far, many studies have applied TMS in healthy volunteers and assessed the behavioral consequences on attention and memory performance. Although many studies indeed could demonstrate that rTMS can lead to significant modulation in cognitive performances even beyond the stimulation itself, most of these studies in fact caused a significant impairment rather than an improvement in cognitive performance. From a scientific point of view this is not a problem per se, as the mere fact that TMS can noninvasively and significantly modulate behavior by itself represents a great value for studying causal brain-behavior relationships. However, one may nonetheless wonder why so view studies have reported TMS-induced cognitive enhancement effects. What are we missing?

I propose that the key to answer these questions lies in the rhythms of cognition. A brain region is never just simply active or not, it oscillates in a specific rhythm. Neurons in a brain region fire together in regular bursts of activation, like a musical orchestra. This leads to rhythmic waves of brain activity with, e.g., 10 cycles per second, or 10 Hz, also called the alpha rhythm. And there are many such brain rhythms.

We used electroencephalography (EEG) to record these oscillations in healthy volunteers during the execution of a spatial attention task. We found that the power of alpha oscillations was enhanced in the hemisphere ipsilateral, and decreased contralateral to the locus of attention. Also, the exact alpha frequency was slightly different between participants, so we also identified the exact individual rhythm for each participant, called the individual alpha frequency (IAF). We now identified not only the location of attention control in the brain but also the individual

rhythms with which these brain regions fire during the performance of an attention control task. Based on these fMRI-EEG findings, we now applied a personalized and participant-tailored neuromodulation protocol, stimulating with transcranial alternative current stimulation (TACS) at IAF the left intraparietal sulcus of each healthy participant. We recorded the effects of our personalized neuromodualtion on both, oscillatory EEG activity pattern and attention performance. This series of experiments revealed that stimulating the brain at this location with IAF indeed causes an alpha lateralization towards one hemisphere as expected (alpha power increase at stimulated site while alpha power decrease contralateral to stimulation). Moreover, we now found that this stimulation protocol caused a performance improvement in our healthy population, enhancing their ability of shifting their attention to a given location. Interestingly, the stronger the effects of our neuromodulation on the EEG pattern, the stronger also the behavioral improvement induced in a given participant, indicating that it is the neural effect induced by personalized neuromodulation that causes these cognitive enhancements.

Inspired by these results, we translated these findings to stroke patients suffering from specific attention control deficits (hemineglect). We applied rhythmic neuromodulation to the unaffected brain hemisphere to boost their cognitive recovery. This clinical study demonstrated that by using this approach we were able to improve the clinical symptoms of these stroke patients significantly, largely improving their attention deficit using individualized alpha oscillation-based neuromodulation.

In my opinion, to really crack the code of human cognition, we need to simultaneously integrate space, using fMRI to localize which brain regions are active, time, using another technique called EEG to measure with high temporal precision these oscillations, and causality, using TMS to manipulate the brain, during Task Performance. We pioneered in developing this set-up and are now capable of simultaneously combining fMRI, EEG, and TMS during Cognition. We hope to not only use this approach in fundamental brain research, aiming to enhance cognitive performance in healthy volunteers, but to also always translate our findings to clinical applications in order to help patients suffering from cognitive deficits following stroke or bran injury or due to neuropsychiatric illness.

COSMETIC NEUROLOGY: ETHICAL CONSIDERATIONS AND PUBLIC ATTITUDES

Erin Conrad & Anjan Chatterjee *

Cognitive enhancement, or "cosmetic neurology" refers to the practice of enhancing cognition and behavior in healthy people (1). Although cognitive enhancement often refers to the enhancement of cognition, it also refers to the enhancement of mood, movement, creativity, social finesse, and other psychological attributes. As our ability to treat disorders of cognition and emotion improves, so too does our ability to intervene in healthy individuals. Enhancement carries the promise of an improved quality of life and productivity well into old age, as well as potential medical and social perils (2). Here, we review current drugs that can be used for enhancement, their potential efficacy, current cultural norms, and the ethical issues that arise from this practice.

Drugs used for cognitive enhancement

Like its namesake, cosmetic surgery, which was first developed to treat disfiguring injuries resulting from World War I trench warfare, cognitive enhancement has roots in wartime applications (3). Advances in treatment for facial disfigurements from injuries in the field over time were applied to healthy people. This practice was in part driven by financial incentives and eventually cultural acceptance. Analogously, methamphetamine, one of the earliest enhacing drugs, was widely used in Germany during World War II to stimulate battle-weary soldiers (4,5). A medical officer reported early use of this drug during a 1942 battle involving German soldiers encircled by Russian troops at the Eastern Front. The exhausted soldiers were each given two tablets of methamphetamine and subsequently managed to break out of the encirclement, many becoming "euphoric" during the fight (6). Cognitive enhancement, also driven by financial

* Department of Neurology, Perelman School of Medicine, University of Pennsylvania, USA.

and social forces, has expanded beyond the military to the classroom, the workplace, and the home.

Stimulants

Stimulants include amphetamines, methylphenidate, atomoxetine, and modafinil. Many stimulants are currently approved to treat ADHD in the United States, where physicians are allowed to prescribe drugs for off-label uses. Stimulants increase noradrenergic and dopaminergic transmission in frontoparietal attentional systems and the striatum (7). Studies report evidence for improved attention (8), shorter reaction time (9-11), more accurate short term memory (10,12,13), and improved language learning (14). Stimulants mitigate performance decrements following sleep-deprivation (15). Chess players on stimulants take longer to consider each move, improving their performance in untimed games, but display worse performance in more traditional games in which there is a time limit for each move (16). Performance-enhancing effect of stimulants may not be mediated by directly increasing intelligence per se, but rather as a secondary effect of either increased wakefulness, vigilance, or motivation (17). Some suggest that these drugs are better thought of as drive drugs than cognitive enhancers.

Cholinergic medications

Cholinergic medications, including acetylcholinesterase inhibitors, acetylcholine precursors, and the direct nicotine agonist, increase normal cholinergic stimulation of the cerebral cortex via the nucleus basalis and cholinergic stimulation of the hippocampus via the medial septal nuclei and the nuclei of the diagonal bands of Broca (7,18). Acetylcholine acts upon nicotinic and muscarinic receptors in the brain, and both receptors are important in cognition. Cholinergic medications improve learning and memory in part by guiding the development and maintenance of neuronal synaptic connections (22). Acetylcholinesterase inhibitors improve cognitive performance across several domains in patients with Alzheimer's disease and other forms of dementia (19-21). They may improve episodic and verbal memory among healthy adults (23,24). In one preliminary study with commercial pilots, low doses of cholinesterase inhibitors improved performance during emergencies in

flight simulations (25). Like stimulants, the effect of these drugs may be mediated through increased levels of arousal (by potentiating the action of cholinergic nuclei in the midbrain reticular formation), as they also are more effective when a person is sleep-deprived (23,26,27).

Others

Glutamatergic medications such as memantine, used to treat Alzheimer's disease, may improve visual memory in healthy adults (28,29). Calcium channel blockers improve memory acquisition, possibly by affecting cerebral circulation (30,31). Insulin resistance in diabetics is correlated with age-associated cognitive decline. The antihyperglycemic medication metformin may protect against this decline in patients with diabetes and pre-diabetes (32,33). Over-the-counter drugs used for enhancement include caffeine, an adenosine receptor antagonist that increases vigilance and working memory (9); ginkgo biloba, which has been proposed to improve cognition through its antioxidant properties, though the evidence of efficacy is sparse (34,35); Bacopa monnieri, which may improve delayed word recall in older adults (36); piracetam, which has cholinergic and glutamatergic effects and has mixed evidence for enhancement efficacy (37); and curry (presumably through curcumin) which may improve Mini Mental Status Exam scores among the elderly (38). Young professionals use lysergic acid diethylamide (LSD) and psilocybin mushrooms in doses smaller than those used recreationally to augment mood, creativity, concentration, and problem-solving. This practice, known as "microdosing", is particularly popular in Silicon Valley (39,40).

Prevalence of cognitive enhancement

The prevalence of cognitive enhancement varies widely across surveys depending on the nature of the survey, the drug being used, and the survey participants (41). With this caveat in mind, enhancement appears common. Among students, reported lifetime use rates range from 5% to 40% and 18% for medical students specifically (42-48). Among professionals, 9% of surgeons, 28% of poker players, and 19% of professionals in economics report using illicit or prescription drugs for

enhancement (49-51). Adults also use pills outside of school and work to improve their cognitive performance in daily life. Most of these data are from American populations. However, 15% of German elderly adults reported using Ginkgo biloba for enhancement purposes (52).

Potential advantages

The current benefits of cognitive enhancement are unclear, and probably small

The enhancing effect of drugs on cognitive testing is inconsistent across trials, with little to no effect demonstrated in meta-analyses (15,23). Effects on more practical measures of intellectual success are also unimpressive. Stimulants, the most commonly used cognitive enhancement drugs among students, do not actually improve GPA (53). Some studies find that people on these drugs are more confident of their improved performance, even when such improvement is expressed in objective test measures (54,55).

Despite these modest results, many scientists, ethicists, and physicians are optimistic about their potential future benefits. Our improving understanding of cognitive neuroscience, the increasing prevalence of dementia in the aging population, and the need for treatments for conditions like depression, addiction and attention deficit disorder, will likely encourage the development of new and more efficacious enhancement drugs (56,57).

Benefits to the individual

Cognitive enhancement offers the promise of improved performance, enhanced learning potential, increased motivation, facilitated social interactions, better mood, and improved ability to recover from stress (58,59). Both methylphenidate and lorazepam lessen the effect of emotions on memory (60), and beta blockers prevent post-traumatic symptoms in car-crash victims (61). Perhaps these drugs can be used to dull other painful - albeit less clinically significant - memories.

Cognitive enhancement may also enhance our autonomy (62,63). Our capacity for self-determination depends on our ability to act as rational agents. Improved verbal processing strengthens our ability

to critically analyze others' claims and viewpoints, protecting us from deception. Enhanced memory gives us a more complete picture of ourselves and our world, aiding in self-reflection. And improved logical reasoning facilitates our free choice.

Cognitive enhancement may have particular utility among older adults. Aging begets expected non-pathological cognitive decline, as distinct from dementia. Vocabulary and general knowledge tend to improve as we get older, but almost all other measures of cognition, including processing speed, attention, memory, visuospatial ability, and executive function start declining as early as the third decade of life (64). Although this decline is a part of healthy aging, it can greatly impact people's lives. Many are embarrassed by increasingly frequent tip-of-the-tongue episodes when trying to remember the names of acquaintances. Difficulty performing more complex executive tasks may lead to serious errors in managing finances. And as people live longer and the retirement age increases, cognitive changes may impact the ability of older adults to flourish and keep up with their younger colleagues.

Benefits to society

Professionals such as pilots, physicians, and firefighters whose attention, reaction time, and problem-solving ability are critical for protecting the public may be able to perform their duties more safely with cognitive enhancement drugs, particularly under conditions of stress or sleep deprivation (65-68). Sleep deprived professionals can be dangerous. The case of Libby Zion, who died under the care of overworked medical residents, spurred advocacy for the regulation of resident work hours (69,70). But even today, residents routinely work 24+ continuous hours without sleep, and the current physician shortage, combined with the aging population, makes it unlikely that we will have an abundance of well-rested physicians in the near future. Given the lack of available social solutions to the physician shortage, should pharmacologic solutions be considered?

Enhancing the decision-making capacity of judges, whose decisions are less dependent on rapidilty but of equal consequence to those of physicians, may improve justice (71). Retrials prompted by judges falling asleep mid-case show us that judges are subject to fatigue no less

than physicians and pilots (72). Judges reportedly make more lenient parole decisions at the beginning of the day and immediately after lunch (73), although the non-random order of prisoners without attorney representation may be a factor in this effect (74). The use of cognitive enhancement by judges might mitigate these random influences on justice.

More intelligent and creative thinking may also enhance economic productivity and accelerate new discoveries and inventions (76). Paul Erdős, the author of over 1,000 mathematics papers, frequently used stimulants to enhance his mathematical prowess. In 1970 a friend concerned for his health bet him $500 that he couldn't stop amphetamines for a month. Erdős accepted the bet and won. However, he was frustrated by his lack of academic progress while off amphetamines, and told his friend at the end of the bet, "You've set mathematics back a month" (77).

We may also use interventions for moral enhancement. Some psychiatric disorders (most notably antisocial personality disorder) are characterized in part by a disregard for the rights of others. Therapy aimed at improving moral behavior in individuals with these disorders could be considered treatment (78). Such therapies could also apply to less pathological moral deficiencies. One method would be to alter the underlying impulses that provoke immoral behavior. Just as naltrexone is used clinically to curb cravings for alcohol, drugs might be used to mitigate violent impulses or feelings of racism (79). Conversely, we might take a pill that promotes empathy, trust, or altruism (oxytocin and SSRIs have this effect to some degree) (76,80,81). Stimulants, cholinergic agents, and other cognitive enhancers discussed above could improve our ability to reason in morally ambiguous situations, assuming we start with good motives (80,82).

Limits to our knowledge

Any discussion of the advantages and disadvantages of cognitive enhancement relies on adequate information about their efficacy and adverse effects. Unfortunately, our knowledge is limited and may remain so for the foreseeable future.

Placebo effects

A pervasive issue in trying to understand the specific effects of enhancing drugs is determining the extent of placebo effects (83,84). The belief that drugs are helpful often contributes to their demonstrable beneficial effects (85). For example, people often feel better about their performance on stimulants even when there is no measurable improvement (86). At a societal level, the greater the general belief that enhancements work, regardless of whether that belief is generated by the media or what peers say, the more likely people will experience positive effects of these medications. Such beliefs, if widespread, are likely to influence public policy regardless of limited scientific support.

Bias

Several impediments exist to research on the effects of enhancing medications in healthy people. Most funding agencies do not support such research, making systematic research programs difficult. The lack of funding and regulatory burdens prevents large multicenter randomized controlled trials. Accumulated data can be biased in fields with few researchers and small true effect sizes that might not be meaningful (87). Inadequate statistical power, hence insufficient evidence of generalizability, is an endemic problem in studies of enhancements. These studies typically enroll few participants. Often the drugs are given once, and if repeated, only for short durations. Because studies that show significant effects are more likely to be published, well-designed negative studies are not accounted for in any systematic manner. This publication bias is common in neuroscience (88). As such, reviews of this literature and various meta-analyses may overestimate the effects of currently available enhancement medications.

Ethical concerns of cognitive enhancement

Safety

Many physicians, scientists, and regulators worry that the medical risks and side effects outweigh the modest benefits of cognitive enhancement drugs. Stimulants have been subject to particular scrutiny. The established effect of stimulants on heart rate and blood pressure has caused concern

over potential cardiovascular risks, leading the FDA to issue a black box warning in 2006 for all amphetamines and methylphenidate (89,90). However, since this warning, large retrospective cohort studies have demonstrated no increased risk of cardiovascular events with the use of any ADHD drugs by young adults or children (91,92). The relative cardiovascular safety of these drugs in young adults may not apply to older people with underlying atherosclerotic and incipient cardiovascular disease.

Other potentially concerning side effects of stimulants include decreased appetite, insomnia, and irritability (93). Given the action of stimulants on the dopaminergic reward pathways, and given their similarity to drugs of abuse such as methamphetamine and cocaine, dependence and addiction are also concerns. However, prospective cohort studies have not found an increased risk of substance use disorders among people prescribed stimulants for ADHD (94,95).

These are risks of cognitive enhancement drugs when used to treat disease. We do not know the long-term effects of these drugs in *healthy* people. New, less-studied drugs present additional safety concerns (17,96). Some physicians argue that safety requirements for drugs should be more stringent when they are used for enhancement than when used to treat disease. Healthy people have less to gain and more to lose (97).

Some underscore the discrepancy between the actual and perceived benefits of cognitive enhancement (13,98). For instance, despite the lack of evidence for stimulants affecting academic performance, improving grades remains the primary reason students take stimulants (53). If the hype surrounding cognitive enhancement outstrips the science, then users may unknowingly put themselves at risk for little benefit.

Inadvertent cognitive changes and trade offs

In addition to medical risk, cognitive enhancement pills may produce unintended psychological trade-offs (99). For instance, although stimulants show some benefit for cognitive function among sleep-deprived individuals, over longer periods of sleep deprivation, stimulants increase wakefulness but *not* cognitive performance, potentially instilling overconfidence in their users (54,55). In 2003, American pilots in Afghanistan spotted ground fire that was part of a Canadian military

training exercise. Misinterpreting the exercise as hostile, the pilots - who were on amphetamines at the time to combat sleep deprivation - ignored an order to hold their fire, shooting and ultimately killing four of the Canadian soldiers. The pilots claimed that the drugs clouded their judgement (100).

Gaining function in one cognitive domain may compromise others (101,102). By activating the noradrenergic system, stimulants may aggravate test anxiety. Also, enhancing concentration might harm the unfocused thought necessary for creativity (103). There is some evidence that stimulants might impede performance on tasks that require cognitive flexibility (104). Amphetamines had no effect on overall performance on a battery of creativity tests, however there was a small negative effect among the most creative individuals (105). There are other potential trade-offs such as enhancing consolidation of long-term memories could reduce the adaptability of memory to changes in the environment (101).

Social danger

Even when cognitive enhancement works as intended, an individual's enhanced intelligence, creativity, and productivity might carry some risk to others. History offers examples (atomic bombs, biological weapons, cell phones, etc.) in which scientific progress can contribute to dangerous social results. Cognitive enhancement could potentially accelerate the development of harmful inventions. Of course, this risk exists with *any* intervention that improves intelligence, including basic education, but we consider the benefits of these cultural forms of enhancement to outweigh the risks. Some philosophers suggest that the solution to the dangers of cognitive enhancement - both cultural and pharmaceutical - is the development of moral enhancement as discussed above, and cautioned against cognitive enhancement that does not go hand in hand with moral enhancement (76).

Enhancement versus treatment

Cosmetic neurology, like cosmetic surgery, deviates from medicine's traditional goal of treating disease (106). One can question the importance of the treatment-enhancement distinction with a thought experiment. Imagine two equally short children - one afflicted with growth hormone

deficiency and the other with short parents - who both want access to growth hormone pills. Although growth hormones would be treatment in the first child and enhancement in the second, the practical effects of the pills would be identical in both children. By extension, why differentiate between cognitive treatment and cognitive enhancement (107)?

The treatment-enhancement distinction is particularly ambiguous in age-associated cognitive changes. Although age-related cognitive decline is not considered pathological, its mechanisms, and more importantly its results, are similar to those of disease-related cognitive decline. Whereas cognitive enhancement is generally aimed at enhancing a person's baseline, in the elderly cognitive enhancement seeks to restore function to a prior baseline. Some argue that the enhancement-restoration distinction is morally relevant and makes cognitive enhancement more permissible in the elderly than in young people (108). However, as mentioned earlier, the potential risk of adverse effects also likely increases among the elderly complicating an individual's decision to take advantage of current available enhancement medications.

Inauthentic pills

A major criticism of cognitive enhancement pills in surveys of public opinion is that drugs are unnatural. The public is generally more accepting of vitamins, caffeine, and other natural supplements than they are of pharmaceuticals (109). Even when the same enhancing substance is considered, people find it more morally acceptable if it is delivered by pill than by injection (110). Pills are also considered less acceptable than non-pharmacological cognitive enhancement (such as exercise or computer training) (111). Safety explains some of the difference, as people perceive pharmacological cognitive enhancement to be less safe than natural supplements (112). The bias against pharmaceuticals may depend on familiarity with the industry. A survey of medical students found no difference in acceptability between the use of pharmaceuticals and natural supplements for enhancement (113).

Inauthentic achievements

Achievements with the aid of cognitive enhancement may be interpreted as inauthentic, even cheating in competitive contexts such

as standardized tests (114). As with the use of calculators in school and specialized gear in athletics, "cheating" is defined by the pre-established rules of the game. So cognitive enhancement is only cheating if schools and other regulators say so. Regardless of how we define cheating, if a student, aided by a pill, does well on a test, then the pill arguably cheapens the success. But what if the pill is taken one month prior to the test, and the pill allows the student to study harder and retain more information? What if they take the pill years before the test, and the pill heightens their intelligence in a lasting way, making the test accurately reflect their newfound intelligence? Some argue that this intelligence is itself inauthentic, as it is the result of neither inborn potential nor hard work, discussed further below (115).

Inauthentic selves

Will cognitive enhancement drugs erode our character by enabling intelligence through easier means ("gain without pain") (116)? Every new development that improves quality of life, from anesthesia to air conditioning, could also be argued to reduce character-building suffering. Yet we generally accept these convenient technologies (59). But perhaps altering our intelligence rather than just our room temperature poses a greater risk to the human essence (106). The President's Council on Bioethics opined in 2003 that using unnatural means to change our thinking risks "flattening our souls" (117). This discussion encroaches upon concepts that vary across different individuals, cultures, and religions, making it challenging to definitively argue that human essence is harmed or not by cognitive enhancement (115). The notion of changing ourselves through education, religion, travel, or even pills is not new or necessarily bad. Some describe experiences with psychedelic drugs that produced positive changes in their sense of self (118). If it is acceptable to alter personhood with these external agents, then why not with cognitive enhancement?

Coercion

The potential use of cognitive enhancement for competition raises the question of whether the decision to use cognitive enhancement can be undertaken freely. If a student's peers are taking cognitive enhancement drugs, then the student may feel compelled to take drugs to level the

playing field. As people age, they might feel pressure to enhance their cognition to keep up with or compete with younger workers, especially in a technologically changing and challenging workplace. On the other hand, any method of self-improvement - including learning to read - risks social coercion for similar reasons (115). Social pressure to enhance oneself is not problematic in itself. But if cognitive enhancement is bad for *other* reasons, then the potential for coercion makes it even worse.

In addition to implicit pressures to keep pace with others, employers could explicitly demand that employees take pills to improve their performance. This is not a remote concern: in the case of friendly fire on Canadian soldiers in Afghanistan, the American pilots claimed that they felt compelled by their superiors to use amphetamines or be dismissed from the mission (100). This explicit coercion could be legislated against, although such legislation may have limited practical effect. It would be hard to prove that an employer gave unequal treatment because of an employee's unwillingness to use cognitive enhancement (119). Explicit pressure might also arise in situations where benefits to the group might outweigh the rights of an individual. For example, should post-call medical residents be required to take drugs that counter errors made more likely by fatigue and sleep deprivation? Do physicians have a moral responsibility to use enhancements (120).

Unequal access

Cognitive enhancement may produce injustice through unequal access. Inequality is not inevitable: if cognitive enhancement were freely available to the public, it might mitigate rather than exacerbate inequalities by creating cognitive opportunities for the socially disadvantaged (121). This optimistic possibility contrasts with the current social reality, particularly in the US, in which opportunities are disproportionately available to the wealthy. Where cognitive enhancement is available for pay, economic advantages become cognitive advantages (115).

Children and adolescents

Children and adolescents are a special case. On the one hand, their developing brains stand to benefit more from the effects of enhancing pills on neuroplasticity. However, this window of development also puts them

at greater risk. It is also unclear who should decide which children receive cognitive enhancement. Should a particular parents' wishes determine if a child is exposed to the potential risks and benefits of cognitive enhancement drugs? On the other hand, leaving the decision to the state would conflict with parents' autonomy over raising their children. Citing these special concerns, the American Academy of Neurology issued guidance opposing cognitive enhancement for children (122).

Social considerations

Inevitability

Regardless of the debate in the literature, cognitive enhancement is to some degree inevitable (31,123). A recent Netflix Documentary released in March, 2018, recounts the current widespread use of cognitive enhancement among students and workers in some sectors (124). The widespread use of prescription stimulants on college campuses suggests that banning cognitive enhancement is practically impossible. It would be even more challenging to ban the use of over-the-counter medications for cognitive enhancement, as these are readily available to anyone. And if we did try to prohibit the use of over-the-counter medications for cognitive enhancement, where would we draw the line? If we ban ginkgo biloba, why not coffee?

Given that banning cognitive enhancement would be difficult (and not clearly desirable), sociologists have turned their attention toward public policy that might foster responsible use. Universities that oppose cognitive enhancement could establish a social norm against it by defining cognitive enhancement in their honor codes as cheating (125). We may be able to regulate cognitive enhancement drugs similarly to other legal non-prescription psychoactive drugs, such as nicotine and alcohol, with taxes, limited distribution, and age restrictions. However, as with alcohol and nicotine, this would not preclude abuses within or outside the legal system (126). We could even license cognitive enhancement, requiring users to demonstrate an understanding of the risks before being allowed to purchase drugs. But, counterproductively, this would discourage those who have less cognitive capacity and thus could benefit the most from cognitive enhancement from pursuing it (115).

Public opinion

Cultural norms about the use of enhancements have not coalesced into a consensus. Attitudes about enhancement are influenced by cultural contexts that vary (127). Physicians, who would do the prescribing, may need to think beyond traditional disease models of care (1,128–130). Physicians are typically pragmatic about prescribing enhancements, but also ambivalent, viewing the practice as alleviating suffering while being wary of exaggerating social inequities (131,132). Approaching enhancement as a public health issue may advance the discussion (133).

Clinical neuroscientists and ethicists can lay the groundwork for broader public discussions. As of now, academics do not agree (134). Some regard the ethical concerns as exaggerated or ill-conceived (98,135). The attitude among the public also varies. Most of our information comes from surveys of young people who show a divide between those who use enhancers and those who do not (136). Non-users more than users are concerned about medical safety and questions of fairness. Generally, both users and non-users think that the decision to use enhancements is a matter of personal choice and oppose formal coercive policies, such as requiring use of enhancements in high performance jobs (e.g., physicians, pilots).

Involving the public in the debate on cognitive enhancement is essential. First, it advances the ethical discussion: the public offers a diverse array of moral viewpoints and may anticipate future ethical considerations. Involving the public also prevents physicians, scientists, and ethicists from operating in isolation from the population they serve. Understanding which elements of cognitive enhancement the public finds acceptable and which they find morally concerning can help guide the development of cognitive enhancement drugs and shape socially conscious public policy. Many surveys, interviews, and focus groups that gather opinion regarding cognitive enhancement, demonstrate considerable variability in respondents' opinions but largely reflecting the concerns raised by ethicists (136-147). One limitation of these studies is that they typically query students and primarily asked about the student use of cognitive enhancement. Involving the larger public and addressing use in and out of the workplace will reveal a broader range of opinions toward the growing public use of cognitive enhancement.

Acknowledgment

This essay is adapted from a chapter titled, *Pharmacological Cosmetic Neurology*, to appear in **Cognitive Changes and the Aging Brain**, Heilman KM, Nadeau S (eds), Cambridge University Press.

References

1. Chatterjee A. Cosmetic neurology: The controversy over enhancing movement, mentation, and mood. Neurology. 2004;63(6):968-74.

2. Chatterjee A. Cosmetic neurology and cosmetic surgery: parallels, predictions, and challenges. Cambridge Quarterly of Healthcare Ethics. 2007;16(2):129-37.

3. Haiken E. Venus envy: a history of cosmetic surgery. Baltimore, Maryland: The Johns Hopkins University Press; 1997.

4. Snelders S, Pieters T. Speed in the Third Reich: metamphetamine (Pervitin) use and a drug history from below. Soc Hist Med. 2011;24(3):686–99.

5. Vearrier D, Greenberg MI, Miller SN, Okaneku JT, Haggerty DA. Methamphetamine: history, pathophysiology, adverse health effects, current trends, and hazards associated with the clandestine manufacture of methamphetamine. Disease-a-Month. 2012 Feb;58(2):38-89.

6. Steinkamp P. Pervitin (methamphetamine) tests, use and misuse in the German Wehrmacht. In: Eckart WU, editor. Man, Medicine, and the State: the Human Body as an Object of Government Sponsored Medical Research in the 20th Century. Stuttgart: Steiner; 2006. p. 61-71.

7. Husain M, Mehta MA. Cognitive enhancement by drugs in health and disease. Trends Cogn Sci. 2011 Jan;15(1):28-36.

8. Sostek AJ, Buchsbaum MS, Rapoport JL. Effects of amphetamine on vigilance performance in normal and hyperactive children. J Abnorm Child Psychol. 1980 Dec;8(4):491-500.

9. Koelega HS. Stimulant drugs and vigilance performance: a review. Psychopharmacology. 1993;111(1):1-16.

10. Pigeau R, Naitoh P, Buguet A, McCann C, Baranski J, Taylor M, et al. Modafinil, d-amphetamine and placebo during 64 hours of sustained mental work. I. Effects on mood, fatigue, cognitive performance and body temperature. J Sleep Res. 1995;4(4):212-28.

11. Baranski JV, Pigeau R, Dinich P, Jacobs I. Effects of modafinil on cognitive and meta-cognitive performance. Human Psychopharmacology: Clinical and Experimental. 2004 Jul;19(5):323-32.

12. Elliott R, Sahakian BJ, Matthews K, Bannerjea A, Rimmer J, Robbins TW. Effects of methylphenidate on spatial working memory and planning in healthy young adults. Psychopharmacology. 1997 May;131(2):196-206.

13. Bagot KS, Kaminer Y. Efficacy of stimulants for cognitive enhancement in non-attention deficit hyperactivity disorder youth: a systematic review. Addiction. 2014 Apr;109(4):547-57.

14. Breitenstein C, Wailke S, Bushuven S, Kamping S, Zwitserlood P, Ringelstein EB, et al. D-amphetamine boosts language learning independent of its cardiovascular and motor arousing effects. Neuropsychopharmacology. 2004 Sep;29(9):1704-14.

15. Repantis D, Schlattmann P, Laisney O, Heuser I. Modafinil and methylphenidate for neuroenhancement in healthy individuals: A systematic review. Pharmacol Res. 2010 Sep;62(3):187-206.

16. Franke AG, Gränsmark P, Agricola A, Schühle K, Rommel T, Sebastian A, et al. Methylphenidate, modafinil, and caffeine for cognitive enhancement in chess: A double-blind, randomised controlled trial. Eur Neuropsychopharmacol. 2017 Mar;27(3):248-60.

17. Franke AG, Lieb K. Pharmacological neuroenhancement: substances and epidemiology. In: Hildt E, Franke AG, editors. Cognitive Enhancement: An Interdisciplinary Perspective. Dordrecht, Netherlands: Springer Netherlands; 2013. p. 17-27.

18. Fond G, Micoulaud-Franchi J-A, Brunel L, Macgregor A, Miot S, Lopez R, et al. Innovative mechanisms of action for pharmaceutical cognitive enhancement: A systematic review. Psychiatry Res. 2015;229(1):12-20.

19. Winblad B, Engedal K, Soininen H, Verhey F, Waldemar G, Wimo A, et al. A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD. Neurology. 2001 Aug 14;57(3):489-95.

20. Wesnes KA, McKeith IG, Ferrara R, Emre M, Del Ser T, Spano PF, et al. Effects of rivastigmine on cognitive function in dementia with lewy bodies: a randomised placebo-controlled international study using the cognitive drug research computerised assessment system. Dement Geriatr Cogn Disord. 2002;13(3):183-92.

21. Rowan E, McKeith IG, Saxby BK, O'Brien JT, Burn D, Mosimann U, et al. Effects of donepezil on central processing speed and attentional measures in Parkinson's disease with dementia and dementia with Lewy bodies. Dement Geriatr Cogn Disord. 2007;23(3):161-7.

22. Ferreira-Vieira TH, Guimaraes IM, Silva FR, Ribeiro FM. Alzheimer's disease: Targeting the Cholinergic System. Curr Neuropharmacol. 2016;14(1):101-15.

23. Repantis D, Laisney O, Heuser I. Acetylcholinesterase inhibitors and memantine for neuroenhancement in healthy individuals: a systematic review. Pharmacol Res. 2010 Jun;61(6):473-81.

24. FitzGerald DB, Crucian GP, Mielke JB, Shenal BV, Burks D, Womack KB, et al. Effects of donepezil on verbal memory after semantic processing in healthy older adults. Cogn Behav Neurol. 2008 Jun;21(2):57-64.

25. Yesavage JA, Mumenthaler MS, Taylor JL, Friedman L, O'Hara R, Sheikh J, et al. Donepezil and flight simulator performance: effects on retention of complex skills. Neurology. 2002 Jul 9;59(1):123-5.

26. Chuah LYM, Chee MWL. Cholinergic augmentation modulates visual task performance in sleep-deprived young adults. J Neurosci. 2008 Oct 29;28(44):11369-77.

27. Chuah LYM, Chong DL, Chen AK, Rekshan WR 3rd, Tan J-C, Zheng H, et al. Donepezil improves episodic memory in young individuals vulnerable to the effects of sleep deprivation. Sleep. 2009 Aug;32(8):999-1010.

28. Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ. Memantine in moderate-to-severe Alzheimer's disease. N Engl J Med. 2003 Apr 3;348(14):1333-41.

29. Rammsayer TH. Effects of pharmacologically induced changes in NMDA-receptor activity on long-term memory in humans. Learn Mem. 2001;8(1):20-5.

30. Watfa G, Rossignol P, Kearney-Schwartz A, Fay R, Bracard S, Felblinger J, et al. Use of calcium channel blockers is associated with better cognitive performance in older hypertensive patients with subjective memory complaints. J Hypertens. 2010 Dec;28(12):2485-93.

31. Rose SPR. "Smart drugs": do they work? Are they ethical? Will they be legal? Nat Rev Neurosci. 2002 Dec;3(12):975-9.

32. Ng TP, Feng L, Yap KB, Lee TS, Tan CH, Winblad B. Long-term metformin usage and cognitive function among older adults with diabetes. J Alzheimers Dis. 2014;41(1):61-8.

33. Luchsinger JA, Ma Y, Christophi CA, Florez H, Golden SH, Hazuda H, et al. Metformin, Lifestyle Intervention, and Cognition in the Diabetes Prevention Program Outcomes Study. Diabetes Care. 2017 Jul;40(7):958-65.

34. Solomon PR, Adams F, Silver A, Zimmer J, DeVeaux R. Ginkgo for memory enhancement: a randomized controlled trial. JAMA. 2002 Aug 21;288(7):835-40.

35. Birks J, Grimley Evans J. Ginkgo biloba for cognitive impairment and dementia. Cochrane Database Syst Rev. 2007;2:CD003120.

36. Calabrese C, Gregory WL, Leo M, Kraemer D, Bone K, Oken B. Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial. J Altern Complement Med. 2008 Jul;14(6):707-13.

37. Flicker L, Evans JG. Piracetam for dementia or cognitive impairment. Cochrane Database Syst Rev. 2001;2:CD001011.

38. Ng T-P, Chiam P-C, Lee T, Chua H-C, Lim L, Kua E-H. Curry consumption and cognitive function in the elderly. Am J Epidemiol. 2006 Nov 1;164(9):898-906.

39. Solon O. Meet the Silicon Valley-ites taking tiny hits of LSD to boost performance. Wired. 2016 Aug 24.

40. Johnstad PG. Powerful substances in tiny amounts: An interview study of psychedelic microdosing. Nordic Studies on Alcohol and Drugs. 2018;35(1):39-51.

41. Franke AG, Bagusat C, Rust S, Engel A, Lieb K. Substances used and prevalence rates of pharmacological cognitive enhancement among healthy subjects. Eur Arch Psychiatry Clin Neurosci. 2014 Nov;264(Suppl 1): S83-90.

42. Singh I, Bard I, Jackson J. Robust resilience and substantial interest: a survey of pharmacological cognitive enhancement among university students in the UK and Ireland. PLoS One. 2014 Oct 30;9(10): e105969.

43. Dietz P, Striegel H, Franke AG, Lieb K, Simon P, Ulrich R. Randomized response estimates for the 12-month prevalence of cognitive-enhancing drug use in university students. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2013 Jan;33(1):44-50.

44. Babcock Q, Byrne T. Student perceptions of methylphenidate abuse at a public liberal arts college. J Am Coll Health. 2000 Nov;49(3):143-5.

45. McCabe SE, Knight JR, Teter CJ, Wechsler H. Non-medical use of prescription stimulants among US college students: prevalence and correlates from a national survey. Addiction. 2005 Jan;100(1):96-106.

46. Arria AM, O'Grady KE, Caldeira KM, Vincent KB, Wish ED. Nonmedical use of prescription stimulants and analgesics: associations with social and academic behaviors among college students. J Drug Issues. 2008;38(4):1045-60.

47. Arria AM, Wilcox HC, Caldeira KM, Vincent KB, Garnier-Dykstra LM, O'Grady KE. Dispelling the myth of "smart drugs": cannabis and alcohol use problems predict nonmedical use of prescription stimulants for studying. Addict Behav. 2013 Mar;38(3):1643-50.

48. Emanuel RM, Frellsen SL, Kashima KJ, Sanguino SM, Sierles FS, Lazarus CJ. Cognitive enhancement drug use among future physicians: findings from a multi-institutional census of medical students. J Gen Intern Med. 2013 Aug;28(8):1028-34.

49. Franke AG, Bagusat C, Dietz P, Hoffmann I, Simon P, Ulrich R, et al. Use of illicit and prescription drugs for cognitive or mood enhancement among surgeons. BMC Med. 2013 Apr 9;11(1):102.

50. Caballero J, Ownby RL, Rey JA, Clauson KA. Cognitive and performance enhancing medication use to improve performance in poker. J Gambl Stud. 2016 Sep;32(3):835-45.

51. Dietz P, Soyka M, Franke AG. Pharmacological neuroenhancement in the field of economics-poll results from an online survey. Front Psychol. 2016 Apr 19;7: 520.

52. Franke AG, Heinrich I, Lieb K, Fellgiebel A. The use of Ginkgo biloba in healthy elderly. Age. 2014;36(1):435-44.

53. Arria AM, Caldeira KM, Vincent KB, O'Grady KE, Cimini MD, Geisner IM, et al. Do college students improve their grades by using prescription stimulants nonmedically? Addict Behav. 2017 Feb;65:245-9.

54. Baranski JV, Pigeau RA. Self-monitoring cognitive performance during sleep deprivation: effects of modafinil, d-amphetamine and placebo. J Sleep Res. 1997 Jun;6(2):84-91.

55. Sharp C. Cognitive enhancers--performance or problem? Occup Med. 2016 Mar;66(2):88-9.

56. Dekkers W, Rikkert MO. Memory enhancing drugs and Alzheimer's Disease: enhancing the self or preventing the loss of it? Med Health Care Philos. 2007;10(2):141-51.

57. Arce E, Ehlers MD. The mind bending quest for cognitive enhancers. Clinical Pharmacology & Therapeutics. 2017;101(2):179-81.

58. Brand R, Wolff W, Ziegler M. Drugs as instruments: describing and testing a behavioral approach to the study of neuroenhancement. Front Psychol. 2016 Aug 17;7:1226.

59. Chatterjee A. Framing pains, pills, and professors. Expositions. 2008;2(2):139-46.

60. Brignell CM, Rosenthal J, Curran HV. Pharmacological manipulations of arousal and memory for emotional material: effects of a single dose of methylphenidate or lorazepam. J Psychopharmacol. 2007 Sep;21(7):673-83.

61. Pitman RK, Sanders KM, Zusman RM, Healy AR, Cheema F, Lasko NB, et al. Pilot study of secondary prevention of posttraumatic stress disorder with propranolol. Biol Psychiatry. 2002 Jan 15;51(2):189-92.

62. Clewis RR. Does Kantian ethics condone mood and cognitive enhancement? Neuroethics. 2017;10(3):349-61.

63. Schaefer GO, Kahane G, Savulescu J. Autonomy and enhancement. Neuroethics. 2014;7(2):123-36.

64. Harada CN, Love MCN, Triebel KL. Normal cognitive aging. Clin Geriatr Med. 2013 Nov;29(4):737-52.

65. English V, Sommerville A. Boosting your brainpower, ethical aspects of cognitive enhancements: a discussion paper. London, United Kingdom: British Medical Association; 2007. 42 p.

66. Lucke J, Partridge B. Towards a smart population: a public health framework for cognitive enhancement. Neuroethics. 2013;6(2):419-27.

67. Maslen H, de Sio FS, Faber N. With cognitive enhancement comes great responsibility? In: Koops B-J, Ilse O, Romijn H, Swierstra T, van den Hoven J, editors. Responsible Innovation 2. Switzerland: Springer International Publishing; 2015. p. 121-38.

68. Batéjat DM, Lagarde DP. Naps and modafinil as countermeasures for the effects of sleep deprivation on cognitive performance. Aviat Space Environ Med. 1999 May;70(5):493-8.

69. Lerner BH. A case that shook medicine. The Washington Post. 2006 Nov 28;

70. Lerner BH. A life-changing case for doctors in training. The New York Times. 2009 Mar 3;

71. Chandler JA, Dodek AM. Cognitive enhancement in the courtroom. In: Jotterand F, Dubljevic V, editors. Cognitive Enhancement: Ethical and Policy Implications in International Perspectives. New York: Oxford University Press; 2016. p. 329-45.

72. Grunstein RR, Banerjee D. The case of "Judge Nodd" and other sleeping judges—media, society, and judicial sleepiness. Sleep. 2007;30(5):625-32.

73. Danziger S, Levav J, Avnaim-Pesso L. Extraneous factors in judicial decisions. Proc Natl Acad Sci. 2011 Apr 26;108(17):6889-92.

74. Weinshall-Margel K, Shapard J. Overlooked factors in the analysis of parole decisions. Proc Natl Acad Sci U S A. 2011 Oct 18;108(42):E833.

75. Rachlinski JJ, Johnson SL, Wistrich AJ, Guthrie C. Does unconscious bias affect trial judges? Notre Dame Law Review. 2009;84(3):1195-246.

76. Persson I, Savulescu J. The perils of cognitive enhancement and the urgent imperative to enhance the moral character of humanity. J Appl Philos. 2008;25(3):162-77.

77. Hoffman P. The man who loved only numbers: the story of Paul Erdos and the search for mathematical truth. New York, New York: Hyperion; 1998. 301 p.

78. Carter S. Could moral enhancement interventions be medically indicated? Health Care Anal. 2017 Dec;25(4):338-53.

79. Douglas T. Moral enhancement. J Appl Philos. 2008 Aug;25(3):228-45.

80. Shook JR. Neuroethics and the possible types of moral enhancement. AJOB Neurosci. 2012;3(4):3-14.

81. Ahlskog R. Moral enhancement should target self-interest and cognitive capacity. Neuroethics. 2017 Apr 26;10(3):363-73.

82. Harris J. Moral enhancement and freedom. Bioethics. 2010;25(2):102-11.

83. Kirsch I. The emperor's new drugs: exploding the antidepressant myth. UK: The Random House Group; 2009.

84. Rutherford BR, Mori S, Sneed JR, Pimontel MA, Roose SP. Contribution of spontaneous improvement to placebo response in depression: a meta-analytic review. J Psychiatr Res. 2012 Jun;46(6):697-702.

85. Benedetti F. Mechanisms of placebo and placebo-related effects across diseases and treatments. Annu Rev Pharmacol Toxicol. 2008;48:33-60.

86. Ilieva I, Boland J, Farah MJ. Objective and subjective cognitive enhancing effects of mixed amphetamine salts in healthy people. Neuropharmacology. 2013 Jan;64:496-505.

87. Ioannidis JPA. Why most published research findings are false. PLoS Med. 2005 Aug;2(8):e124.

88. Button KS, Ioannidis JPA, Mokrysz C, Nosek BA, Flint J, Robinson ESJ, et al. Power failure: why small sample size undermines the reliability of neuroscience. Nat Rev Neurosci. 2013 May;14(5):365-76.

89. Wilens TE, Hammerness PG, Biederman J, Kwon A, Spencer TJ, Clark S, et al. Blood pressure changes associated with medication treatment of adults with attention-deficit/hyperactivity disorder. J Clin Psychiatry. 2005 Feb;66(2):253-9.

90. Nissen SE. ADHD drugs and cardiovascular risk. N Engl J Med. 2006;354(14):1445-8.

91. Habel LA, Cooper WO, Sox CM, Arnold Chan K, Fireman BH, Arbogast PG, et al. ADHD medications and risk of serious cardiovascular events in young and middle-aged adults. JAMA. 2011;306(24):2673-83.

93. Cooper WO, Habel LA, Sox CM, Arnold Chan K, Arbogast PG, Craig Cheetham T, et al. ADHD drugs and serious cardiovascular events in children and young adults. N Engl J Med. 2011;365(20):1896-904.

93. Busardò FP, Kyriakou C, Cipolloni L, Zaami S, Frati P. From clinical application to cognitive enhancement: the example of methylphenidate. Curr Neuropharmacol. 2016;14(1):17-27.

94. Biederman J, Monuteaux MC, Spencer T, Wilens TE, Macpherson HA, Faraone SV. Stimulant therapy and risk for subsequent substance use disorders in male adults with ADHD: a naturalistic controlled 10-year follow-up study. Am J Psychiatry. 2008 May;165(5):597-603.

95. Barkley RA, Fischer M, Smallish L, Fletcher K. Does the treatment of attention-deficit/hyperactivity disorder with stimulants contribute to drug use/abuse? A 13-year prospective study. Pediatrics. 2003 Jan;111(1):97-109.

96. Brühl AB, Sahakian BJ. Drugs, games, and devices for enhancing cognition: implications for work and society. Ann N Y Acad Sci. 2016 Apr;1369(1):195-217.

97. Banjo OC, Nadler R, Reiner PB. Physician attitudes towards pharmacological cognitive enhancement: safety concerns are paramount. PLoS One. 2010 Dec 14;5(12):e14322.

98. Partridge BJ, Bell SK, Lucke JC, Yeates S, Hall WD. Smart drugs "as common as coffee": media hype about neuroenhancement. PLoS One. 2011 Nov 30;6(11):e28416.

99. Schermer M. Changes in the self: the need for conceptual research next to empirical research. Am J Bioeth. 2009 May;9(5):45-7.

100. Shanker T, Duenwald M. THREATS AND RESPONSES: MILITARY; Bombing Error Puts a Spotlight On Pilots' Pills. New York Times. 2003 Jan 19;

101. Schermer M, Bolt I, de Jongh R, Olivier B. The future of psychopharmacological enhancements: expectations and policies. Neuroethics. 2009;2(2):75-87.

102. Davis NJ. A taxonomy of harms inherent in cognitive enhancement. Front Hum Neurosci. 2017 Feb 14;11.

103. Heilman KM, Nadeau SE, Beversdorf DO. Creative innovation: possible brain mechanisms. Neurocase. 2003 Oct;9(5):369-79.

104. Beversdorf DQ, Hughes JD, Steinberg BA, Lewis LD, Heilman KM. Noradrenergic modulation of cognitive flexibility in problem solving. Neuroreport. 1999 Sep 9;10(13):2763-7.

105. Farah MJ, Haimm C, Sankoorikal G, Smith ME, Chatterjee A. When we enhance cognition with Adderall, do we sacrifice creativity? A preliminary study. Psychopharmacology. 2009 Jan;202(1-3):541-7.

106. Fukuyama F. Our posthuman future: consequences of the biotechnology revolution. New York, New York: Farrar, Straus and Giroux; 2002. 272 p.

107. Daniels N. Normal functioning and the treatment-enhancement distinction. Camb Q Healthc Ethics. 2000 Summer;9(3):309-22.

108. Reiner PB. Distinguishing between restoration and enhancement in neuropharmacology. Virtual Mentor. 2010 Nov 1;12(11):885-8.

109. Caviola L, Faber NS. Pills or push-ups? Effectiveness and public perception of pharmacological and non-pharmacological cognitive enhancement. Frontiers in psychology. 2015;6:1852.

110. Scheske C, Schnall S. The ethics of "smart drugs": moral judgments about healthy people's use of cognitive-enhancing drugs. Basic Appl Soc Psych. 2012;34(6):508–15.

111. Specker J, Schermer MHN, Reiner PB. Public attitudes towards moral enhancement. Evidence that means matter morally. Neuroethics. 2017 Jul 27;10(3):405-17.

112. Bergström LS, Lynöe N. Enhancing concentration, mood and memory in healthy individuals: an empirical study of attitudes among general practitioners and the general population. Scand J Public Health. 2008 Jul;36(5):532-7.

113. Kudlow PA, Naylor KT, Xie B, McIntyre RS. Cognitive enhancement in Canadian medical students. J Psychoactive Drugs. 2013 Sep;45(4):360-5.

114. Greely H, Sahakian B, Harris J, Kessler RC, Gazzaniga M, Campbell P, et al. Towards responsible use of cognitive-enhancing drugs by the healthy. Nature. 2008;456(7223):702-5.

115. Bostrom N, Sandberg A. Cognitive enhancement: methods, ethics, regulatory challenges. Sci Eng Ethics. 2009 Sep;15(3):311-41.

116. Kass LR. Ageless bodies, happy souls: biotechnology and the pursuit of perfection. The New Atlantis. 2003 Spring;1(1):9-28.

117. President's Council on Bioethics (U.S.), Kass L. Beyond therapy: biotechnology and the pursuit of happiness. New York, New York: Harper Perennial; 2003. 352 p.

118. Elliot C. American bioscience meets the American dream. Am Prospect. 2003;14(6):38.

119. Appel JM. When the boss turns pusher: a proposal for employee protections in the age of cosmetic neurology. J Med Ethics. 2008 Aug;34(8):616-8.

120. Enck GG. Pharmaceutical enhancement and medical professionals. Med Health Care Philos. 2014 Feb;17(1):23-8.

121. Ray KS. Not just "study drugs" for the rich: stimulants as moral tools for creating opportunities for socially disadvantaged students. Am J Bioeth. 2016;16(6):29-38.

122. Graf WD, Nagel SK, Epstein LG, Miller G, Nass R, Larriviere D. Pediatric neuroenhancement: ethical, legal, social, and neurodevelopmental implications. Neurology. 2013 Mar 26;80(13):1251-60.

123. Cakic V. Smart drugs for cognitive enhancement: ethical and pragmatic considerations in the era of cosmetic neurology. J Med Ethics. 2009 Oct;35(10):611-5.

124. Klayman A. Take your pills. USA: Netflix; 2018.

125. Sattler S, Sauer C, Mehlkop G, Graeff P. The rationale for consuming cognitive enhancement drugs in university students and teachers. PLoS One. 2013 Jul 17;8(7):e68821.

126. Lucke J, Partridge B, Forlini C, Racine E. Using neuropharmaceuticals for cognitive enhancement: policy and regulatory issues. In: Clausen J, Levy N, editors. Handbook of Neuroethics. Netherlands: Springer Netherlands; 2014. p. 1085-100.

127. Shook JR, Galvagni L, Giordano J. Cognitive enhancement kept within contexts: neuroethics and informed public policy. Front Syst Neurosci. 2014 Dec 5;8:228.

128. Synofzik M. Ethically justified, clinically applicable criteria for physician decision-making in psychopharmacological enhancement. Neuroethics. 2009;2(2):89-102.

129. Bostrom N. Drugs can be used to treat more than disease. Nature. 2008;451(7178):520-520.

130. Ravelingien A, Braeckman J, Crevits L, De Ridder D, Mortier E. "Cosmetic neurology" and the moral complicity argument. Neuroethics. 2009;2(3):151-62.

131. Ott R, Lenk C, Miller N, Neuhaus Bühler R, Biller-Andorno N. Neuroenhancement - perspectives of Swiss psychiatrists and general practitioners. Swiss Med Wkly. 2012 Nov 27;142:w13707.

132. Hotze TD, Shah K, Anderson EE, Wynia MK. "Doctor, would you prescribe a pill to help me … ?" a national survey of physicians on using medicine for human enhancement. Am J Bioeth. 2011 Jan;11(1):3-13.

133. Outram SM, Racine E. Developing public health approaches to cognitive enhancement: an analysis of current reports. Public Health Ethics. 2011;4(1):93-105.

134. Heinz A, Kipke R, Heimann H, Wiesing U. Cognitive neuroenhancement: false assumptions in the ethical debate. J Med Ethics. 2012 Jun;38(6):372-5.

135 Zohny H. The myth of cognitive enhancement drugs. Neuroethics. 2015;8(3):257-69.

136. Schelle KJ, Faulmüller N, Caviola L, Hewstone M. Attitudes toward pharmacological cognitive enhancement-a review. Front Syst Neurosci. 2014 Apr 17;8:53.

137. Bell S, Partridge B, Lucke J, Hall W. Australian university students' attitudes towards the acceptability and regulation of pharmaceuticals to improve academic performance. Neuroethics. 2013;6(1):197-205.

138. Aikins RD. Academic performance enhancement: a qualitative study of the perceptions and habits of prescription stimulant–using college students. J Coll Stud Dev. 2011;52(5):560-76.

139. Desantis AD, Hane AC. "Adderall is definitely not a drug": justifications for the illegal use of ADHD stimulants. Subst Use Misuse. 2010;45(1-2):31-46.

140. Dodge T, Williams KJ, Marzell M, Turrisi R. Judging cheaters: is substance misuse viewed similarly in the athletic and academic domains? Psychol Addict Behav. 2012 Sep;26(3):678-82.

141. Fitz NS, Nadler R, Manogaran P, Chong EWJ, Reiner PB. Public attitudes toward cognitive enhancement. Neuroethics. 2014;7(2):173-88.

142. Franke AG, Bonertz C, Christmann M, Engeser S, Lieb K. Attitudes toward cognitive enhancement in users and nonusers of stimulants for cognitive enhancement: a pilot study. AJOB Prim Res. 2012;3(1):48-57.

143. Franke AG, Lieb K, Hildt E. What users think about the differences between caffeine and illicit/prescription stimulants for cognitive enhancement. PLoS One. 2012;7(6):e40047.

144. Partridge B, Bell S, Lucke J, Hall W. Australian university students' attitudes towards the use of prescription stimulants as cognitive enhancers: Perceived patterns of use, efficacy and safety. Drug Alcohol Rev. 2013;32(3):295-302.

145. Partridge B, Lucke J, Hall W. A comparison of attitudes toward cognitive enhancement and legalized doping in sport in a community sample of Australian adults. AJOB Prim Res. 2012;3(4):81-6.

146. Sabini J, Monterosso J. Judgments of the fairness of using performance enhancing drugs. Ethics Behav. 2005;15(1):81-94.

147. Sattler S, Forlini C, Racine É, Sauer C. Impact of contextual factors and substance characteristics on perspectives toward cognitive enhancement. PLoS One. 2013;8(8):e71452.

COGNITIVE ENHANCEMENT AND DOPING IN SPORT

Jean-Noël Missa *

This paper is intended as a contribution to the debate on the future of sport, confronted as it is with the problem of doping (including cognitive doping). Even assuming that doping-free competitive sport is preferable to sport which tolerates certain forms of doping subject to medical supervision, the soundness of the policy currently pursued by the World Anti-Doping Agency (WADA) and international sports authorities is open to question. The relative ineffectiveness of anti-doping controls raises serious ethical and sports justice issues. A very large number of doped athletes manage to slip through the anti-doping net. As a result, the two main aims of WADA's policy – to enable athletes to compete on a level playing field and to eradicate doping – are not achieved[1]. The problem is a structural one. The anti-doping policy implemented by WADA since 1999 may be regarded as a large-scale social experiment. Nearly 15 years on, it is time to take stock of this experiment and determine whether the current policy of prohibition is the best approach to reducing the harmful effects of doping. Recent cases show that doping is endemic to some sporting disciplines such as cycling. The investigation by USADA into Lance Armstrong's US Postal team shows that, in the early 2000s, most cyclists competing in the Tour de France were using prohibited substances. From our point of view, the important thing, therefore, is to look at doping in sport from a pragmatic standpoint, based on an ethics of consequences. From an ethical standpoint, we feel there are two key factors: minimising the risks to athletes' health and ensuring fairness in sport. From the standpoint of risks to health, it is by no means certain that WADA's current policy is the best possible approach given that, in

* National Fund for Scientific Research, Belgium; Université Libre de Bruxelles, Belgium.

[1] The World Anti-Doping Code contains the following passage (page 11): "The purposes of the World Anti-Doping Code and the World Anti-Doping Programme which supports it are to protect the athletes' fundamental right to participate in doping-free sport and thus promote health, fairness and equality for athletes worldwide […]" (World Anti-Doping Code, www.wada-ama.org).

practice, it permits the development of clandestine doping on a large scale. From the standpoint of fairness in sport, the current policy is far from satisfactory given that its ineffectiveness puts non-doped athletes at a disadvantage in relation to those who dope in secret. This leads to a highly immoral situation in which the winner is often the "best cheat", in other words the shrewdest, smartest and luckiest competitor. Furthermore, independently of health and fairness issues, WADA's prohibitionist policy produces a number of very worrying adverse effects. It should therefore be possible to discuss the doping issue without any taboos or preconceptions. For this purpose, the various stakeholders (athletes in particular) should be allowed to air their views freely. This is a complex problem to which there is no simple solution. A wide-ranging societal debate, free from prejudice, should therefore be launched on the consequences of anti-doping policy, the legitimacy of using performance enhancement techniques in sport and the sports policy that should be advocated if athletes are to practise their sport under the best possible conditions.

1. New developments in the debate on performance enhancement

The debate on performance enhancement in sport has obviously been going on for a long time, but it has evolved significantly in the last few years. In our view, there are two reasons for these new developments: the setting up of the World Anti-Doping Agency and the emergence of enhancement medicine.

The setting up of the World Anti-Doping Agency (WADA)

The stepping up of the fight against doping after the Festina affair in the 1998 Tour de France led to the establishment of the World Anti-Doping Agency (WADA) and to the adoption of a prohibitionist philosophy officially espoused by the sports authorities. WADA's mission is to promote, co-ordinate and monitor the fight against doping in sport in all its forms. It was founded in 1999 as an independent international organisation. It is composed in equal parts of, and funded in equal parts by, the sports movement and governments. It monitors the conformity of sport with the World Anti-Doping Code, a document harmonising the

rules on doping in all sports and all countries. The setting up of WADA put an end to the relative laxity seen in the fight against doping in the closing decades of the 20th century. This political will to eradicate doping led to the suspension of many sportsmen and women from competition for varying periods and, indirectly, to the imprisonment of such an illustrious athlete as Marion Jones. Some doctors and philosophers think today that the goal of eradicating doping in sport is an unattainable ideal. Believing WADA's policy to be counterproductive, they advocate various pragmatic approaches allowing doping under medical supervision.

The emergence of enhancement medicine

The second factor that gives the question of performance enhancement a philosophical and ethical dimension it did not previously possess is the inclusion of the issue of doping in a wider context, that of enhancement medicine. The blurring of the boundaries between traditional therapeutic medicine and enhancement medicine is one of the main features of 21st century biomedicine. In modern biomedicine, new therapeutic drugs and techniques can be used not only to treat a patient but also to enhance certain human abilities. A recent survey showed that it had become routine practice in American universities to take cognition enhancers to improve academic performance[2]. The substances used by athletes to enhance their performance, such as amphetamines, erythropoietin (EPO), corticosteroids or growth hormone, were used initially for therapeutic purposes. In the same way, medical techniques such as gene therapy or stem cell injection may potentially be used for enhancement purposes in athletes. This development represents a change of paradigm in medical practice. Within traditional, therapeutic medicine, imperceptibly, another type of medicine has developed, whose aim is no longer to cure but to enhance, "doping medicine". In his book *Better than Well*, the philosopher and bioethicist Carl Elliot analysed the many different facets of enhancement technologies in modern American society[3]. In the last ten years or so, first in the United States, then in Europe, many authors - doctors, philosophers, bioethicists, lawyers etc - have focused on the issue

[2] B. Maher, Poll results: look who's doping, *Nature*, vol. 452, 2008, p. 674-675.

[3] C. Elliott, *Better than well: American medicine meets the American dream*, New York, W.W. Norton, 2003.

of enhancement technologies[4]. Medicine is no longer solely therapeutic. Some people expect it to contribute to performance enhancement and human "improvement", including in sport. In this context, competitive sport could become one of the main testing grounds for enhancement. Athletes are often ready to take risks, including the risk of using doping products or experimental technologies, to enhance their performances. To win competitions, break records or earn medals, some athletes are ready to become the subjects of a vast experiment conducted hitherto in secret. The coming together of sport and enhancement biotechnology raises ethical, philosophical and sports policy questions to which there are no straightforward answers. The policy of prohibiting and punishing doping is certainly not the only possible strategy. There are ethical positions (and policies) other than that underlying WADA's work at present. We will need to await confirmation of the ineffectiveness and likely failure of the current anti-doping policy before other solutions are tested in the field. Some people today, advocates of liberal ethics, are already calling for supervised legalisation of enhancement technologies in sport. Their arguments deserve to be taken seriously, even if legalisation may have undesirable consequences of its own.

2. Biotechnology, enhancement and sport: the example of gene therapy

"What is clear ... is just how impatient some coaches and athletes are to find new and ingenious ways to cheat. First it was steroids, then EPO [erythropoietin], then human growth hormone – and now the illicit grail seems to be gene therapy."

(T. Friedmann, O. Rabin, T.S. Frankel, "Gene doping and sport", *Science*, 327, 2010, p. 647-648).

[4] For a historical, philosophical and ethical approach to enhancement technologies, the following works may be consulted: J.-N. Missa and L. Perbal, *"Enhancement".* Éthique et philosophie de la médecine d'amélioration, Paris, Vrin, 2009; Julian Savulescu & Nick Bostrom (ed.), *Human Enhancement*, Oxford Univ. Press, 2009; J. Harris, *Enhancing Evolution. The Ethical Case for Making People Better*, Princeton Univ. Press, 2007.

In the 20th century, doping in sport evolved in line with advances in pharmacology (amphetamines, steroids, growth hormone, EPO etc). For a number of years now, the development of gene therapy has brought new tools for enhancing performances in sport. The potential uses of gene therapy in sport provide a perfect illustration of the blurring of the boundaries between therapeutic and enhancement medicine. Gene therapy offers techniques for genetic modification of physiological functions related to athletic performance. Genetic recombination techniques can be used not only to alleviate the symptoms of diseases such as muscular dystrophy, but also to enhance muscular vigour in the elderly or improve athletes' performances. Dozens of genes affecting athletes' performances and susceptible to modification by genetic recombination have been identified. Scientists have created transgenic mice endowed with exceptional "athletic abilities"[5].

One of the first experiments in genetic recombination with potential consequences in terms of enhancing sports performances was conducted by Se-Jin Lee, a professor of molecular biology at John Hopkins Medical School in Baltimore. Lee identified the function of myostatin, a protein which tells muscles when to stop growing[6]. Experimenting on mice, Lee inactivated the gene that codes for myostatin production. He obtained mice with oversized muscles. When he published his findings, Se-Jin Lee received emails from patients suffering from muscular conditions, but also from athletes and bodybuilders keen to increase their muscle strength artificially, and enthusiastic about the idea of testing gene therapy on their own bodies. In 1998, H. Lee Sweeney, professor of physiology at the University of Pennsylvania, published the results of an experiment on a mouse genetically modified to produce IGF-1 (insulin-like growth factor), a substance involved in muscle anabolism. Sweeney's muscular mice were dubbed "Schwarzenegger mice" by the American press. Sweeney was also contacted by many athletes wishing to take rapid advantage of the advances in science. He was even approached by the trainer of an American football team and the coach of a wrestling team who were

[5] See in this connection: T. Friedmann, O. Rabin, M.S. Frankel, Gene doping and sport, *Science*, 327, 2010, p. 647-648.

[6] Alexandra C. McPherron, Ann M. Lawler, Se-Jin Lee, Regulation of skeletal muscle mass in mice by a new TGF-ß superfamily member, *Nature*, 1997, 387, p. 83-90.

prepared to submit their entire teams to genetic experimentation. He says that even when he explained to them that it was dangerous, some athletes were still prepared to act as guinea-pigs[7].The possibility of "gene doping" has also received a boost from the work of a team led by Richard Hanson. The mice genetically modified by Hanson possess outstanding athletic qualities.

The improvement in their performances is spectacular. On a treadmill, they can run up to six kilometres at a speed of 20 metres per minute, whereas normal mice stop after 200 metres. These modifications are linked to overexpression in the skeletal muscle of a gene, that of the enzyme "phosphoenolpyruvate carboxykinase" (PEPCK-C). This enzyme is involved in the production of glucose, which cells use as their primary source of energy, and glycerol, which is found in fat. The enhanced ability of the mice to run is explained by their oxygen consumption, which is increased by 40%, and the small quantity of lactic acid they produce.

If, thanks to new gene technology, athletes were able to inhibit the expression of the myostatin gene and increase their production of IGF-1 or PEPCK-C, the change would be recorded in their genome. At this stage, the only way of identifying the modification would be muscle biopsy, a technique that would be hard to imagine as part of regular anti-doping controls. Some athletes and trainers are keeping a close eye on developments in this research into the genetic factors underlying sports performances. Attempts have already been made to use genetic technology in sport. A Chinese genetic laboratory was offering its services in the field of genetic recombination before the Beijing Olympics in 2008. It is not known whether these attempts at gene therapy for enhancement purposes resulted in actual DNA recombinations and whether the desired effects were achieved, but all the evidence suggests that the advent of these techniques in the world of sport is imminent. According to Sweeney, some methods of genetic recombination are so easy to carry out that students of molecular biology could perform them. Since 2003, WADA's genetics committee has funded research programmes to detect the presence of artificially recombined genes in the organism or viruses serving as gene transfer vehicles. So far, however, no project has resulted in a validated

[7] M.Wenner, How to be popular during the Olympics: Be H. Lee Sweeney, Gene doping expert, *Scientific American*, 15 August 2008 (www. Scientificamerican.com).

blood or urine test. Gene doping can only be detected by performing a biopsy of athletes' muscle tissue. The day these enhancement techniques become a reality in sport, they will be extremely difficult to detect. For anti-doping controllers, identifying the "cheats" will be a very tricky business, even more so than at present. But doping is not necessarily cheating. Everything depends on one's philosophy of sport and the rules one wishes to adopt on performance enhancement in sport.

3. The inefficacy and adverse effects of anti-doping policy

WADA has developed an anti-doping ideology similar to that underpinning the war on drugs. In terms of consequentialist ethics, it is by no means obvious that this is the best attitude to adopt. Some people today think that the eradication of doping in sport is an inappropriate solution condemned to failure[8]. They advocate a pragmatic approach allowing certain forms of doping under medical supervision. WADA members tend all too often to present the fight against doping as a battle between Good and Evil, without questioning the rightness of this approach or considering its possible adverse effects[9]. What is needed is to encourage the emergence of a public debate on the ethical and philosophical foundations of a radical anti-doping policy and think about the effects of such a policy on athletes' lives. We have identified some arguments which are all too often overlooked in discussions on performance enhancement in sport and which call into question the effectiveness and relevance of current anti-doping policy.

[8] See for example B. Kayser, A. Mauron, A. Miah, Current anti-doping policy: a critical appraisal, *BMC Medical Ethics*, 2007, 8, 2; J. Savulescu, B. Foddy, Ethics of performance enhancement in sport: Drugs and gene doping', *in* R E. Ashcroft, A. Dawson, H. Draper & J.R. McMillan, (ed.), *Principles of Health Care Ethics*, 2nd ed., London, John Wiley & Sons, 2007, p. 511-520; J. Savulescu, B. Foddy, Le Tour and failure of zero tolerance: Time to relax doping controls', *in* R. Ter Meulen, G. Kahane, J. Savulescu (ed.), *Enhancing Human Capacities,* Oxford, Wiley Blackwell, 2009; Andy Miah, *Gene Doping: A reality, but not a threat*, 2 May 2005, www.andymiah.net.

[9] See in this connection Verner Moller, *The Ethics of Doping and Anti-Doping*, London, Routledge, 2010; Paul Dimeo, *A History of Drug Use in Sport (1876-1976)*, London, Routledge, 2007.

3.1. Anti-doping policy is ineffective because WADA is incapable of enforcing the rules it lays down in the World Anti-Doping Code

The central problem with anti-doping policy is that WADA and the sports authorities are incapable of enforcing the rules laid down in the World Anti-Doping Code. The tougher anti-doping policy adopted since 1998 has not succeeded in containing doping. There has been a steady stream of "scandals"[10]. In some disciplines such as athletics and cycling, a considerable number of athletes continue to use substances despite several decades of doping control. Athletes who dope adapt to testing policy. New substances (biosimilar EPOs, IgF1, secretagogues etc) are appearing on the Tour and already circulating in sports circles. In the United States, the Mitchell Report, the outcome of a large-scale investigation into the problem of doping in sport, showed that the establishment of stricter controls does not eliminate illegal substance use but causes athletes to choose different, less easily detectable, or undetectable substances[11]. The USADA investigation into the US Postal team showed that, in 2000 (the year in which a test to detect EPO was developed), racing cyclists abandoned EPO and went back to blood transfusion techniques which are very difficult to detect[12]. Victor Conte, the main protagonist in the Balco affair asked a chemist, Patrick Arnold, to procure for him a new undetectable synthetic steroid - THG, known as "the Clear" because it allowed athletes to avoid being tested positive. Conte supplied "the Clear" to American athletes and baseball players. This substance was unknown to the anti-doping authorities until a former associate of Conte, the trainer Trevor Graham, delivered a syringe containing traces of it to Don Catlin, head of a laboratory specialising in anti-doping testing. Conte offered top athletes (Marion Jones, Tim Montgomery, Dwain Chambers etc) doping programmes. He marked on a calendar the type of substance to take: E for EPO, G for growth hormone, I for insulin etc. The phased programme allowed athletes to enjoy the full effects of the substances

[10] In cycling, for example, the affairs involving Landis, Ricco, Vinokourov, Rasmussen, Contador, Armstrong etc.

[11] *Report to the Commissioner of baseball of an independent investigation into the illegal use of steroids and other performance enhancing substances by players in major league baseball*, George J. Mitchell, DLA PIPER US LLP, 13 December 2007 (http://files.mlb.com/mitchrpt.pdf).

[12] See appendices to Statement from USADA Regarding the U.S. Postal Service Pro Cycling Team Doping Conspiracy: http://cyclinginvestigation.usada.org/.

without any abnormal physiological variables. Conte "pre-tested" athletes before competitions. He recorded his athletes' blood and urine test results in a notebook and had them checked regularly by a private laboratory to avoid any unpleasant surprises in the official tests. The relative ineffectiveness of testing raises some serious ethical and sports justice issues. A very large number of doped athletes manage to slip through the net. This places non-doped athletes at a disadvantage in relation to those who dope in secret. This in turn leads to a highly immoral situation in which the winner is often the best "cheat". The situation is unlikely to get any better with the advent of biosimilar drugs and the emergence of cell and gene therapy. New drugs which may be mentioned include biosimilar EPOs (official or counterfeit), EPO modulators, biosimilar growth hormones, secretagogues (which stimulate the pituitary gland to produce growth hormone), the muscle growth factors IgF1 and bFGF, which are currently undetectable by anti-doping tests, selective modulators of androgen receptors, muscle resorption inhibitors (which act by neutralising myostatin), fat burning activators (which target the SIRT1 genes by activating the PPAR-delta protein), AMP-kinase agonists… Some of these drugs, most of which are undetectable by current anti-doping tests, are already being used by professional athletes. Where cell and gene therapy is concerned, bioproduction of red blood cells from stem cells is likely to develop in the near future. Cell therapy has already become a reality in competitive sport with the use of PRP (platelet-rich plasma) methods, which are based on the richness of platelets in growth factor. Local injection of these platelets can speed up cartilage, tendon, bone and muscle repair. These cell therapy methods can be used in sports preparation to maximise performance, and not solely for injury repair purposes. Gene therapy also raises the issue of doping and deviance in elite sport. In a nutshell, if anti-doping tools are already unable to detect pharmacological doping effectively, they are likely to be completely overwhelmed by the emergence of biotechnological methods[13]. Under these circumstances, the objective of allowing athletes to "compete on an equal footing" is not attained today and will be even less so in future. Undeniably, therefore, the anti-doping system based on coercive testing

[13] See in this connection Gérard Dine, Le dopage sportif et son avenir, in Hottois, G., Missa, J-N., Perbal, L., *Encyclopédie du Trans/posthumanisme*, Vrin, 2015.

has failed. This is clear from the remark which former Balco boss Victor Conte made to British sprinter Dwain Chambers when he came to join the team of American sprinters (Marion Jones, Tim Montgomery, etc.) who were being supplied with doping substances by Conte: "They are cheating you, Dwain. You're a very talented athlete but you are not competing at a level playing field. The system allows people to cheat"[14].

3.2. Doping is the logical consequence of the spirit of competitive sport: maximising performance

The ban on doping introduces a structural contradiction into competitive sport. Athletes are expected to surpass themselves, but at the same time the means to that end are prohibited, on a controversial basis. Doping is nothing but the logical consequence of the quest for maximisation of performance. The nature of competitive sport prompts athletes to supplement their training with a biomedical preparation. It might seem paradoxical to ban a practice which is consistent with the logic of competitive sport: improving performance at any cost. Athletes are expected to surpass themselves and break records, but at the same time they are banned from having recourse to doping. Without the use of enhancement techniques or substances, there is little chance of any athlete beating in the near future the time of 10'49 recorded by Florence Griffith Joyner in the 100 metres or of any cyclist doing better than Marco Pantani's time of 36 minutes and 45 seconds in the climb to Alpe-d'Huez (in 1997). Some records are impossible to break with a "natural" body. One might obviously take the view that this quest for better performances is absurd and that people should give up trying to break records, but this would spell the end of competitive sport - an unrealistic and undesirable goal.

3.3. Doping is not inconsistent with the "spirit of sport": it is part of the reality, the logic and the history of competitive sport

The preamble to the World Anti-Doping Code states that "doping is fundamentally contrary to the spirit of sport"[15]. That is an untruth.

[14] Victor Conte, quoted in Dwain Chambers, *Race against me*, Libros, London, 2009, p. 61.

[15] The "spirit of sport" is defined as follows in the World Anti-Doping Code: "Anti-doping programs seek to preserve what is intrinsically valuable about sport. This intrinsic value is often referred to as 'the spirit of sport', it is the essence of Olympism; it is how we play true. Doping is fundamentally contrary to the spirit of sport." (World Anti-Doping Code, www.wada-ama.org)

Doping is an integral part of competitive sport, its reality, its history, its logic, and hence its very essence, to use the language of ontology[16]. Doping is endemic to some disciplines such as athletics and cycling. Let us take the example of cycling. Amphetamines, corticosteroids, anabolic steroids, EPO, PFC, gene doping… Every period has had its favourite substance. After the Second World War, amphetamines became the drug of choice for cyclists. Few cyclists at the time did not use amphetamines. The bodily signs of stimulant use could even play a part in champions' race strategies[17]. In the jargon of the *peloton*, doping was "*la charge*", the load, and many thought that the Tour de France would not really have been the Tour without its share of "loaded" competitors. Brought from the USA by American soldiers, amphetamines became the drug of choice of post-war cyclists. They relieved pain and made them want to pedal faster. Félix Levitan, co-director of the Tour De France, commented lucidly in a 1965 issue of "*Miroir des sports*" that anyone who doesn't use doping substances is "doomed in advance to defeat". A syringe of amphetamines pushed back the pain barrier. Riders were no longer aware of their limits. They became cycling machines. Until final victory, when everything was fine. Or until a system overload caused the human "boiler" to explode, as in the case of Tom Simpson, who collapsed and died in 1967 while riding up Mont Ventoux. In the jargon of the *peloton*, a "boiler" (*chaudière*) was a doped rider. The post mortem carried out on Simpson's body showed that death was due to the absorption of amphetamines combined with the effects of heat, fatigue and alcohol. Amphetamines were one of the most widely used substances in the 1970s and 80s. In his book *Nous étions jeunes et insouciants*, Laurent Fignon, twice winner of the Tour de

[16] For a history of doping, see, for example, Paul Dimeo, *A History of Drug Use in Sport (1876-1976)*, London, Routledge, 2007.

[17] Amphetamines, "la bomba" in Italian cycling jargon, gave cyclists an energy boost at the end of a stage, but they could also stop them sleeping and recovering during the night. In his book *Fallen Angel. The Passion of Fausto Coppi*, cycling historian William Fotheringham recounts that, before a mountain stage in the Giro, Coppi asked one of his team-mates, the *gregario* Ettore Milano, to check out the eyes of his main rival, Swiss champion Hugo Koblet. "To my immense pleasure, said Milano, I noticed that Koblet had eyes that would scare you. At once I went to Fausto and said to him "Look Koblet has 'drunk'– his eyes are in the back of his head." "Mine are too", said Fausto." On the strength of this evidence, Coppi launched an attack on his rival in the Stelvio climb and won the 1953 Giro (W. Fotheringham, *Fallen Angel. The Passion of Fausto Coppi*, London, Yellow Jersey Press, 2009; R. Moore, *Stelvio, Rouleur, Issue Seven*, 2007, p. 40).

France, admits that he used corticosteroids and explains that, in cycling jargon, the expression *faire le metier* (doing one's job) meant using doping products[18].

Erythropoietin (EPO) first appeared in the *peloton* in around 1990. EPO stimulates red blood cell production. Obtained artificially through genetic engineering, EPO is prescribed for some patients with kidney failure treated by dialysis, or to treat severe anaemia. In cycling, it has helped to enhance performances. The pattern is always the same: from therapy to enhancement. In the 1990s and the 2000s, it was virtually impossible to win the Tour without using EPO. In his testimony before the US anti-doping agency, a former loyal team-mate of Lance Armstrong explained the circumstances in which he and Armstrong had been forced to use EPO from 1995 onwards: "We got crushed in the Milan San Remo race and coming home from the race Lance Armstrong was very upset. As we drove home Lance said in substance 'this is bull shit, people are using stuff and we are getting killed'. He said in substance that he did not want to get crushed any more and something needed to be done. I understood that he meant the team needed to get on EPO"[19]. Interviewed by Oprah Winfrey in 2013, Lance Armstrong said that doping was essential to win the Tour. According to Armstrong, using banned substances was part of the cyclist's job: "That's like saying we have to have air in our tyres or we have to have water in our bottles. That was, in my view, part of the job"[20]. EPO use could be combined with the older practice of self-transfusion. After a course of EPO treatment, blood was taken from the cyclist during the winter when there were no tests, then kept refrigerated and ready for use in competitions. Cyclists' rooms were like medical laboratories, with drugs, blood packs and micro-centrifuges to test the haematocrit level. To enter the professional cycling fraternity, the initiation ritual of doping was virtually obligatory. Newcomers who showed any talent always thought that they could compete in cycling

[18] Laurent Fignon, *Nous étions jeunes et insouciants*, Paris, Grasset, 2009, p. 89.

[19] See affidavit of George Hincapie in "Appendices and supporting materials", Statement from USADA Regarding the U.S. Postal Service Pro Cycling Team Doping Conspiracy: http://cyclinginvestigation.usada.org/.

[20] See transcript of Oprah Winfrey's interview with Lance Armstrong: http://armchairspectator.wordpress.com/2013/01/23/full-transcript-lance-armstrong-on-oprah/.

without using doping products. Their young bodies recovered quickly and they could win races and even hold their own against adversaries said to use doping products. Then, as the frequency and number of races increased, they very soon realised the gap between themselves and those whose performances were "assisted". Acceptance was gradual. First of all they were given substances which were harmless but were administered by injection. This first step enabled them to get over the initial psychological barrier, because, in the young cyclist's mind, injection was synonymous with doping. The next step came logically. Because performance was enhanced by a recovery product, they moved on to ordinary corticosteroid pills recommended by a team-mate who assured them that there was no risk. Initially, the benefit was obvious. But in due course, as dependence set in, they saw no reason not to step up the dose and no reason to refuse more powerful substances, such as steroids, amphetamines and EPO. All riders experienced this inexorable spiral. Some resisted longer than others, but they all, or most of them, eventually weakened, to keep their jobs as professional cyclists or out of love for the sport. Of course, doping was not official team policy. But those who took nothing were well aware that their contracts would not be renewed. They also knew that they had no chance of being among the candidates for final victory. Doping is an integral part of cycling culture[21]. To say that doping is contrary to the spirit of sport is to deny the history and reality of sport. Doping is at the core of competitive sport[22]. The nature of professional sport leads athletes to supplement their training with a biomedical preparation. One may regret this fact and live in nostalgia for a pure sport which never existed. But it is hard to deny that the use of doping and biomedical technology fits readily into the philosophy of maximising performance which underpins elite

[21] To convince oneself of this, one has only to read a few biographies or personal accounts by cyclists or prominent figures from the world of cycling. See, for example: Erwann Menthéour, *Secret défonce*, Paris, Jean-Claude Lattès, 1999; Roger Bastide, *Doping. Les surhommes du vélo*, Paris, Solar, 1970; Paul Kimmage, *Rough Ride*, London, Yellow Jersey Press, 2001; Philippe Gaumont, *Prisonnier du dopage*, Paris, Grasset, 2005.

[22] In a remarkable sociological survey based on personal accounts by cyclists, Christophe Brissonneau, Olivier Aubel and Fabien Ohl showed that doping is part of the professional culture of cycling. For many cyclists, doping is not cheating. Doping is doing one's job. (*L'épreuve du dopage*, Paris, PUF, 2008).

sport. Is it not paradoxical, therefore, to seek to ban conduct which stems from the basic philosophy of competitive sport? Would it not be more consistent to concede that biomedical enhancement of performances is an integral part of the elite athlete's preparation[23]. Maximising performance by developing natural talent through training and aiming for the best possible biomedical preparation - this defines the spirit of modern sport much better than the fine sentiments and naïve generalisations about the spirit of sport contained in the World Anti-Doping Code.

4. The many adverse effects of the anti-doping policy

4.1. Threat to the privacy of the athletes

The proponents of anti-doping policy believe that if a larger number of new resources were employed, doping could gradually be eliminated. This attitude inevitably leads to a larger number of bureaucratic, legal and police constraints on professional sports: random tests, biological passports, cryopreservation of blood samples with a view to subsequent testing, searches in competitors' rooms, and perhaps even one day muscle biopsies to counter genetic doping… Is it reasonable that athletes who devote their entire life to their chosen sport should be subject to such constraints? The fight against doping violates their privacy. Random tests can be carried out at any time, during, prior to, or after a competition, and athletes have to inform the authorities of their every move. If an athlete fails to turn up for three random tests within an 18-month period, he or she may be suspended from competing[24]. The severity of doping control procedures is clearly escalating. WADA recently recommended that

[23] This is the position defended by Kayser, Mauron and Miah: "Elite athletes are also constituted by scientific knowledge and this is a valued aspect of contemporary sport. As such, translating doping enhancements into earned advantages – having the best scientists on one's team – would more closely align to the values of competition than leaving it all to chance, unequal access to illicit practices, and the cleverness of undetected cheating" (Current anti-doping policy: a critical appraisal, *BMC Medical Ethics*, 2007, 8 :2).

[24] In the World Anti-Doping Code, www.wada-ama.org, the rule reads as follows: "Any combination of 3 missed tests and/or failures to file whereabouts information within an 18-month period may be considered a doping violation".

tests should be carried out in the middle of the night[25]. But in what other sector of society would it be acceptable to submit people to such constraints? More thought should be given to whether it is appropriate to treat athletes as potential delinquents who have to constantly keep anti-doping organisations informed of their whereabouts. Athletes are beginning to rebel and to demand respect for their privacy. Rafael Nadal, the tennis-player, recently criticised the doping control procedure, saying "I feel like a criminal". He complained that he had to report his whereabouts for at least one hour a day, seven days a week. In Belgium, 65 athletes have initiated legal proceedings against the World Anti-Doping Agency, claiming that doping controls are intrusive and breach European privacy laws.

4.2. Criminalising and demonising athletes

The outcome of WADA's current policy is the criminalisation and demonisation of athletes. In the name of anti-doping policy and by insisting that sportsmen and women should be somehow cleaner than clean which, in some sports, ignores the historical and cultural background to the sport in question, the sports authorities have initiated a ferocious "witch hunt", a merciless puritan crusade, which can have terrible consequences for the life of those who get caught out. Many athletes have been suspended and others have had to put an end to their career. We already mentioned above the issue of the persecution of athletes. Take Pantani[26] as an example. The Italian climber could not stand being hounded by the media and the judicial authorities following his disqualification from the 1999 Giro. It is plausible to say that this pressure was one of the main causes of his premature death in 2004. Few

[25] "WADA recommended that "a more varied, targeted and aggressive approach to catching cheating riders be a priority for the UCI. This should include, but not be limited to, increasing the number of anti-doping tests, testing in less acceptable hours with a greater chance of detecting substances and/or methods with short detection windows" (*Independent Observers Report on the Antidoping Testing Carried by the UCI at 2010 Tour de France*, quoted *in* S. Farrand, Italian riders question need for night time anti-doping tests, 30, October 2010- cyclingnews.com).

[26] See the following books and documents on Pantani: M. Rendell, *The Death of Marco Pantani*, London, Weidenfeld & Nicholson, 2006; P. Brunel, *Vie et mort de Marco Pantani*, Paris, Grasset, 2007; Cito, Cosimo, *Il fantasma del Galibier*, Limina, Arezzo, 2010; and the box-set of seven DVDs on the life of Pantani: P. Bergonzi, E. Vicennati, *Tutto Pantani. Una vita in salita*, La Gazzetta dello Sport & Rai Trade, 2008.

people will remember that Ivan Gotti won the 1999 Giro. The race will forever be remembered as the fall of Marco Pantani, destroyed at the height of his career by the presumption that he was taking drugs just 48 hours before final and inevitable victory. From one day to the next the champion was no longer a hero but a pariah. A champion like Pantani definitely did not deserve to be treated so badly.

In the United States, the authorities use the *perjury trap* to exert pressure on athletes suspected of doping. An athlete who, after taking an oath, makes a false statement to a federal agent, for example by denying that he or she has used doping substances, is liable to a fixed term of imprisonment. In America, the perjury trap is an incredible weapon for getting people involved in doping cases to testify[27]. That was what led to the sentencing of Victor Conte, the main protagonist in the Balco affair, bringing in its wake the downfall of athletes who had worked with him, in particular Marion Jones. On 5 October 2007, she was brought before a New York court where she admitted that she had used THG (a synthetic steroid produced by the Balco laboratory) between September 2000 and July 2001. Following her confession, the International Association of Athletics Federations (IAAF) cancelled all her results prior to September 2000 and the IOC stripped her of the 5 medals she had won at the Sydney Olympic Games. Finally, Marion Jones was given a six-month prison sentence for lying to federal investigators. "No consideration was taken for the fact that she has been shamed, that she has lost her medals, that she has been brought to financial ruin. She has paid a terrible human price already"[28], said Georges Hulse, one of her cousins, after the verdict was announced in early 2008. In January 2010, a journalist of the BBC asked Marion Jones the following question: "Was it right that you went to jail?" After a long silence, Jones replied: "I don't think it was right. My reputation, fame and fortune were lost. Learning that lesson would have benefited society more than putting me away for six months."[29]

[27] See M. Fainaru-Wada, L. Williams, *Game of Shadows*, New York, Gotham Books, 2006, p. 191.
[28] L. Zinser, Judge Sentences Jones to 6 Months in Prison, *New York Times*, 12, January 2008.
[29] Inside Sport. The Marion Jones Story, BBC, 4 December 2010.

4.3. Health risks caused by illegal doping and paternalism

Anti-doping proponents claim, quite rightly, that doping can be dangerous for the athlete's health. There have indeed been fatal accidents caused by doping. But, in the majority of cases, these accidents have taken place in a context where the doping substances had been illegally prescribed, most frequently by trainers with no medical background. The consequence of the anti-doping policy is therefore that it obliges athletes to take illicit doping substances, without any kind of medical supervision, to ensure that they are not caught by the anti-doping police. Only the most well-off athletes can afford to seek the advice of a private doctor for their biomedical preparation. Some people now think that if doping under medical supervision were made legal, it would paradoxically reduce the risks for the athletes' health by avoiding the need to take doping substances illegally. Legalisation would put an end to the unhealthy paternalistic attitude of protecting athletes and making sure that they do not yield to the temptation of taking certain risks. What justifies such paternalism and protectionism towards athletes? Did they not choose this sort of life? Are they not fully informed adults? Are they not free to choose whether or not to take certain risks after calculating whether the benefits that could be gained are worth the risks? And if the risks are sometimes greater, are the possible benefits not just as great? Constantly, in our everyday lives, both professional and private, it is possible and legitimate to wonder about the degree of freedom and conscience with which individuals choose to act or not act in very diverse situations. That does not, however, mean that we can decide what is best for those individuals and then intervene to prevent them from harming themselves when they have access to the information that allows them to decide for themselves. After all, is high-level sport not a source of major risks in itself, in particular in certain fields? There is an undeniable risk factor in cycle racing, for example. The number of cyclists who have died during races or training is impressive [30]. For example, the *campionissimi* Gino Bartali and Fausto Coppi both lost a brother: Serse Coppi crashed because of a blocked wheel in the final sprint of part of the *Tour de Piémont* 1951 and died shortly after his fall. *Gino il pio*'s brother was killed in a cycling

[30] One only has to look at the "*List of professional cyclists who died during a race"* in Wikipedia (http://en.wikipedia.org).

accident in 1936. Would it be reasonable to forbid the sport in the name of the athlete's health on the pretext that it is dangerous?

4.4. Continual rewriting of sports history

Who won the 100m final at the Sydney Olympic Games? Marion Jones? She was the first to cross the finishing line, but in 2007, she was disqualified on grounds of doping[31]. So that cannot be the right answer. Ekaterini Thanou? The Greek sprinter finished second in this race. She is listed as the official winner but the IOC did not want to give her the gold medal because she had been involved in other doping cases. Thanou officially won the 100m at the Sydney Games but she had to make do with the silver medal[32]. "Who won the 100m final at the Sydney Olympic Games?" is therefore a question to which there has been no answer and the women's 100m final at the Sydney Games was a race without a winner. A similar situation arose during the 2006 Tour de France. Floyd Landis, the American cyclist, won the Tour in July before testing positive for testosterone in August. A long legal process led to his disqualification and, in October 2007, the famous yellow jersey was handed over to Oscar Pereiro, who had come second in the race. As a result of the snail-pace workings of the law, more than a year went by before the official winner of the 2006 Tour was announced. "At last! It took too long, far too long to announce the winner. He was a belated winner but a true winner", said Christian Prudhomme, Director of Tour. A true winner? Very few fans of cycle racing and the

[31] On 5 October 2007, Marion Jones admitted that she had taken doping substances prior to the Sydney Games. On 9 October she handed her medals back to the American Olympic Committee and on 12 December, the IOC formally stripped her of her medals. Nevertheless, the IOC did not want to award the medals to anyone else. It announced that the updating of the rankings as a result of Marion Jones' disqualifications would not be automatic as the Balco scandal might involve other athletes. In December 2007, Jacques Rogge, President of the IOC, announced that the medals would only be redistributed if the IOC was convinced that the investigations would not reveal further cases of doping.

[32] In 2004, Ekaterini Thanou was one of the favourites to win the 100m at the Athens Olympic Games. Before the Games, Thanou and her compatriot, the sprinter Kenteris, failed to appear for a random anti-doping test on the pretext that they had been involved in a motorcycle accident. They had already missed two random tests in the past. Thanou and Kenteris withdrew from the Games. In August 2008, the executive committee of the Olympic organisation barred Thanou from competing in the Beijing games for indecent conduct and for dishonouring the Olympic Movement. In May 2010, Thanou announced that she was putting an end to her career.

Tour de France are prepared to consider Pereiro as the true winner of the 2006 Tour. Like the final of the women's 100m at the Sydney Games, the 2006 Tour is a Tour without a true winner. The possibility of condemning athletes retroactively further reinforces the current process of continually re-writing sports history. The conservation of samples for eight years - as authorised under the World Anti-Doping Code - and retroactive tests make it possible to detect at a later date doping substances that were undetectable at the time of their use and this serves as a sword of Damocles. We now need to be patient to find out who really won a race. You thought that Armstrong was the seven-time winner of the Tour de France (from 1999 to 2005)? The anti-doping authorities will soon tell you you were wrong. Armstrong was caught in the anti-doping net[33]. His fall into disgrace has left a major void in the record of Tour winners. The 1999 to 2005 Tours are tours without a winner as the title was not given to anyone else. This poses huge problems of justice in sports. According to the sports authorities, no cyclist deserved to receive the yellow jersey between 1999 and 2005 because the vast majority of athletes were taking drugs. Nobody was capable of ensuring that the rules of the World Doping Code were respected. That is an abysmal failure of the anti-doping policy, a failure of the system that was supposed to allow athletes to compete on an equal footing without taking drugs. The system does not guarantee fairness. Bjarn Riis, for example, another winner of the Tour, had more luck than Lance Armstrong, Floyd Landis or Alberto Contador. He was allowed to keep his yellow jersey despite having admitted that he had taken doping substances to ensure his victory in 1996[34]. The anti-doping authorities are inconsistent in the way they apply penalties to competitors who are found guilty of doping and this inconsistency is incompatible with the fairness of sport. The result of an increasingly stringent anti-doping policy is a curious rewriting of history. If this process of permanent re-

[33] See the documents concerning the Armstrong affair published by the American Anti-Doping Agency: Statement from USADA Regarding the U.S. Postal Service Pro Cycling Team Doping Conspiracy (http://cyclinginvestigation.usada.org/).

[34] On 25 May 2007, Bjarn Riis acknowledged that he had taken EPO during his sports career and in particular during the 1996 Tour de France, which he had won. On 7 June 2007, his name was struck off the list of winners of the Tour de France and no other winner was nominated for 1996. He was reinstated by the organisers of the Tour de France in July 2008, with a reference to his confession.

assessment of the virtue of the winners continues, the conclusion will be that no one has ever won the Tour de France or a 100m final while respecting the genuine "spirit of sport".

5. WADA's whole philosophy is based on naturalistic and bioconservative principles

Competitive sports are not based on an egalitarian philosophy. Equality is far from being the core value of professional sports. Indeed, competitive sports are profoundly inegalitarian. To put it in a nutshell, the athletes who win are those who have the best genetic potential and who benefit from the best training conditions and medical supervision. The expression "*to compete on a level playing field"* is misleading. When the World Anti-Doping Agency forbids the use of technologies or doping substances to guarantee fairness and equality in respect of athletes throughout the world, it is implicitly defending a naturalist philosophy which sees sport as the unbiased referee of natural inequalities. From this standpoint, being fair means respecting these inequalities. WADA therefore defends a competitive sport whose role is to highlight natural inequalities. This philosophy rewards athletes who are the most genetically and physiologically gifted, the human "animal" which is the strongest, the fastest and which has the most stamina. By upholding the principle of respecting a "fact of nature", this philosophy reflects the bioconservative approach to enhancement medicine. Those who preach anti-doping sometimes even transform the WADA's naturalist philosophy into a naturalist religion. In this religious philosophy, doping becomes an absolute sin. And athletes who take drugs must confess their sin in order to ensure their redemption. John Fahey, WADA President, claims that seeing Armstrong's teammates, such as Tyler Hamilton, confess that they had been doping had "restored his faith in human nature"[35]. Travis Tygart, USADA Chief Executive, said "'riders should be given a chance to voluntarily confess

[35] "Fahey said 'seeing cyclists like Tyler Hamilton and White confess their doping past was extremely welcome and restored his faith in human nature to see that is a sentiment that is still in sport'. 'They've at least said they're sorry and that's a step ahead of some others, who continue to deny reality' said John Fahey" (WADA to consider global amnesty for drug cheats, http://www.news.com.au/sport/more-sport/wada-to-consider-global-amnesty-for-drug-cheats/story-fndukor0-1226498924207).

and detail doping'". Once they have confessed, those who have repented would then be granted a "pardon" and an "amnesty" by a "Truth and Reconciliation" commission[36]. In this quasi-religious philosophy, anti-doping takes on the form of a thorough-going Puritan crusade. Would it not be more intelligent to ask oneself some questions on the merits of an anti-doping policy which obliges athletes to take drugs - and then invites them to confess - and constantly promises a renewal of the sport without doing anything to put an end to doping.

[36] "Tygart said 'cycling should adopt a truth and reconciliation commission'. Tygart, and others, believe 'riders should be given a chance to voluntarily confess and detail doping'" (US Anti-Doping Agency chief Travis T Tygart insists truth and reconciliation commission will help heal cycling, The Telegraph, 22 October 2012, http://www.telegraph.co.uk/sport/othersports/cycling/9626900/US-Anti-Doping-Agency-chief-Travis-T-Tygart-insists-truth-and-reconciliation-commission-will-help-heal-cycling.html).

THE NEUROSCIENCE OF WORKING MEMORY CAPACITY AND TRAINING

***Torkel Klingberg* ***

Thank you very much. It is an honor to be here. Thank you for the invitation.

I have been obsessed with working memory for the last twenty years so I am gone share some of my thoughts on working memory capacity and training. So, I will start talking about: the neural basis of working memory, then we go into working memory training and transfer to attention, the more application side of this; and also touch upon the relationship between working memory and mathematics in the end.

So, what it is working memory? It is the ability to keep information in mind for a short period of time. Here it is an example of visuo-spatial memory tasks. So, a person points at certain boxes here. You should keep that in memory so that you could point at the same boxes in the same order. So right now, you are keeping four positions in your working memory, so that you could perform this, point at them in the same order like this. That sounds easy. Now you try to do that a little more bit difficult task, again keeping in mind the positions. And now your brain is starting to hurt a little bit. So roughly just half of you would succeed is this task. So, this illustrates one basic characteristics of working memory – its limited capacity. And if you take a task like this and gradually make it more difficult, you can record the capacity limit of an individual - how many items you can keep in your working memory. And this is an example of a visuo-spatial working memory task. It is visual and spatial information that you keep in mind during this task.

And the surprising thing is that a simple task like this, if you measure the capacity and how different individuals differ in their capacity this correlates with the wide range of other abilities. So, it is correlated with attention, more specifically selective top-down attention, when you

* Karolinska Institute, Stockholm, Sweden.

control your selective attention. It is also correlated, quite highly, with non-verbal reasoning ability or the fluid intelligence. It is correlated with mathematics and reading ability. And there are also a number of groups with impaired working memory, such as children with ADHD, where you generally have deficit in working memory; children born extremely prematurely and children after cancer treatment, so both the radiations and cytotoxic treatment affect probably the white matter and affects working memory capacity and you have working memory and attention deficits after traumatic brain injury.

So, this is a central very important cognitive function and people have studied working memory, different versions of working memory tasks since at least the seventies, we know about the neuroscience of it. And monkey studies used very simple versions of working memory. What you can see here is a monkey looking at the cross in the middle of the screen, a cue is presented to the right here, the monkey is supposed to keep is gaze fixed here but remember this position during this delay, so this is the delay where information is kept in working memory and then when this cross disappears the monkey moves his/her gaze to this position to indicate that they knew where the cue was. And this was beginning to be study by Joaquin Fuster (1971) and Kubota and Niki (1971) in the beginning of the nineteen-seventies and later Patricia Goldman-Rakic (1989) and they have shown that neurons, mostly in the pre-frontal cortex, but also in the posterior parietal cortex respond with increased sustained activity during the delay and it seems also to be coded in a stimulus specific way. So certain neurons keep certain spatial positions in mind.

So, the neuroscience from monkeys has been tried to be translated to human studies, where we can look at this with neuroimaging and it actually maps quite nicely to imaging findings. In human studies we also have consistent activity in parietal and pre-frontal areas and more recently people have shown that you can actually read out the content of working memory from the brain signals in the parietal cortex. So, if you remember one dot, you can reconstruct that memory in the parietal cortex. Here are subjects trying to remember two dots and although it is a fuzzy image you can actually read out the information.

And connecting the physiology and human neurophysiology, people have developed neural network models so this is worked by Wang and

Albert Compte and others developing network models so what we are looking at here is pyramidal cells that should represent the cells in parietal or prefrontal cortex, small inhibitory neurons here. If you try to remember an item at 180º degree, a neuron will code for that and will form a bump, so by recurrent activity here, information is kept in mind over delay. And using studies like this we can see the same thing here. The network here. So, this cells code for different positions in space, so degrees, where you see a cue that you should remember. Here we see the same cells aligned up from 0º to 380º. So here we have the network of excitatory cells and inhibitory cells. A stimulus is presented here and is kept in mind by recurrent positive persistent activity. Here we have a small distracter. It distracts the network a little bit but the information is actually kept during the entire delay here.

Using these models, you can come up with hypothesis about what constitutes a better working memory and these networks generally show that higher functional connectivity gives you a better working memory. So, if you have stronger connectivity between these neurons, you have a more stable and better working memory capacity and this higher connectivity also give you higher firing rate. You can also have input to a coding region. So, if you have parietal cortex here that keeps information in mind, you can have prefrontal area giving input to this parietal region and that results in a higher capacity and more resistant, being able to keep the information in mind despite distractions.

If we go to human working memory there are many kinds of working memory. You can keep many types of information in mind. I do not think that all of these tasks reflect the same type of memory actually but there are also similarities. Most consistently we have similarities in this parietal and prefrontal network like this.

And this network is also very similar to the network you see in studies of top-down attention. And this is one illustration out of many, showing this, that the areas that you have activate by both working memory and attention can be seen in black or blue within subjects and you can see these black and blue regions here in the parietal cortex and at least two different sites or three here in the pre-frontal cortex. So, there is a specific very close link to top-down attention.

And this can also be seen in inattention in ADHD, the clinical type of inattention. So, children with ADHD, as I have mentioned, have impaired their working memory capacity. It is specifically linked to the inattentive symptoms in ADHD. Not the hyperactivity or the impulsivity. And it is also the inattention in ADHD that predicts poor academic performance. Hyperactivity in ADHD does not. And working memory similarly predicts academic performance. So, giving this link and given what we know about working memory I thought it will be a good idea to try to improve working memory twenty years ago which now I have tried to do.

So, we developed a method that later was commercialized as Cogmed. I was together and built up this company but left it a couple of years ago. Published that in 2002 and 2005 mainly sustained visuo-spatial working memory training and this is a screen shot. The task is very similar to the one that you tried in the beginning of this talk. You remember the position of lamps lightening up here. Jaeggi et al. (2008) was the next one trying this dual n-back task. An example of that you can see here. And then there has been many other versions of working memory training. They are not having the same type of effect but they are starting now to have quite a lot of research in this field.

If we talk only for Cogmed training there are now more than hundred studies from different groups over the world published on research with this and several hundreds if we include the other methods to.

This method that we used is pretty straightforward, it is repeated performance with feedback and without specific strategy instructions. It is more of an implicit training of cognitive functions. It is adaptive difficulty close to capacity limit and we know this to be a key factor. So, what I mean by that is if you have a capacity of six items, that is where you should be doing the training, trying to remember five or six or seven items, because in many control groups that we have had the control groups used the same types of software but with easy trials, so the control group tried to only remember two items for example. Therefore, all the differences we were looking at was between training on difficult items and easy items to get a good placebo simply, because it is difficult. We had mainly visuo-spatial working memory tasks because of the closer link to visuo-spatial selective attention and also evidence that this is an ability where kids with ADHD have more problems.

It is pretty intense and extensive. When we started this, it was more intense and extensive that the one we had tried before at all and the reason we could do that was that we used internet and computers rather than kids having go to the hospital or to a teacher.

The second study we did, we had subjects randomized to adapted difficult versions or controlled version, double-randomized and double-controlled blinded and we could see improvements to non-trained task so this is still visuo-spatial working memory but it is not the same type of stimulus, is not the same type of response, etc. and we can show an improvement in the treatment group relative to the placebo group that was retained at the three months follow-up.

We see now from different studies, different groups, transferred to a number of different working memory tasks. Visuo-spacial working memory tasks, but also tasks called complex working memory tasks such as in the Haveman testing battery. So, it is not exactly the same type of tasks. We see cross-modals transfer from visual space only training to verbal type of tasks (Thorell et al., 2009). For example, we can see transfer from this type of training to ability to remember instructions so that is tests were kids are given an instruction of a thing to do and then you test their ability to remember the instruction and carry out it (Holmes et al., 2009; Bergman-Nutley & Klingberg, 2014). And I think this is a kind of nice working memory task because it shows the clinical relevance or ecological validity of working memory.

If we pan out and not only look at Cogmed working memory training but general working memory training there are now a lot of meta-analyses. Here are six meta-analyses of transfer to non-trained tasks (Spencer-Smith, 2015; Melby-Lervåg, 2013; Schwaighofer, 2015; Rapport, 2013; Cortese, 2015; Peijnenborgh, 2015) and we can see the effect sizes are around .6 for this different type of trainings. So, we can improve working memory capacity.

Now there are two implications of this. First of all, it is an experimental tool to study brain plasticity associated with higher cognitive functions. It could also be an experimental tool I think to study what is happening during development. But then also there is the potential usefulness as clinical tool to enhance attention. Next, I am going to say a few words about each of this.

As an experimental tool, these network models and what we know from monkey physiology and imaging gives us some indication of what higher capacity might look like. We made one of the first studies to look at neural correlates of working memory training. In this case we had two different experiments with a slight different set up. I will not show all of it here, but the general finding was increased BOLD response in parietal and pre-frontal regions, which we know, since before, are closely correlated with capacity. From monkey physiology we also know that working memory capacity is linked to dopamine levels in a non-linear way often described as the inverted U curve, so there is an optimal level of dopamine for working memory performance.

We have also looked at dopamine. In one study we had 13 healthy volunteers, did five weeks of training (Klingberg et al., 2005). We measured working memory capacity before and after. We mapped the brain regions activated by working memory performance and the receptive density of D1 and D2, dopamine receptors, before and after and using both linear and non-linear models we could show that there was a correlation between baseline performance and improvement and the change in D1 cortical receptor density. And this is also paralleled now by studies in mice doing working memory training actually where they also see changes in cortical D1 receptors (McNab, Klingberg et al., 2009). So, dopamine seems to be a key factor here, also not only for capacity, but also for training and this is also seen is some studies of the genetics of working memory training.

Here is one sample of that. We had 251 children, between 6 and 16, doing 25 days of training and here is how they improved during training so that is only on the trained tasks (Söderqvist et al., 2013). Here is the percentage change on the trained tasks over these individuals so in general they improved about 20%, 25% on the trained tasks, but there is a large variability here and we wanted to see if that had anything to do with any candidate genes previous linked to learning or working memory capacity and we found two of these snips associated with DRD2 receptors, that were related to training improvement. So, what that looks like here is depending on which version you have you improve differently much.

There has been links now to both, to DAT-1 and to DRD2 receptors concerning genetics and working memory training and these two

receptors they also work in close proximity so DRD2 is the receptor reacting to dopamine and DAT-1 is the one picking up dopamine from the synaptic cleft and also a lot of imaging studies pointing to the striatum as important for the training effects (Olesen et al, 2004; Dahlin et al., 2008; Backman et al., 2011). So, capacity associated with frontal-parietal areas, striatum possibly having to do with the plasticity of the system.

Here is the summary from our recent review. We have tried to summarize research on the neuroscience of working memory training and that has been both imaging studies in green here we can see that we have modulation of frontal-parietal activity, some studies showing increase and some showing decrease and this is a bit difficult to pick out still. One big confounding, in many of these studies, is the reaction time, the time on tasks, often when you train on a task you get faster, if you get faster you solve it in a few hundred million seconds earlier and you get less BOLD responses, so it is difficult to say anything about the mechanisms but we know the regions that are involved at least and we have this fronto-parietal network that is consistently modulated. And a lot of studies both using fMRI and EEG showing higher functional connectivity between frontal and parietal cortex, which is interesting but it goes together with the stimulation studies suggesting that functional connectivity is a key to capacity.

And changes in striatal dopamine release from pet studies. We have genetic studies showing gene independent differences dopamine signaling that affects how much we improve from working memory training.

A number of studies has also come up from Christos Constantinides lab where they looked at monkeys doing working memory training. What they see there is increasing firing rate during the delay, so increased after training in higher frequency. We also see more neurons with delay activity. So, this is of course not new neurons, there is no neurogenesis in the pre-frontal cortex, but rather, probably, neurons that are devoted to this task that were not as devoted before through changes in connectivity. And again, the pink area shows the suggestions from computational studies, suggesting that we have strengthening of inter-network connectivity contributing to this capacity.

As I said, there are two fields from working memory training. One the more experimental and the other can be potentially useful as

an intervention and in that case for what. And people have, as I said, working memory has been correlated with a lot of stuffs, so in principle you could expect to be a treatment for everything, so people have looked at attention, people have looked at IQ, mathematics, reading, dementia, school performance, etc. and many of these fields you do not see an effect. For example, for IQ there is no consistent evidence I would say that working memory training enhances IQ, but on the other hand IQ is very difficult to measure so perhaps in the future we could define a small section of or some particular aspects of IQ that could be enhanced. Similarly, mathematics and reading are a very broad field and there are not consistent effects here. I will get back to mathematics. I would say that right know the most consistent effects are for attention, which is not surprising given the close link between working memory and attention.

In our 2005 study we used questionnaires asking about ADHD symptoms about inattention and showed that this is improvements in the treatment group and in the control group after training and after follow-up. There were a significant decrease in inattentive symptoms but not for hyperactivity and impulsivity, which again makes sense. And a pretty OK effect size immediately after of 0.7 here (Klingberg et al., 2005).

Another study was done in young and older healthy adults by Brehmer et al. (2012). This is an independent research group doing randomized controlled, blinded study, of the same type of training. They had young and old subjects and they could first show that you had transferred to non-trained tasks in this task called PASAT, which is remembering and adding a stream of digits that are presented to you. But they also used a measure of inattention in everyday life and found a significant decrease of attentiveness in both old and young subjects.

Another study, again randomized controlled blinded study looked at children with ADHD (Green, Schweitzer et al. 2012). They used a task called Restricted Academic Setting Task (RAST) and that is a kid is put in what looks like a school bench and given a boring task to do and then there are a lot of toys surrounding and they are been filmed and all aspects of their behavior is being recorded and that recording is afterwards rated by blinded raters, regarding a lot of symptoms, such as if they are fidgeting and if they are exactly looking at what they are supposed to look rather than looking out at the window or at the toys besides them.

And that turned out to be one the most significant effect when the kids were looking at what they were supposed to look at or were looking at somewhere else. But the overall symptoms was an improvement also for the treatment group relative to the control group. I think this is a very nice type of measurement because it also gets the ecological valid aspects of attention and working memory and I don't think that you see this kind of effects if you ask a teacher ratting ADHD symptoms only.

There has been another, at least 3 others randomized controlled studies of this. This is 66 children randomized controlled study showing an improvement in inattention. This is again a randomized controlled blinded study of the same type of Cogmed working memory training showing effects for kids, who were cancer survivors, showing improvement in inattention in everyday life.

There are also a lot of other studies that are not all of them randomized controlled, with active control groups. Overall you see an effect size of around 0.4 for the attention effects (Spencer-Smith & Klingberg, 2015) and this is getting back to your point here Rainer about effect sizes, which I think it is a very important question regarding all of these types of interventions and the question is "Should we be happy with 0.4 or not?". First of all, I think that this can be improved. I think that we will learn for each category of children or adults this works or not works. For example, I think one of the most negative findings is the one by Chacko where they had five years old from low SES areas, problematic families, where around 50% of the kids also had oppositional defiant disorder, so this is a very difficult group to attack and probably we should not, probably one the of the least responsive group. If we, by having a lot of studies, gradually know for each group it works better or worse I think that we will be able to improve the overall effect sizes too.

But even it turns out that it is only 0.4 I think we should be happy. For example, the effect of SSRIs on severe depression is not stellar and it is around 0.3 if we talk about severe depression. If we talk about moderate depression it is even lower. If we look at methylphenidate, if we look at the cognitive effects. So, we know that it makes kids seat still in class but if we look to the cognitive effects and measure them, objectively, the effects are around 0.26. If we are looking at other non-drug effects such as physical training we have an effect size on working memory around 0.13

and this is the immediate effect, directly after physical exercise. If we look at the long-term effect it is close to 0. So, I think that even if we stay with an effect size of 0.4, we should be happy with this. It is very difficult to change cognitive abilities in the long run.

There has been interest in a lot of different fields for what memory training could be useful for. One of them is mathematics. So why mathematics? Well we know that working memory capacity is correlated with arithmetical performance in both children with and without known learning difficulties (Henry & MacLean, 2003; Kytttälä et al, 2003; Maybery & Do, 2003; Alloway et al., 2005, 2009; Geary et al. 2009; Meyer et al. 2010). Working memory capacity also predicts future development of arithmetical ability (Jarvis & Gathercole, 2003; Gestern et al., 2005; Bull et al., 2008; Dumontheil & Klingberg, 2012) and working memory and reasoning ability contribute partly unique variance to predict arithmetic (Alloway & Alloway, 2010; Dumontheil & Kingberg, 2012).

So, we have been looking at this in some studies. This is a study from a large longitudinal developmental study we used. So, we picked out brain activity when kids performed working memory tasks in the scanner and we can show that this signal in itself predicts future math scores 2 years later, above and beyond what can be predicted from cognitive measures at the same time.

We have also tried to dig in to the details of the parietal cortex that we heard about previously here regarding attention. In this study we looked at different aspects of different parts of the parietal cortex and could show that we have overlap, in this case specifically in the frontal part here, overlap is involved in both visuo spatial working memory and mathematics. There were some interesting trans here too that in younger children we saw a relationship for both working memory and mathematics. Later it was only mathematics. So possible generally spatial attention, spatial working memory area that gets tune into being more and more of a mathematical area. So, there are a lot of links between visuo spatial working memory and mathematics.

Know what happens during training? Well it is not as simple as we would expect. So, there are least now six different studies looking at the effect of working memory training (Dahlin et al., 2013; Holmes et al.,

2013; Holmes et al., 2009; Dunnings et al., 2013; Bergman-Nutley, 2014; Roberts, 2016).

All of this is Cogmed working memory training and its effects on mathematics and in some we see significant effects. In some we see small non-significant effects. In some, with a lot more subjects, we see small but significant effects, and large study with no effects at all. But of course there are a lot of problems. Mathematics is not one thing. There are many aspects of mathematics. We don't automatically learn new concepts in mathematics just because you can pay attention or keep information in mind. So, I think that in the future we should learn and look at more specific aspects of mathematics.

But we wanted to look at this and see "Could it possibly be the case that you should do working memory training and mathematics at the same time?" And we were also independently interested in learning about mathematical training. So, we had a study with combined working memory and number-line training. So why number-line training? Well I don't have really time to go into this but there is lot of evidence suggesting that the link between working memory and mathematics partly has to do with the spatial aspect of mathematics and that the number-line representation of numbers is especially important and that is number-line there you make a connection between the spatial point and the number. So, we had four groups. One group doing only reading training. One group doing 50% reading training, 50% memory training. One group doing 50% reading training, 50% number-line training; and one group doing 50% number-line training and 50% working memory training. So, they did these for 30min per day for eight weeks, for an average 38 days. So, it is about 19 hours of training (Nemmi et al., 2016). This was 6 years old mostly typically developing children, some of them with low working memory, most often they do it in a class environment like this, with i-pads. So, we developed, together with two other mathematical researchers Pekka Räsänen and Ola Helenius, this mathematical training tool where kids have a number-line here so in this very easy task they see the number 6 and then they take their index finger and drag, so they really interact with the screen, and drag out a number-line or a victory to this point here - 6. So just this easy task it combines different representations of what a number actually is. It is a symbol but it also a

place on the number-line where is neighbored with 5 and 10, it is length that corresponds to the meaning of the number but they can also make the connection to counting, by counting these smalls squares.

We also included working memory tasks, a couple of them, all of them visuo-spatial. We had pre- and post-measures, a battery of working memory tasks, a battery of mathematical tasks and we did imaging on subgroup of these children. We analyzed it in a factorial way and what we found was that there was no effect of only doing working memory training so on average they did not improve more because they had working memory training. We do have a significant effect of doing the number-line training but there wasn't interaction between working memory baseline performance and whether they did working memory training and on average we can see here the group that performed best was the group that combined working memory training and number-line training. But the interesting thing with this study was I think all the interactions we had. So, this is one example of the interactions, so what we see here is performance at baseline, so all of this are z-scores so they are centered around zero, so zero minus does not mean that you get worse, zero means that you are average. So, based on what performance you had at working memory in baseline the game from doing working memory training is different. So, if we do a split-half measurement, the kids with higher working memory at baseline actually improve more from doing working memory training. They gain more mathematical improvements than the others. Here is some illustration of the same thing. We split up kids based on working memory performance and based on mathematical performance and we see about three-fold differences in how they respond to different types of training depending on their baseline performance and first we analyzed this linearly but it might not be only linear effects. Here is showing the same thing here, how kids respond to working memory training based on baseline mathematical performance and based on working memory performance we can see very non-linear trans here to.

Then we also looked at brain imaging to see if we had effects there. So, we had both measures of grey matter density and brain activity and we could show that for a number of regions, those in red here, they gave us information about how the kids improved on specific types of training. So, for example, the case of working memory training was related to the

amount of grey matter volume they have in the right parietal cortex. So, if you have a high grey matter volume or a low grey matter volume, you respond differently to the different types of training. And this contribute significantly up and above behavioral measures.

I will not go into details of interpreting all of this but I think it is a basic proof of principle that individuals differ in how they respond to different types of cognitive training and this or mathematical training and behavioral measures might contribute to this profile, brain imaging might also contribute to this profile.

What we are doing right now is this program, the mathematical program combined with cognitive training is based from this non-profit foundation. So, we are getting a lot of kids now that are trained with this so since we put this out, for free on app store and google play, we now have a quarter of a million kids registering during the last one and a half year for this, which gave us a lot of data to try to further improve this and see if we can find the cognitive profiles and how they respond to different types of training.

And what is also nice is that this type of mathematical training is totally non-verbal, is not a single world, either in the mathematics or on the working memory training, which means that the same program can be used and it is used in smaller studies around the world. We have a pilot study in India, in rural Australia, Uruguay and running several projects in Mexico also to try to help kids learn mathematics by this way.

So, to conclude, working memory training improves working memory and that is not a trivial thing in itself. For example, it could be a pretty good thing to be able to remember instructions better in everyday life.

The most consistent findings is in its ability to improve attention in everyday life and this make a lot of sense giving the close association between working memory and attention.

Regarding other tasks, such as mathematic, IQ, reading, grades it is still inconclusive. I think, of course, we need more studies, we need to look more carefully at this specific outcomes measures and specific groups.

For the future directions, I think we need better measures of inattention, ADHD rating scales will not do in the future for research. We need tasks ecological valid and objective measures of inattention.

The question of effect sizes is very important and it also has implications for what kind of research you should do. People in the beginning, including us, were very enthusiastic, did studies with twenty subjects. It will not work in the future. If we expect sizes around 0.3, 0.4, 0.5 it means that we also need to have hundreds of children in the training groups in order to see effects.

There is a lot of interest and ongoing studies about combined training, so that means working memory training plus something else, such as working memory training plus mathematics as I show, or plus other cognitive functions. We heard here, earlier, about tDCS or other kind of direct current stimulation, alternating current stimulation (tACS) or random noise stimulation (tRNS). We have tried that and it failed. It only made the working memory training work less well. Other groups have also failed, but some groups have positive findings and I do think that it could be a very interesting field in the future to look at.

Some studies are starting to look at the combination of drugs including drugs that affect the dopamine system because we know about the link, also looking at the combination of physical and cognitive training. But, whatever the combination is, studies such as the last one that I show here, emphasized that we should also be thinking more in individualized training. The kind of combination you should have, how you should do it, what you should do, might depend on the individual. And I think that continued research, specially continued research combining cognitive and neuroscience research will be the way forward and we that I would like to thank you very much for your top-down attention.

DERANGEMENT OF THE SENSES OR ALTERNATE EPISTEMOLOGICAL PATHWAYS? ALTERED CONSCIOUSNESS AND HUMAN POTENTIALS [1]

Etzel Cardeña [1/*]

Le poète se fait voyant par un long, immense
et raisonné dérèglement de tous les sens.
(The poet becomes a seer through a long, immense
and systematic derangement of the senses)

Arthur Rimbaud, in a letter to Paul Demeny, May 15, 1871

The outrageously precocious 16-year-old Arthur Rimbaud, about to demolish the conventions of the poetry of his time, wrote that a visionary artist needed to embark into a long and systematic derangement of the senses. He then proceeded to embody the worst stereotype of a bohemian, imbibing various types of drugs and having drunken brawls with his lover, the also poet Paul Verlaine, who ended up shooting him in the wrist. At 21, after changing forever the nature of poetry, Rimbaud retired from the world of letters to become a trader in coffee beans, rifles, and slaves. Despite Rimbaud's recommendation to an incipient poet, some would interpret his story as a cautionary tale for those seeking to affect their consciousness, but this paper focuses on the positive changes related to alterations of consciousness, granting that at times some alterations are related to deleterious medical and/or psychological effects. I will first clarify basic concepts about altered consciousness, discuss strengths and weaknesses of the "normative" waking state of consciousness, review research on how altered consciousness relates to enhanced psychophysiological functions, and then discuss whether alterations of consciousness can provide alternate valid epistemological pathways to that of the normative state of consciousness.

---

[1] This is an abbreviated version of a paper with a similar title (Cardeña, 2018a). I am thankful for Prof. Caroline Watt's editorial assistance.

* Lund University, Sweden.

Altered Consciousness

In his treatise on religious experiences, William James set up the agenda for the study of alterations of consciousness, along with their potential functions:

> "Our normal waking consciousness, rational consciousness as we call it, is but one special type of consciousness, whilst all about it, parted from it by the filmiest of screens, there lie potential forms of consciousness entirely different… at a touch they are there in all completeness, definite types of mentality which probably somewhere have their field of application and adaptation." (James, 1902/1958, p. 298)

But even earlier, in his magisterial and best-selling *Principles of Psychology* (1890) James sought to integrate the ordinary with other states of consciousness, for instance in his chapter on the Self, in which he covered both its traditional sense and its alterations in dissociation and possession. A comprehensive psychology that would integrate our understanding of various states of consciousness was, however, stillborn, with academic psychology choosing a behaviorist stance that proscribed the study of conscious experience, and a clinical psychology too eager to split asunder human nature into sane or pathological. Only the marginalized psychical research/parapsychology community continued to systematically investigate the characteristics and potential functions of altered consciousness (e.g., Sidgwick, 1915).

Mainstream psychology would have to wait for decades until the political and intellectual movements of the 60s embraced the exploration of states of consciousness through psychedelics, meditation, and other means. A short but very rich article by Arnold Ludwig (1966) contributed a definition of "altered states of consciousness" and Charles Tart (1975) and Robert Ornstein (1986) arguably became the most important theoreticians in the area. Despite these contributions and the many empirical studies since, a discussion of altered consciousness as a necessary component in the social and biological sciences has been mostly absent, although there are signs of some integration of the topic into psychology (Cardeña, Lynn, & Krippner, 2017) and other disciplines (Cardeña & Winkelman, 2011).

Included in my use of *altered consciousness* are three different but interrelated concepts: *altered* (or alternate, see Zinberg, 1977) *state of consciousness, altered trait of consciousness,* and *induction procedures* to elicit altered states. Natural concepts are "fuzzy" and have vague boundaries (Lakoff, 1973) and these three are not an exception. I endorse Tart's (1975, p. 5) definition of a distinct (or discrete) altered state of consciousness (ASC) as a "unique, dynamic pattern or configuration of psychological structures, an active system of psychological systems," which differs qualitatively from the individual's ordinary state of consciousness, and can be recognized by the individual him/herself (e.g., someone recognizing a near-death-experience as a very different state from the ordinary one) or sometimes by an observer (e.g., in a variety of more -or-less nonconscious states; Noirhomme & Laureys, 2011).

Whereas ASCs are by definiton transitory and reversible, typically lasting from seconds to some days, an *altered trait (of consciousness)*, a term probably coined by the historian of religion Huston Smith (1995), denotes lasting changes of consciousness in which the baseline state of consciousness has been permanently changed. For instance physiological and cognitive changes that occur only during or shortly after meditation may become a part of the normative state of consciousness of those who have maintained a serious meditation practice for a very long time (Goleman & Davidson, 2017). There are also qualitative differences in the baseline state of consciousness across people that do not involve any practice, such as synesthesia (i.e., experiencing a stimulus in more than one modality, such as always seeing a color associated to a musical tone), which occurs in the normal, waking state of a few people whereas the majority may never experience it or only when in an ASC (Marks, 2014).

And how might ASCs be induced? The list of methods by Ludwig (1966) remains a good introduction: reduction or increase of exteroceptive stimulation and/or motor activity (e.g., decrease in restricted environment stimulation or REST; intense movement and sound in prolonged energetic dancing rituals); increased or decreased alertness or mental involvement (or, more generally, use of higher cognitive processes to affect the normative state, as in meditation and hypnosis); and presence of somatopsychological factors (including psychoactive drugs as well as more recent techniques such as transcranial magnetic stimulation; Dieguez &

Blanke, 2011). Tart (1975) further discussed how personality/cognitive and external variables can disrupt or maintain the equilibrium of a state of consciousness, as in the case of remaining asleep by maintaining a quiet and dark environment. A method of induction is, however, but one variable in the potential alteration of a state of consciousness. Other, interacting, variables include cognitive dispositions, set and setting, cultural facilitation, and so on (Tart, 1975). Laughlin, McManus, and d'Aquili (1992) pointed out as well that whereas some cultures are polyphasic and value alterations of consciousness and facilitate their manifestation through rituals and others techniques, monophasic ones, like contemporary Western cultures, prioritize the waking, normative state and marginalize or minimize alterations of consciousness.

To illustrate the interaction of induction procedures with personality traits, a hypnotic induction may have large experiential and neurodynamic effects on people who have the disposition to respond strongly to hypnosis (i.e., high hypnotizables) but have small and/or contrary effects in those who do not (i.e., low hypnotizables) (e.g., Cardeña et al., 2013). And not only are traits and states interactive processes, but conscious experience is ever changing, and even within the "same" state there may be noticeable changes. For example, people responsive to minimal-suggestion hypnosis may initially experience unusual somatic alterations, while later on they will report mostly imaginative and transcendent experiences (Cardeña, 2009). And even within the "same" group, for instance high hypnotizables, there may be important variations. Research reveals that among highly responsive individuals there are at least two main groups, one that tends to experience imagery in response to suggestions, whereas the other tends to experience lack of cognitive control (Terhune & Cardeña, 2010). Unfortunately very few studies on potential altered consciousness have distinguished and systematically evaluated altered traits, altered states, and their potential interaction with induction procedures.

The Limitations of the Normative State

The focus of this paper is on the potential benefits of alterations of consciousness, but it is pertinent to first discuss the normative, waking

state, ignoring for the moment individual and cultural differences. For a discussion of some individual differences in the baseline, waking state, such as having a lot of or little imagery see Hurlburt & Schwitzgebel (2007). For cultural differences, mediated by environmental pressure, a good example is that the hunter-gatherer Semaq Beri show much better olfactory sensitivity than the neighboring sedentary Semelai, for whom subtle animal odors do not have much survival value (Majid & Kruspe, 2018).

In his paper on "Basic Problems of Consciousness," Natsoulas (1981, p. 162) characterized the normative waking state as prioritizing "distinctions among *what is, what might be, what is not,* and *what cannot be,"* thus having survival value, although he also posed the question "Does the normal waking state consistently involve the pursuit of truth about the world?" (p. 164). In a less nuanced discussion of the topic, Kallio and Revonsuo (2003, pp. 141-142) concluded that any other state than the normative one "creates phenomenal contents of consciousness that misrepresent or create delusional beliefs of the surrounding world and oneself." This assertion assumes that the waking state does not misrepresent reality, a conclusion that has been vigorously challenged in many fronts.

Even while granting that the ordinary state must have adaptive value or humans would have perished, the naïve realism perspective equating the contents of the waking state of consciousness with an accurate representation of "reality" has been seriously challenged by philosophers for milennia. More recently, some important theoretical physicists have concluded that one of the implications of quantum mechanics is that we cannot apprehend reality, which remains "veiled", but only verify the results of particular ways of measurement (d'Espagnat, 2006), and that some form of mentality is intrinsic to that measurement (Kastrup, Stapp, & Kafatos, 2018). Second, various cognitive and philosophical models have concluded that the content of ordinary consciousness should not be taken literally. For instance cognitive psychologist Donald Hoffman (2009) has shown through evolutionary game theory that it is detrimental to have a very precise apprehension of "reality" given the processing demands that would be required. Instead, he concludes that waking consciousness is only required to maintain basic adaptive behaviors, and concludes that

our perception is a simulation (for other views of conscious contents as illusions see Frankish, 2017). Consistent with the view of very limited capacities are analyses showing that conscious awareness can only process a very small fraction of incoming sensory stimulation (Wilson, 2002), which is itself very limited (e.g., humans can perceive only a very small fraction of the electromagnetic spectrum).

The human waking state seems particularly primed to detect relatively large, changing stimuli (Ornstein, 1986), exerting some organization and control (but not much, as evidenced by the difficulties in deliberately maintaining a focus of attention for more than a few moments), biased towards supporting previous expectations, beliefs, and so on. The waking state is geared to attending to expectable or survival-relevant changing stimuli over subtle, unchanging, or trivial unusual ones (Bruner & Postman, 1949; Ornstein, 1986), usually while exhibiting a strong egocentric bias (e.g., Pronin, Lin, & Ross, 2002).

Typically missing from the discussion of the limitations of waking consciousness is the hypothesis adumbrated by James that other states of consciousness may have their function and perhaps circumvent some of the limitations of the waking state. Various religious traditions have also questioned the waking state as an ultimate purveyor of reality, concluding, among other things, that when we are awake we are really in some ways asleep because we do not realize the true nature of things, or that we apprehend reality through the "veil of Maia" of our desires (Hinduism), or through "a glass darkly" (Christianity' St. Paul). Earnest followers of these traditions have often adopted ascetic and introspective practices, which may induce alterations of consciousness, to become aware of general and personal cognitive biases. Ludwig (1966) distinguished between maladaptive and adaptive functions of ASC. The former are not discussed in this paper. For adaptive expressions he listed healing, social functions such as cohesion, and offering different modes of knowledge. I will concentrate on his first and third categories, presenting in the remaining of the paper examples of altered consciousness associated with enhanced psychophysiological functioning and with plausible alternate perspectives on "reality" (social functions of altered consciousness are discussed in Whitehead, 2011). Five caveats are worth stating:

1) I do not claim that altered consciousness is the only way to achieve some of the enhancements I describe below.

2) The relation between potential alterations of consciousness and associated effects does not necessarily assume a causal effect, unless this has been specifically evaluated in a study.

3) I will not be covering "small" changes to consciousness that may slightly improve mood or enhance the experience of life such as the use of caffeine or psychedelic microdosing (Cardeña, 2011; Kitchens, 2018).

4) Many studies have not collected data on which specific alterations occurred.

5) The literature of traditional practices in the East and West have mentioned some of the abilities listed below for which there is scientific evidence, but they have also listed others such as mentally destroying statues or living for hundreds of years for which I could find no empirical evidence (for a review see Cardeña, in press).

Altered Consciousness and Enhanced Psychophysiological Functions

Overviews of exceptional psychophysiological functions have been published, in relation to religious practices by Thurston (1925/2013), and in relation to sports and contemplative practices by Murphy (1992). Although they made implicit or explicit connections to altered consciousness in many cases, that was not the focus of their work. In this section I review research on consciousness alterations and unusual psychophysiological manifestations.

Somatic systems

The literature on the clinical uses of hypnosis contains many experiments as well as case studies giving evidence of what T. X. Barber (1984) called "changing 'unchangeable' bodily processes," in which the "unchangeability" is contrasted with what tends to occur in the waking state. With respect to dermatological conditions, an old but still worth citing case is Mason's (1952), who treated a patient with a genetic condition (congenital erythodermia) believing it to be psychosomatic. The photos in his paper show that a severe and pervasive condition that had not responded previously to any treatment started healing dramatically in a matter of days. More generally, but less attention-grabbing, is a study by

Spanos, Williams, and Gwynn (1990) showing a hypnotic intervention to be the only effective treatment against warts as compared with salicylic acid, placebo, or no treatment. There is also considerable evidence that hypnosis may affect directly and indirectly the gastric system, particularly in the treatment of irritable bowel syndrome (Schaefert, Klose, Moser, & Häuser, 2014). A general review by Benham and Younger (2008) found evidence that hypnotic interventions can affect blood pressure, enlarge breasts, improve gastric motility, improve asthma, affect allergic reactions, treat dermatological conditions, affect the immune system, perhaps affect wound healing, and improve gastric conditions, but deplored the lack of a programmatic evaluation of mediation processes.

There have also been single observations of unusual healings of intractable conditions related to altered consciousness, such as an inoperable brain condition that seemed to heal in conjunction with having a near-death-experience (Dossey, 2011). It is important to mention that to call such cases "spontaneous remission" just provides a label rather than an explanation. Furthermore, apparently successful non-allopathic healing ministrations have been related to alterations of consciousness, although there has been little systematic research on the topic (Krippner & Achterberg, 2014; see also Esalen Center for Theory and Research's online "Database of Extraordinary Human Function," https://www.esalen.org/ctr/scholarly-resources/database).

Heart rate control

Laboratory studies with single individuals (e.g., Green & Green, 1977) and small groups (e.g., Wenger, Bagchi, & Anand, 1961) of long-term yoga practitioners have reported their ability to willingly induce heart fibrillation, and slow down or even momentarily stop the heart rate. A meta-analysis reported that Yoga practice can affect heart rate variability, although many of the studies conducted had methodological limitations (Tyagi & Cohen, 2016).

Stigmata and bleeding control

Stigmata, very rare and apparently spontaneous and uncontrolled wound marks or bleeding, typically in the locations identified with Christ's (depicted) crucifixion, have been observed in dozens of individuals

throughout history (Thurston, 1925/2013), some of them reporting an intense attentive and emotional focus on Christ's ordeal (Murphy, 1992). A few cases have been evaluated systematically to rule out fraud and general medical conditions such as hematidrosis (e.g., Margnelli, 1999).

Genuine stigmata do not seem to be under the person's control, but there are reports of precise beginning or stopping of bleeding with an Eastern meditator (Murphy, 1992) and a Western one (Green & Green, 1977). Hypnosis research also provides some evidence of the ability to control the vascular system. For instance, specific hypnotic suggestions to experience a phlebotomy evoked similar physiological reactions to those of participants undergoing the procedure, but mere hypnosis or rest did not produce that effect (Casiglia et al., 2017). There have also been observations and a laboratory study of Islamic Sufi dervishes inflicting themselves severe body damage with razor, glass, and similar materials, exhibiting little or no bleeding and very rapid healing (Hall, 2011). The Sámi Nordic tradition describes healers who can stop the bleeding of other humans and sentient beings (Sexton & Buljo Stabbursvik, 2010), but I could not find an experimental study of this claim.

Reduced metabolism

Ascetic yogis have claimed to reduce or even suspend their need for food, water, and even oxygen. Kothari, Bordian, and Gupta (1973) tested a yogi buried in a pit for eight days without access to water or food, who seemed to stop his heart until just before being brought out, at which point he was emaciated. There have also been case and group studies with yogis showing decrease of O_2 consumption between 40% (Craig Heller, Elsner, & Rao, 1987) and 32% (Telles, Reddy, & Nagendra, 2000). There is also evidence of an altered trait in that baseline respiration rate among long-term meditators with retreat practice was significantly lower than that of non-meditators (Wielgosz, Schuyler, Lutz, & Davidson, 2016).

Ability to withstand cold temperature

Ascetic practices can involve enduring very cold temperatures and studies support the ability to generate exceptional body heat in such circumstances. *G Tum-mo* yoga involves the intention to generate bodily heat while meditating in very cold environments. Benson et al. (1982)

found that three long-term practitioners could raise the temperature of their fingers and toes by up to 8.3° C. A later study of the same practice suggests that the mediating mechanisms include controlled breathing and visualization (Kozhevnikov, Elliott, Shephard, & Gramann, 2013).

The holder of various world records for enduring cold temperatures, Wim Hof, has been studied in the lab. His practice of hyperventilation and attentional focus produced significantly larger changes in cortisol release and immune response attenuation than those of a control group (Kox et al., 2012). Some of these researchers (Kox et al., 2017) later trained a group in Hof's physical and meditation techniques, and, after inoculation of bacterial endotoxin, compared them to a control group. The trained individuals exhibited substantial increases in the release of epinephrine and a reduction of the cytokine inflammatory response to the endotoxin. Although this set of studies is exemplary in studying thoroughly a person with an extraordinary ability and then using his techniques to train others, Kox et al. (2017, p. 7379) falsely claim that "Hitherto, both the autonomic nervous system and innate immune were regarded as systems that cannot be voluntarily influenced" when the decades-long research on biofeedback pioneered by Miller (Dienstfrey, 1991) has shown some voluntary control of autonomic activity, and research on hypnosis (e.g., Olness, Culbert, & Uden, 1989) and meditation (e.g., Davidson et al., 2003) had found the same for immune responses.

Skin temperature control can be very precise. Hypnotically trained individuals produced opposite changes of temperature in each hand (Maslach, Marshall, & Zimbardo, 1972), and an Indian swami showed the same phenomenon between the sides of a hand (Green & Green, 1977).

Analgesia

There are many descriptions of intentional infliction of painful stimuli in the context of religious ritual with apparent imperviousness to the pain, including in the Malaysian Thaipusam festival (Simons, Ervin, & Prince, 1988), some Sufi dervish practices (Hall, 2011), and the ascetic Christian tradition (Thurston, 1925/2013). In *Vodou*, not reacting to burning and painful stimuli can be used as a demonstration of being possessed (Broch, 1985), and probably the most researched medium in history, Mrs. Piper, did not evidence pain to noxious stimuli while she

was in an altered state although in her ordinary state later she had blisters and enduring pain (Gauld, 1982). Systematic research in both hypnosis and meditation are consistent with the ability to overcome pain while in an altered state. Anand, Chhina, and Singh (1961) describe two yogis who, while meditating, could maintain their hands in 4° C water for 45-55 minutes without evidencing discomfort. Zen meditators exhibited lower pain sensitivity in a thermal pain paradigm as compared with a control group; their ability was correlated with slow respiration rate and meditation experience, and probably mediated by reduced connectivity between executive and pain-related cortices (Grant, Courtemanche, & Rainville, 2011; Grant & Rainville, 2009). In hypnosis research similar experimental pain paradigms have shown that those who are responsive to suggestions can withstand exposure to painful stimuli considerably better than those who are not (e.g., Hilgard & Hilgard, 1975/2013), and the analgesic effect is linked to specific cortical dynamics (Rainville et al., 2002). The analgesic effects of hypnotic suggestions in laboratory and clinical samples were found to be medium to strong in a meta-analysis (Montgomery, DuHamel, & Redd, 2000) and small in a meta-analysis of mindfulness meditation (Hilton et al., 2017). So far I have emphasized phenomena with a more central somatic component and will now discuss those with a more direct cognitive component.

Perceptual sensitivity

Murphy (1992) listed reports by athletes and contemplative practitioners of extraordinary sensory abilities after intense focusing activities, including enhanced vision, hearing, touch, smell, taste, and even synesthesia. There is some experimental evidence for enhanced visual perception. Participants in a mindfulness meditation retreat increased their discrimination sensitivity to two tasks involving light flashes, whereas a control group did not (Brown, Forte, & Dysart, 1984). In another study, practitioners in a focusing meditation retreat exhibited significant increases in perceptual sensitivity/stimuli discrimination (related to hours of practice) across time and in comparison with a waiting-list group (MacLean et al., 2010).

Attention control and cognitive deautomatization

Meditation practices include self-generated attempts to exert greater control or awareness of attentional and related cognitive processes. Enhancements have been found for, among others, selective attention (Jha et al., 2007), continuing to pay attention to repetitive stimuli (Antonova et al., 2015; Kasamatsu & Hirai, 1966), and vigilance/sustained attention (MacLean et al., 2010). The findings, however, have not been completely consistent (Cardeña, Sjöstedt, & Marcusson-Clavertz, 2015; Lao, Kissane, & Meadows, 2016), perhaps due to comparing different types of meditation and amount of hours spent in them (Goleman & Davidson, 2017).

Furthermore, meditation and hypnosis have been shown to reduce or even sometimes annul what had been previously been considered automatic, unchangeable cognitive processes, including the Stroop effect (Raz, Moreno-Íñiguez, Martin, & Zhu, 2007), synesthesia (Terhune, Cardeña, & Lindgren, 2013), and "attentional blink" (Slagter et al., 2007).

Creativity

Creative insights in science and the arts have been related to alterations in consciousness, including deep relaxation and transitional awake-sleep-awake states (Mavromatis, 1987), dreaming (Hartmann, 1996), and "microdosing" on psychedelics (Kitchens, 2018). A few controlled studies support a relation between creative insights and more associative, less rigid cognitive states, including: a) visual arts originality while taking psychedelics (e.g., Krippner, 1985), b) improved creative drawing after hypnotic suggestions (Council et al., 2007), and c) enhanced creative problem solving while mildly intoxicated with alcohol (Benedek et al., 2017).

Positive affect

Although not universally so, mystical-type states of consciousness are typically described as blissful and serene, whether they arise spontaneously, through the use of hallucinogens or following hypnotic or meditation procedures (Cardeña, 2005; Griffiths et al., 2006; Wulff, 2014). As a participant in a hypnosis experiment describing her simultaneous experiences put it: "All the feelings that are good just surround me... It's

really great" (Cardeña, 1988, p. 128). A sense of equanimity and positive affect seems to become a more permanent feature in the case of long-term meditators (Easterlin & Cardeña, 1998/1999), which may parallel reduced amygdala reactivity even while not meditating (Desbordes et al., 2012).

Personality change

Altered traits may follow even one experience of an altered state of consciousness. A study on the effects of controlled ingestion of psilocybin showed an increase of the trait *openness to experience*, mediated by having a more comprehensive mystical experience (MacLean et al., 2011). Long-term increases in spirituality, concern for others and the environment, appreciation of life, and decreases in fear of death, materialism, and competitiveness have resulted after near-death (Greyson, 2014) and different types of mystical experiences (Wulff, 2014).

Diagnosis and Treatment

An area deserving further study is whether medical conditions diagnosed later may be inferable from the earlier content of dreams. Studies supporting this contention include cardiac dysfunction (Smith, 1987), cancer, (Burk, 2015), and a case study of viral encephalitis (Sacks, 1973). It may be that somatic dysfunction at a very subtle level and not detectable at a conscious level nonetheless affects dream content. There is also the possibility that dreams may precognize an event into the distant future and before, perhaps, there is any detectable somatic marker (see below).

There is much more research on the use of hypnosis and meditation in the treatment of diverse medical and psychological conditions. Besides producing analgesia and changes in epidermic and gastric systems, there is consistent evidence that hypnosis can be helpful in the treatment of anxiety, depression, stress, sleep disorders, posttraumatic symptomatology, smoking, and obesity (Cardeña et al., 2009; Mendoza & Capafons, 2009). Different meditation approaches have also been profitably used to treat, among others, depression, anxiety, stress, and borderline personality disorders (Goleman & Davidson, 2017). And ingestion of psychedelics in clinical and naturalistic settings has been beneficial in the treatment of alcoholism, anxiety related to death, depression, smoking, and obsessive-compulsive symptoms (Garcia-Romeu, Kersgaard, & Addy, 2016).

Altered Consciousness, Noetic Experiences, and Psi Phenomena

A central component of a mystical experience is its noetic quality, which William James described as "states of insight into depths of truth unplumbed by the discursive intellect… [which] carry with them a curious sense of authority" (William James, 1902/1958, p. 380-381). In more pedestrian prose, it refers to a sense of having gotten a glimpse of a basic aspect of the nature of reality. To give another example from the research with the spontaneous experiences of high hypnotizables, a different person than the one quoted above stated: "This is the best place to be… I am out in the brightness… I am not matter anymore; just nothing physical, not even color. I'm just energy. Things don't happen here… it's a matter of being…here there's no time and no space" (Cardeña, 1988, p. 136-137).

It is very challenging but also potentially very important to try to make sense of the ontological value of such experiences. There is no doubt that some of the "epiphanies" produced by transcendent experiences are clearly false or trite, as exemplified by some of the "insights" that a person may have while intoxicated that later turn out to be absurd, or the spiritual clichés and triteness of many mediumship/channel communications (Hastings, 1991). But the question remains whether the central aspect of a mystical experience of interconnectedness is nothing more than a wish-fulfillment delusion.

Interconnectedness is an essential aspect of reality in the models of some important theoretical physicists (e.g., Bohm, 1986; d'Espagnat, 2006), in religious traditions (e.g., Wulff, 2014) and is an implication of psi phenomena (Marshall, 2015), but these strands by themselves do not provide evidence that transcendent experiences may elicit a valid glimpse of consensual reality. Greater validation would come if alterations of consciousness provided evidence that experients can accurately access information that implies the abeyance of our usual sense of temporal and spatial constraints. For this, it is important to evaluate whether individuals in altered consciousness can better access such information than in the normative state.

Parapsychology or psi is the study of such phenomena as ostensible telepathy, in which a person seems to be affected by the thoughts or emotions of someone else, unmediated by the senses or reason, as when

someone suddenly has a sense of the unexpected death of a beloved one, precisely as that event unfolds unpredictably in another place. Psi research also investigates the ostensible direct effect of intention on physical systems such as random number generators. The use of the scientific method to evaluate the potential validity of psi phenomena has a long history and many eminent scientists have supported this endeavor empirically and/or theoretically (Cardeña, 2015). Comprehensive reviews of the experimental evidence for these phenomena, underlying theories from physics and psychology as well as skeptical counterpoints, are offered in two recent comprehensive anthologies (Cardeña, Palmer, & Marcusson-Clavertz, 2015; May & Sarwaha, 2015) and a review of more than 10 meta-analyses (Cardeña, 2018a).

Research on naturally occurring ostensible psi phenomena has found that they often occur during alterations of consciousness such as dream sleep or *twilight* states between awakening and sleep (Sandwald, 1963). Although finding consistent patterns in the natural occurrence of psi phenomena is basic to ascertain their nature, it is difficult or impossible to evaluate alternative explanations in occurrences during "everyday life." To be able to discard reasonable competing explanations such as biased recollections or randomicity of an occurrence requires experimental paradigms that can control for these and other variables. Many experimental paradigms have systematically evaluated a possible link between altered consciousness and psi phenomena.

Probably the first set of meta-analyses of a relation between altered consciousness and psi scoring was Charles Honorton's (1977). He proposed that during the normative state of consciousness (the very subtle) psi information usually does not become salient given the primacy of perceptual and other processes. His cumulative analyses of research showed significant associations between what he called *internal attention states* (meditation, hypnosis, relaxation, and sensory deprivation) and accurate scoring in psi tasks. Since his publication there have been new or updated literature reviews or meta-analyses, all supporting a relation between psi and altered consciousness, including papers on psi and meditation (Roney-Dougal, 2015), hypnosis (Stanford & Stein, 1994), dreaming (Storm, Tressoldi, & Di Risio, 2010), and psychedelic experience (Luke, 2015).

The area of psi research with the longest and most consistent set of experiments supporting psi phenomena, even after improving the methodology following the guidelines co-proposed by a skeptic (Hyman & Honorton, 1986), follows a procedure called ganzfeld to enhance internal focus. It involves sitting in a comfortable chair, listening to relaxation suggestions, and being exposed to homogeneous visual and auditory stimulation, while trying to detect spatially or temporally distant information chosen randomly. Various meta-analyses of research spanning dozens of labs across the world have reported that participants in ganzfeld choose the correct stimulus at a rate that significantly exceeds chance; furthermore, although the results of experiments using a ganzfeld protocol do not differ significantly from those using other inductions such as meditation or hypnosis, they show a bigger effect than those not using any induction procedure (Storm et al., 2010). Another important meta-analytic finding is that individuals who engage in some type of mental practice (meditators but also artists) perform noticeably better than those who do not (Baptista, Derakhshani, & Tressoldi, 2015).

The assumption of Honorton was that exposure to ganzfeld induces an alteration of consciousness, but this has been rarely evaluated systematically in the psi experiments themselves. More generally, it is known that ganzfeld can elicit alterations of consciousness that differ from being sleepy (Wackermann, Pütz, & Allefeld, 2008), and that such effects interact with traits such as hypnotizability and dissociation (Marcusson-Clavertz, Terhune, & Cardeña, 2012). Nonetheless, when a systematic evaluation of the state of consciousness has been carried out during psi experiments, there has been an association between experiencing an altered state and performing well in the psi task. The specific alterations related to psi include alterations in the sense of time, reduced body awareness, an experience of self-transcendence, increased absorption, and less arousal and internal dialogue (for a review see Cardeña & Marcusson-Clavertz, 2015). A general sense of being in an ASC among high hypnotizables has also been found to have medium to large correlations with psi scoring in two studies using similar protocols (Cardeña & Marcusson-Clavertz, 2019; Marcusson-Clavertz & Cardeña, 2011). In sum, the noetic sense that mystical experiences of interconnectedness describe real events is grounded not only on intense experiences but, more importantly, on

research data showing that altered consciousness seems to allow greater access to, or greater awareness of, information not mediated by the senses or reason, and interpretable as evidencing interconnectedness in nature.

Conclusion

The proposal by James that some forms of altered consciousness have "their field of application and adaptation" has empirical support from multiple areas of research. This review shows evidence for psychophysiological enhancements associated with alternate consciousness, and for the possibility that they may provide valid information. Thus, it is legitimate to conclude that the normative, waking state of consciousness is not optimal for all functions, but should be thought of as having a basic survival value with a number of inbuilt structural and functional limitations. The characterization by Carhart-Harris et al. (2014) of the waking state as leaning towards low entropy, low disorder, and somewhat rigid processing of information (cognitive "stickiness" in meditation terms) is consistent with a generally adaptive strategy. Other states, however, seem to bypass temporarily or more permanently some of these restrictions (although of course they may have their own inbuilt particular limitations). To give but a few instances, meditation and hypnosis increase continuity of attentional focus (Cardeña & Spiegel, 1991; Goleman & Davidson, 2017); dreams and ganzfeld procedures allow, by decreasing exteroceptive stimulation, awareness of subtle information that would otherwise go undetected (Honorton, 1976); psychedelic, near-death, and mystical experience can provide different ways of conceiving of, and feeling about, such important topics as one's death or the centrality of one's being; and dreaming and intoxication with various substances may provide looser and more metaphorical associations than the waking state, which may provide valuable insights about oneself and/or the solution of problems. Olness et al. (1989) pointed out that cyberphysiologic techniques such as hypnosis are more easily learned by children than by adults, so Huxley's idea of early hypnotic training in his novel *Island* has an anchor in research, and meditation techniques are being pioneered in some schools (Goleman & Davidson, 2017).

Although in the last few decades programmatic studies have been launched on the effect of contemplative practices and the effect of psychedelics, many other areas reviewed in this paper have been scarcely researched and are typically ignored in theoretical discussions of consciousness. This may partly reflect the rareness of some phenomena (e.g., stigmata), but it probably has more to do with not treating altered consciousness as a central component of the features of consciousness and cognition. This is unfortunate considering the potential benefits that could accrue, among them resetting the boundaries of what are considered automatic cognitive processes or "unchangeable" physiological processes, developing more powerful therapeutic interventions, evaluating the effect of intention on psychophysiological processes, increasing the likelihood of accurate psi cognition, and, ultimately, understanding better the nature of consciousness, both normative and altered. The attempt by William James, F. W. H. Myers, and others (Kelly et al., 2007), to integrate altered consciousness into general psychology is empirically warranted and deserves greater attention by researchers and theoreticians.

References

Anand, B. K., Chhina, G. S., & Singh, B. (1961). Some aspects of electroencephalographic studies in Yogis. *Electroencephalography and Clinical Neurophysiology, 13,* 452-456.

Antonova, E., Chadwick, P., & Kumari, V. (2015). More meditation, less habituation? The effect of mindfulness practice on the acoustic reflex. *PLoS ONE, 10,* doi.org/10.1371/journal.pone.0123512

Baptista, J., Derakhshani, M., & Tressoldi, P. E. (2015). Explicit anomalous cognition: A review of the best evidence in ganzfeld, forced choice, remote viewing and dream studies. In E. Cardeña, J. Palmer, & D. Marcusson-Clavertz (Eds.), *Parapsychology: A handbook for the 21st century* (pp. 192-214). Jefferson, NC: McFarland.

Barber, T. X. (1984). Changing "unchangeable" bodily processes by (hypnotic) suggestions: A new look at hypnosis, cognitions, imaging, and the mind-body problem. In A. A. Sheikh (Ed.), *Imagery and healing*. Farmingdale, New York: Baywood.

Benedek, M., Panzierer, L., Jauk, E., & Neubauer, A. C. (2017). Creativity on tap? Effects of alcohol intoxication on creative cognition. *Consciousness and Cognition, 56,* 128-134. https://doi.org/10.1016/j.concog.2017.06.020

Benham, G., & Younger, J. (2008). Hypnosis and mind-body interactions. In M.

Nash & A. J. Barnier (Eds.), *The Oxford handbook of hypnosis: Theory, research, and practice* (pp. 393-435). Oxford, UK: Oxford University Press.

Benson, H., Lehmann, J. W., Malhotra, M. S., Goldman, R. F., Hopkins, J., & Epstein, M. D. (1982). Body temperature changes during the practice of g Tum-mo yoga. *Nature, 295,* 234-236.

Bohm, D. (1986). A new theory of mind and matter. *Journal of the American Society for Psychical Research, 80, 113-135.*

Broch, H. B. (1985). Crazy women are performing in Sombali. *Ethos, 13,* 262.282.

Brown, D., Forte, M., & Dysart, M. (1984). Visual sensitivity and mindfulness meditation. *Perceptual and Motor Skills, 58,* 775-784.

Bruner, J. S., & Postman, L. (1949). On the perception of incongruity: A paradigm. *Journal of Personality, 18,* 206–223.

Burk, L. (2015). Warning dreams preceding the diagnosis of breast cancer: A survey of the most important characteristics. *EXPLORE: The Journal of Science and Healing, 11,* 193–198. http://dx.doi.org/10.1016/j.explore.2015.02.008

Cardeña, E. (1988). *The phenomenology of quiescent and physically active deep hypnosis.* Doctoral dissertation. University of California, Davis.

Cardeña, E. (2005). The phenomenology of deep hypnosis: Quiescent and physically active. *International Journal of Clinical & Experimental Hypnosis, 53*, 37-59.

Cardeña, E. (2009). Beyond Plato? Toward a science of alterations of consciousness. In C. A. Roe, W. Kramer, & L. Coly (Eds.). *Utrecht II: Charting the future of parapsychology* (pp. 305-322). New York: Parapsychology Foundation.

Cardeña, E. (2011). Altered consciousness is a many splendored thing. *Journal of Cosmology, 14,* 207-218.

Cardeña, E. (2015). *Eminent people interested in psi.* Retrieved from: http://psi-encyclopedia.spr.ac.uk/articles/eminent-people-interested-ps.

Cardeña, E. (2018). The experimental evidence for parapsychological phenomena: A review. *American Psychologist.* Advance online publication. http://dx.doi.org/10.1037/amp0000236

Cardeña, E. (2018). Derangement of the Senses or Alternate Epistemological Pathways? Altered Consciousness and Enhanced Functining. *Psychology of Consciousness: Theory, Research, and Practice.* Advance online publication. http://dx.doi.org/10.1037/cns0000175

Cardeña, E. (in press). Fantasy or reality? Meditation, psi phenomena, and exceptional physiological abilities. In M. Farias, D. Brazier, & M. Lalljee (Eds.), *Oxford hand book of meditation.* Oxford, UK: Oxford University Press.

Cardeña, E., Jönsson, P., Terhune, D. B., & Marcusson-Clavertz, D. (2013). The neurophenomenology of neutral hypnosis. *Cortex, 49*, 375-385. http://dx.doi.org/10.1016/j.cortex.2012.04.001

Cardeña, E., Lynn, S. J., & Krippner, S. (2017). The psychology of anomalous experience: A rediscovery. *Psychological Trauma: Theory, Research, Practice, and Policy, 4,* 4-22.

Cardeña, E., Maldonado, J., Van der Hart, O., & Spiegel, D. (2009). Hypnosis. In E. Foa, T. Keane, & M. Friedman (Eds.), *Effective treatments for PTSD* (2nd ed., pp. 427-457). New York: Guilford.

Cardeña, E., & Marcusson-Clavertz, D. (2015). States, traits, beliefs, and psi. In E. Cardeña, J. Palmer, & D. Marcusson-Clavertz (Eds.). *Parapsychology: A handbook for the 21st century* (pp. 110-124). Jefferson, NC: McFarland.

Cardeña, E., & Marcusson-Clavertz, D. (2019). *Changes in state of consciousness and psi scoring in ganzfeld and hypnosis.* Submitted for publication.

Cardeña, E., Palmer, J., & Marcusson-Clavertz, D. (2015). *Parapsychology: A handbook for the 21st century* Jefferson, NC: McFarland.

Cardeña, E., Sjöstedt, J. O., & Marcusson-Clavertz, D. (2015). Sustained attention and motivation in Zen meditators and non-meditators. *Mindfulness, 6,* 1082-1087. doi.10.1007/s12671-014-0357-4

Cardeña, E., & Spiegel, D. (1991). Suggestibility, absorption, and dissociation: An integrative model of hypnosis. In J. F. Schumaker (Ed.), *Human suggestibility: Advances in theory, research, and application* (pp. 93-107). Florence, KY: Taylor & Frances/ Routledge.

Cardeña, E., & Winkelman, M. (Eds.). (2011). *Altering consciousness. Multidisciplinary perspectives* (Vol. 1 and 2). Santa Barbara, CA: Praeger.

Carhart-Harris, R. L., Leech, R., Hellyer, P. J., Shanahan, M., Feilding, A., Tagliazucchi, E.,… Nutt, D. (2014). The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in human neuroscience. 8.* https://doi.org/10.3389/fnhum.2014.00020

Casiglia, E., Mazza, A., Ginocchio, G., Onesto, C., Pessina, A. C., Rossi, A., Cavatton, G., & Marotti, A. (2011). Hemodynamics following real and hypnosis-simulated phlebotomy. *American Journal of Clinical Hypnosis, 40,* 368-375. doi.org/10.1080/00029157.1997.10403405

Council, J., Bromley, K. A., Zabellina, D., & Waters, C. G. (2007). Hypnotic enhancement of creative drawing. *International Journal of Clinical and Experimental Hypnosis, 55,* 467-485. doi.10.1080/00207140701506623

Craig Heller, H., Elsner, R., & Rao, N. (1987). Voluntary hypometabolism in an Indian yogi. *Journal of Thermal Biology, 12,* 171-173.

Davidson, R. J., Kabat-Zinn, J., Schumacher, J., Rosenkranz, M., Muller, D., Santorelli, S. F.,... Sheridan, J. F. (2003). Alterations in brain and immune function produced by mindfulness meditation. *Psychosomatic Medicine, 65,* 564-570.

Desbordes, G., Negi, L. T., Pace, T. W., Wallace, B. A., Raison, C. L., & Schwartz, E. L. (2012). Effects of mindful-attention and compassion meditation training on

amygdala response to emotional stimuli in an ordinary, non-meditative state. *Frontiers in Human Neuroscience, 6.* doi.10.3389/fnhum.2012.00292

d'Espagnat, B. (2006). *On physics and philosophy.* Princeton, NJ: Princeton University Press.

Dieguez, S. & Blanke, O. (2011). Altered states of bodily consciousness. In E. Cardeña, E. & M. Winkelman, (Eds.) *Altering consciousness. Multidisciplinary perspectives. Volume II. Biological and psychological perspectives* (pp. 237-262). Santa Barbara, CA: Praeger.

Dienstfrey, H. (1991). Neal Miller, the dumb autonomic nervous system, and biofeedback. *Advances, 7* (4), 33-44.

Dossey, L. (2011). Dying to heal: A neglected aspect of NDEs. *Explore, 7,* 59-62.

Easterlin, B. L., & Cardeña, E. (1998–1999). Cognitive and emotional differences between short and long term vipassana meditators. *Imagination, Cognition, and Personality, 18*, 69–81.

Garcia-Romeu, A., Kersgaard, B., & Addy, P. H. (2016). Clinical applications of hallucinogens: A review. *Experimental and Clinical Psychopharmacology, 24,* 229-268.

Gauld, A. (1982). *Mediumship and survival: A century of investigations*. Chicago, IL: Academy Chicago Publishers.

Goleman, G., & Davidson, R. (2017). *Altered traits: Science reveals how meditation changes your mind, brain, and body.* New York: Avery.

Grant, J. A., Courtemanche, J., & Rainville, P. (2011). A non-elaborative mental stance and decoupling of executive and pain-related cortices predicts low pain sensitivity in Zen meditators. *Pain, 152,* 150-156. doi.10.1016/j.pain.2010.10.006

Grant, J. A., & Rainville, P. (2009). Pain sensitivity and analgesic effects of mindfulness in Zen meditators: A cross-sectional study. *Psychosomatic Medicine, 71,* 106-114. doi.10.1097/PSY.0b013e31818f52ee

Green, E., & Green, A. (1977). *Beyond biofeedback.* Ft. Wayne, IN: Knoll.

Greyson, B. (2014). Near-death experiences. In E. Cardeña, S. J. Lynn, & S. Krippner (Eds.), *Varieties of anomalous experience: Examining the scientific evidence* (2nd ed., pp. 333–367). Washington, DC: American Psychological Association. http://dx.doi.org/10.1037/14258-012

Griffiths, R. R., Richards, W. A., McCann, U., & Jesse, R. (2006). Psilocybin can occasion mystical type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology, 187*, 268 –283. http://dx.doi.org/10.1007/s00213-006-0457-5

Hall, H. (2011). Sufism and healing. In H. Walach & W. G. Jonas (Eds.), *Neuroscience, consciousness and spirituality* (pp. 263-278). New York: Springer.

Hartmann, E. (1996). Outline for a theory on the nature and function of dreaming. *Dreaming, 6,* 147-170.

Hastings, A. (1991). *With the tongues of men and angels. A study of channeling*. Fort Worth, TX: Holt, Rinehart and Winston.

Hilgard, E. R., & Hilgard, J. R. (2013). *Hypnosis in the relief of pain* (Rev. ed.). New York: Brunner-Routledge. (Originally published 1975)

Hilton, L., Hempel, S., Ewing, B. A., Apaydin, E., Xenakis, L., Newberry, S., ... Maglione, M. A. (2017). Mindfulness meditation for chronic pain: Systematic review and meta-analysis. *Annals of Behavioral Medicine, 51*. 199-213. doi: 10.1007/s12160-016-9844-2.

Hoffman, D. (2008). Conscious realism and the mind-body problem. *Mind & Matter, 6*, 87–121.

Honorton, C. (1976). Has science developed the competence to confront the claims of the paranormal? Presidential Address, Parapsychological Association. In J. D. Morris, W. G. Roll, & R.L. Morris (Eds.), *Research in parapsychology, 1975* (pp. 199-223). Metuchen, NJ: Scarecrow.

Honorton, C. (1977). Psi and attentional internal states. In B. B. Wolman (Ed.), *Handbook of parapsychology* (pp. 435-472). Jefferson, NC: McFarland.

Hurlburt, R.T. & Schwitzgebel, E. (2007). *Describing inner experience? Proponent meets skeptic*. Cambridge, MA: MIT Press.

Hyman, R., & Honorton, C. (1986). A joint communiqué: The psi ganzfeld controversy. *Journal of Parapsychology, 50,* 350-364.

James, W. (1890). *The principles of psychology.* New York: Holt.

James, W. (1958). *The varieties of religious experience: A study in human nature.* New York: New American Library. (Original work published 1902)

Jha, A. P., Krompinger, J., Baime, M. J. (2007). Mindfulness training modifies subsystems of attention. *Cognitive, Affective, & Behavioral Neuroscience, 7,* 109-119.

Kallio, S., & Revonsuo, A. (2003). Hypnotic phenomena and altered states of consciousness: A multilevel framework of description and explanation. *Contemporary Hypnosis, 20,* 111–164.

Kasamatsu, A., & Hirai, T. (1966). An electroencephalographic study on the Zen meditation (Zazen). *Folia Psychiatrica et Neurologica Japonica, 20,* 315-336.

Kastrup, B., Stapp, H. P., & Kafatos, M. C. (2018). Coming to grips with the implications of quantum mechanics. *Scientific American Observations.* Retrieved from https://blogs.scientificamerican.com/observations/coming-to-grips-with-the-implications-of-quantum-mechanics/?print=true

Kelly, E. F., Kelly, E. W., Crabtree, A., Gauld, A., Grosso, M., & Greyson, B. (2007). *Irreducible mind: Toward a psychology for the 21st century*. Lanham, MD: Rowman & Littlefield.

Kitchens, S. (2018, May 3). Microdosing micromoment. *The Cut.* Retrieved from: *https://www.thecut.com/2018/05/microdosing-guide-and-explainer.html*

Kox, M., van Eijk, L. T., Zwaag, J., van den Wildenberg, J., Sweep, F. C. G. J., van der Hoeven, J. G., & Pickkers, P. (2017). Voluntary activation of the sympathetic nervous system and attenuation of the innate immune response in humans. *Proceedings of the National Academy of Sciences, 111,* 7379-7384. doi:10.1073/pnas.1322174111

Kox, M., Stoffels, M., Smeekens, S. P., van Alfen, N., Gomes, M., Eljvogels, Y. M., ... Pickkers, P. (2012). The influence of concentration/meditation on autonomic nervous system activity and the innate immune response: A case study. *Psychosomatic Medicine, 74*, 489–494.

Kok, B. E., & Singer, T. (2017). Phenomenological fingerprints of four meditations: Differential state changes in affect, mind-wandering, meta-cognition, and interoception before and after daily practice across 9 months of training. *Mindfulness, 8,* 218-231.

Kothari, L. K., Bordia, A., & Gupta, O. P. (1973). Studies on a yogi during an eight-day confinement in a sealed underground pit. *Indian Journal of Medical Research, 61,* 1645-1650.

Kozhevnikov, M., Elliott, J., Shephard, J., & Gramann, K. (2013). Neurocognitive and somatic components of temperature increases during gtummo meditation: Legend and reality. *PLoS ONE, 8*, e58244. http://dx.doi.org/10.1371/journal.pone.0058244

Krippner, S. (1985). Psychedelic drugs and creativity. *Journal of Psychoactive Drugs, 17,* 235-245.

Krippner, S., & Achterberg, J. (2014). Anomalous healing experiences. In E. Cardeña, S. J. Lynn, & S. Krippner (Eds.), *Varieties of anomalous experience: Examining the scientific evidence* (2nd ed., pp. 273–301). Washington, DC: American Psychological Association. http://dx.doi.org/10.1037/14258-010

Lakoff, G. (1973). Hedges: A study in meaning criteria and the logic of fuzzy concepts. *Journal of Philosophical Logic, 2*, 408-508.

Lao, S-A, Kissane, D., & Meadows, G. (2016). Cognitive effects of MBSR/MBCT: A systematic review of neuropsychological outcomes. *Consciousness and Cognition, 45,* 109-123.

Laughlin, C., McManus, J., & d'Aquili, E. (1992). *Brain, symbol, and experience: Toward a neurophenomenology of consciousness.* New York, NY: Columbia University Press.

Ludwig, A.M. (1966). Altered states of consciousness. *Archives of General Psychiatry, 15*, 225-234.

Luke, D. (2015). Drugs and psi phenomena. In E. Cardeña, J. Palmer, & D. Marcusson-Clavertz (Eds.), *Parapsychology: A handbook for the 21st century* (pp. 149-164). Jefferson, NC: McFarland.

Marks, L. E. (2014). Synesthesia: A teeming multiplicity. In E. Cardeña, S. J. Lynn, & S. Krippner (Eds.), *Varieties of Anomalous experience: Examining the scientific evidence* (2nd ed., pp. 79–108). Washington, DC: American Psychological Association. http://dx.doi.org/10.1037/14258-004

MacLean, K. A., Ferrer, E., Aichele, S. R., Bridwell, D. A., Zanesco, A. P., Jacobs, T. L.,... Saron, C. D. (2010). Intensive meditation training improves perceptual discrimination and sustained attention. *Psychological Science, 21*, 829 – 839. http://dx.doi.org/10.1177/0956797610371339

Majid, A., & Kruspe, N. (2018). Hunter-gatherer olfaction is special. *Current Biology, 28,* 409-413. h ttps://doi.org/10.1016/j.cub.2017.12.014

Marcusson-Clavertz, D. & Cardeña, E., (2011). Hypnotizability, alterations in consciousness, and other variables as predictors of performance in a ganzfeld psi task. *Journal of Parapsychology, 75*, 235-259.

Marcusson-Clavertz, D., Terhune, D. B., & Cardeña, E., (2012). Individual differences and state effects on mind-wandering: Hypnotizability, dissociation and sensory homogenization. *Consciousness and Cognition, 21,* 1097-1108.

Margnelli, M. (1999). An unusual case of stigmatization. *Journal of Scientific Exploration, 13,* 461-482.

Marshall, P. (2015). Mystical experiences as windows on reality. In E. F. Kelly, A. Crabtree, & P. Marshall (Eds.), *Beyond physicalism: Toward reconciliation of science and spirituality* (pp. 39–76). Lanham, MD: Rowman & Littlefield.

Maslach, C., Marshall, G., & Zimbardo, P. G. (1972). Hypnotic control of peripheral skin temperature: A case report. *Psychophysiology, 9,* 600-605.

Mason, A. A. (1952). Case of congenital ichthyosiform erythoderia of Brocq treated by hypnosis. *British Medical Journal, 2,* 422-423.

Mavromatis, A. (1987). *Hypnagogia: The unique state of consciousness between wakefulness and sleep.* London, UK: Routledge & Kegan Paul.

May, E. C., & Marwaha, S. B. (2015). *Extrasensory perception: Support, skepticism, and science.*(2 Vols.). Santa Barbara, CA: Praeger.

Mendoza, M. E., & Capafons, A. (2009). Efficacy of clinical hypnosis: A summary of its empirical evidence. *Papeles del Psicólogo, 38*, 98-116.

Montgomery, G. H., DuHamel, K. N., & Redd, W. H. (2000). A meta-analysis of hypnotically induced analgesia: How effective is hypnosis. *International Journal of Clinical and Experimental Hypnosis, 48,*138-153.

Murphy, M. (1992). *The future of the body: Explorations into the further evolution of human nature.* Los Angeles, CA: Tarcher.

Natsoulas, T. (1981). Basic problems of consciousness. *Journal of Personality and Social Psychology, 41*, 132-178.

Noirhomme, Q., & Laureys, S. (2011). Altering consciousness and neuropathology. In E. Cardeña & M. Winkelman (Eds.), *Altering consciousness. Multidisciplinary perspectives. Volume 2: Biological and psychological perspectives* (pp. 263-278). Santa Barbara, CA: Praeger.

Olness, K., Culbert, T., & Uden, D (1989). Self-regulation of salivary immunoglobulin A by children. *Pediatrics, 83,* 66-71.

Ornstein, R. (1986). *The psychology of consciousness* (Rev. ed.). New York: Penguin.

Pronin, E., Lin, D. Y., & Ross, L. (2002). The bias blind spot: Perception of bias in self versus others. *Personality and Social Psychology Bulletin, 28,* 369-381.

Rainville, P., Hofbauer, R. K., Bushnell, M. C., Duncan, G. H., & Price, D. D. (2002). Hypnosis modulates activity in brain structures involved in the regulation of consciousness. *Journal of Cognitive Neuroscience, 15,* 887-901.

Raz, A., Moreno-Íñiguez, M., Martin, L., & Zhu, H. (2007). Suggestion overrides the Stroop effect in highly hypnotizable individuals. *Consciousness and Cognition, 16*, 331–338.

Roney-Dougal, S. M. (2015). Ariadne's thread: Meditation and psi. In E. Cardeña, J. Palmer, & D. Marcusson-Clavertz (Eds.), *Parapsychology: A handbook for the 21st century* (pp. 125-138). Jefferson, NC: McFarland.

Sacks, O. (1973). *Awakenings.* London, UK: Duckworth.

Sanwald, G. (1963) On the psychology of spontaneous paranormal phenomena. *International Journal of Parapsychology, 5,* 274–289.

Schaefert, R., Klose, P., Moser, G., & Häuser, W. (2014). Efficacy, tolerability, and safety of hypnosis in adult irritable bowel syndrome: Systematic review and meta-analysis. *Psychosomatic Medicine, 76,* 389-398.

Sexton, R., & Buljo Stabbursvik, E. A. (2010). Healing on the Sámi North. *Culture, Medicine and Psychiatry, 34,* 571-589.

Sidgwick, Mrs. H. (1915). A contribution to the study of the psychology of Mrs. Piper's trance phenomena. *Proceedings of the Society for Psychical Research, 28*, 1-657.

Simons, E. R., Ervin, F. R., & Prince, R. H. (1988). The psychobiology of trance. I: Training for Thaipusam. *Transcultural Psychiatry, 25,* 249-266.

Slagter, H. A., Lutz, A., Greischar, L. L., Fracis, A. D., Nieuwenhuis, S., Davis, J. M., & Davidson, R. J. (2007). Mental training affects distribution of limited brain resources. *PLoS Biology, 5*, doi.org/10.1371/journal.pbio.0050138

Smith, H. (1995). Introduction. In *The essential Rumi.* New York: Quality Paperback Book Club.

Smith, R. C. (1987). Do dreams reflect a biological state? *Journal of Nervous and Mental Disease, 175*, 201–207. http://dx.doi.org/10.1097/00005053-198704000-00002

Spanos, N. P., Williams, V., & Gwynn, M. I. (1990). Effects of hypnotic, placebo, and salicylic acid treatments on wart regression. *Psychosomatic Medicine, 52,* 109-114.

Stanford, R. G., & Stein, A. G. (1994). A meta-analysis of ESP studies contrasting hypnosis and a comparison condition. *Journal of Parapsychology, 58*, 235-269.

Storm, L., Tressoldi, P. E., & Di Risio (2010). Meta-analysis of free-response studies, 1992-2008: Assessing the noise reduction model in parapsychology. *Psychological Bulletin, 136,* 471-485.

Tart, C.T. (1975). *States of consciousness.* New York: Dutton.

Telles, S., Reddy, S. K., & Nagendra, H. R. (2000). Oxygen consumption and

respiration following two yoga relaxation techniques. *Applied Psychophysiology and Biofeedback, 25,* 221-227.

Terhune, D. B. & Cardeña, E. (2010). Differential patterns of spontaneous experiential response to a hypnotic induction: A latent profile analysis. *Consciousness and Cognition* 19:1140–50. doi.10.1016/j.concog.2010.03.006

Terhune, D. B., Cardeña, E., & Lindgren, M. (2010). Disruption of synesthesia by posthypnotic suggestion: An ERP study. *Neuropsychologia, 48,* 3360-3364.

Thurston, H. (2013). *The physical phenomena of mysticism.* Hove, UK: White Crow Books. (Originally published 1952)

Tyagi, A., & Cohen, M. (2016). Yoga and heart rate variability: A comprehensive review of the literature. *International Journal of Yoga, 9,* 97-113.

Wackermann, J., Pütz, P., & Allefeld, C. (2008). Ganzfeld-induced hallucinatory experience, its phenomenology and cerebral electrophysiology. *Cortex, 44,* 1364-1378.

Wenger, M. A., Bagchi, B. K., & Anand, B. K. (1961). Experiments in India on "voluntary" control of the heart and pulse. *Circulation, 24,* 1319-1325.

Wielgosz, J., Schuyler, B. S., Lutz, A., & Davidson, R. (2016). Long-term mindfulness training is associated with reliable differences in resting respiration rate. *Scientific Reports, 6,* doi:10.1038/srep27533

Whitehead, C. (2011). Altered consciousness in society. In E. Cardeña & M. Winkelman (Eds.), *Altering consciousness. Multidisciplinary perspectives. Volume 1: History, culture, and the humanities* (pp. 181–202). Santa Barbara, CA: Praeger.

Wilson, T. (2002). *Strangers to ourselves.* Cambridge, MA: Belknap Press.

Wulff, D. M. (2014). Mystical experiences. In E. Cardeña, S. J. Lynn, & S. Krippner (Eds.), *Varieties of anomalous experience: Examining the scientific evidence* (2nd ed., pp. 369–408). Washington, DC: American Psychological Association. http://dx.doi.org/10.1037/14258-013

Zinberg, N. E. (1977). *Alternate states of consciousness: Multiple perspectives on the study of consciousness.* New York: The Free Press.

AYAHUASCA AS A MIND ENHANCER – ITS KNOWLEDGE AND POTENTIAL

Olga Silva [1] ***& Mário Simões*** [2]

Abstract

Ayahuasca is a South American traditional herbal preparation typically produced by decoction of a mixture of Banisteriopsis caapi stem and Psychotria viridis leaf. Among others, it contains as marker compounds the psychedelic 5-HT2A and sigma-1 agonist N,N-dimethyltryptamine (DMT) from P. viridis plus β-carboline alkaloids with monoamine-oxidase (MAO)-inhibiting properties like harmine, harmaline and tetrahydroharmine from Banisteriopsis caapi. These marker compounds, when administered to humans, produce transitory modifications in emotion, thought content, perception and somatic sensations, while the capacity of the individual to interact with its surroundings is significantly preserved. Studies of medium- and long-term ayahuasca's use suggest that brain alterations manifested as increased spiritual tendencies, can be produced. Ayahuasca therapeutic potential of "decentering" is considered important in clinical psychology and psychiatry. It can produce psychological changes in patients like self-transcendence, personal development, the search for psychological wellbeing, better environment adaptation and treatment for some neuropsychiatric disorders, as some research is supporting. Ayahuasca is used as antidepressant, in the treatment of alcohol and drug dependence, in posttraumatic stress disorder (PTSD), Parkinson Disease, Alzheimer and antisocial behavior. This traditional herbal preparation has been object of a wide series of scientific studies, and the results have been proven on its therapeutic potential. However, the variability inherent to the use of biological material from different sources together with different dosages and forms of preparation means that in most cases it is not possible to

[1] University of Lisbon, Faculty of Pharmacy, iMed.Ulisboa, Lisbon, Portugal.
[2] University of Lisbon, Faculty of Medicine, LIMMIT, Lisbon, Portugal.

compare the results obtained by different teams. In this context there is still a way to go, to allow the profit of the integral therapeutic potential of this herbal medicine.

***Key-words*:** Ayahusca, ethnopharmacology, therapeutic potential, herbal medicine, mind enhancer, psychiatric disorders

Introduction

Ayahuasca is a traditional herbal preparation made by decoction according to different traditional recipes, based on Psychotria viridis (Ruciaceae) leaf and Banisteriopsis caapi stem (Malphigiaceae), used fresh or sometimes dried. Other species like Diplopterys cabreraba or other Psychotria spp. and Nicotiana sp., Brugmansia sp. and Brunfelsia sp. are also referred as possible constituents of this herbal preparation.

The traditional use of this interesting and complex hallucinogen South American traditional herbal preparation was already referred since the pre-Colombian on the neo-Inca cultural historical complex. It is commonly known as ayahuasca, caapi or yage and in hoasca (Portuguese language). The first West writing report of ayahuasca indigenous use for "divination, mystification and bewitchment" was made by the Jesuit missionaries Pablo Maroni in 1737 and Franz Xaver Veigl in 1768. However, it is estimated that this preparation will be used for these purposes from about 8000 years. Currently the use of this preparation in religious and ritualistic context is recognized, among others, in different European countries, United States of America, Australia, Peru, Ecuador, Colombia, Bolivia and Brazil and by at least 72 different indigenous tribes of the Amazon.

This paper aims at a brief review of the knowledge obtained through the studies carried out by many authors on this interesting traditional herbal preparation as an entheogenic agent.

Ritual context

Generally, what is sought when attending an ayahuasca session is an inner and transformative experience. Almost always this type of experiences assumes psychological and biographical contents such as

traumatic events in the person's past. Under the influence of the brew, those events are revived, and it is hoped that an answer, or another meaning, emerges in order to change or influence the present situation of life. These situations can be or not traumatic but, anyway, they can be experienced in a new perspective, often pointing to an imagined and wished positive future, remaining a "future memory". It is also possible that significate "encounters" happen with people already deceased for a releasement of a misunderstood relationship or for bringing advice.

This does not necessarily have to occur in a ritualistic environment and some groups organize events as a form of expanding consciousness. This administration can occur in a single intake and, in this case, it would be the sum of two or three doses normally drank in a ritual. In the course of a ritual, normally, one drinks ayahuasca in three to four times, separated by a two hours interval, in a session of 4 to 8 hours duration. On the other hand, these sessions in ritualistic context are accompanied by songs, oriented by the shaman. These chants have a religious connotation, almost always Christian, and in Brazil they are called "Hinários" and in the rest of South America they are called "Ícaros" and their content connotation has much to do with the fauna and Gods of the jungle and even old relatives (grandfather, grandmother) of people who take part in the ceremony.

Phenomenology

It is known that Ayahuasca has a rich phenomenology, normally appearing in a natural context of a ritual. Visions and other phenomena depend also on the personality, the quantity of compounds present in the brew and intention of the experiencer. In summary one can say that set and setting have a prominent role. It is known today that the amount of DMT present frankly increases the phenomenology of visionary type. Just before the visions one feels a light tremor in the eyelids and "everything" starts with geometric patterns and lights in a fantastic sight!

These visions appear with closed eyes and are of various types, including mammals, reptiles, insect like forms and humans. Animals are in the majority snakes and jaguars, but, curiously, also another type of insect like, for example, mantis. Sometimes visions of deceased ancestors

or living persons also make their appearance. These visions have a special feature, in the sense that it is possible to interact with the characters observed.

In addition to the aforementioned animals, insects or people it often arises scenes according to the motivation to drink the brew, in a vision that corresponds to a response or a searched solution of a problem or question. Other times it feels like a flight of the own conscience to another time and space, in the past or in the future, as it were a "soul flight". Then, experiences of clairvoyance or precognition arise, respectively, concerning situations taking place, in another space, at the same moment of the intake or a situation in the future. Other times still appear visions linked to the transcendent, the ominous, visions that are inscribed in a mystical experience or evoking a near- death experience.

The kind of transformative experiences are of the emotional kind. They range from an inner pacification, through a "cleaning" of the mind, to a self-knowledge of the best and the worst of oneself. Ethical issues are taking in account and there is an inner promise that it does not happen again. Sometimes it arises a state of ecstasy, a feeling of integration and belonging in a Divine and Universal project.

Still in these high emotional experiences, it often arises a direct confrontation with the own emotions of the past and of the present and even eventually with respect to the future, normally connected with personal relations. Frequently, in relation to this aspect, there is an increased empathy, compassion or a benevolence that translates in a better relational capacity. It can even touch the "contact "with the Divine, which is often called as the "tremendum et fascinans misterium".

Very often, after these experiences, the subjects change their attitudes to their previous lives, becoming more ethical, spiritual and less materialistic.

Marker compounds

Traditional herbal preparations produced by decoction of the mixture of Banisteriopsis caapi stem and Psychotria viridis leaf contains alkaloids as main marker compounds, namely N,N-dimethyltryptamine (DMT) from P. viridis and β-carboline alkaloids like harmine, harmaline and tetrahydroharmine from Banisteriopsis caapi.

DMT is an indole alkaloid endogenous in animals and in species from different botanical genus like Phalaris, Delosperma, Acacia, Desmodium, Mimosa, Virola, and Psychotria. This compound when ingested causes brief and episodic visual hallucinations at high concentration and may have a role in normal animals' physiological and/or psychopathology. DMT interacts with ionotropic and metabotropic receptors. In special, it is an agonist of serotonin (5-HT) receptors, namely of 5-HT1A, 5-HT1B, 5-HT1D, 5-HT2A, 5-HT2B, 5-HT5A, 5-HT6 and 5-HT7 receptors (affinities ranging from 39 nM to 2.1 μM) an of TAAR and sigma-1 receptors. DMT is substrate for both cell-surface serotonin uptake transporters (SERTS) and neuronal vesicle monoamine transporters (VMAT2).

In humans, DMT (dimethyltryptamine fumarate salt form) doses of 0.1 and 0.05 mg/kg iv are not hallucinogenic: at 0.05 mg/Kg iv dose a somaesthetic effect was verified and at 1 mg/Kg iv changes in perception were also observed. Doses between 0.1-0.2 mg/kg were described as enhancing the intensity of feeling and affection, cognition and volition and 0.2 mg/kg iv was the threshold dose for hallucinogenic effects.

The β-carboline alkaloids type harman are well known reversible and competitive monoamine oxidase inhibitors. EC50 values of 8x10-8 M for harmine, 6x10-8 M for harmaline and 1.4x10-5 M for tetrahydroharmine (THH) were obtained concerning the monoamine-oxidase A inhibition (MAO-A) but higher concentrations were required for both harmine and harmaline to inhibit MAO-B. Although THH is a poor MAOI can acting as a 5-HT reuptake inhibitor.

Pharmacological and Clinical Evidence

General context

Since the last century ayahuasca has aroused the interest of the scientific community. Ethnobotany, ethnopharmacology and most recently oncology and central nervous system diseases and in special neuropsychiatric disorders are the main subject areas of interest. In fact, from 2011 until now, according to Web of Science and Pubmed databases, more than 100 scientific studies were conducted concerning these 2 last research fields, most of them related with the ayahuasca use in addition problems and depression.

Preclinical data

Scientific studies are manly correlated or made with two of the ayahuasca major compounds, namely DMT and harmine and based on preclinical studies on cell and animal models. In this way it was possible to prove the anticancer activity and the usefulness on central nervous system diseases treatment like depression, Parkinson and addition of these two compounds.

In a review article published in 2016 the authors summarized the in vivo studies aimed at the therapeutic effects of ayahuasca and its β-carboline alkaloids. Most of these studies were performed with harmine and harmane and confirmed the antidepressant activity of these compounds. Ayahuasca has also been shown to be active in depression and anxiety and addictions.

Clinical data

Ayahuasca is being object of a widespread investigation, namely in a variety of neuropsychiatric disorders. The most researched uses are on treatment of resistant depression and addictions, namely alcohol and heroin with excellent results, often in a single intake. Even anxious syndromes and the post-traumatic stress disorder are indications associated with a psychotherapy program. There is also some literature supporting its use in Parkinson's disease as well in Alzheimer's dementia.

Toxicology

Until January 2018 only 13 studies were referred in Pubmed concerning ayahuasca AND toxicity. In one of these studies the reproductive effects after chronic exposure to ayahuasca were evaluated using male Wistar rats. A no-observed-adverse-effect-level for chronic and reproductive effects were observed with 2× the ritualistic ayahuasca dose, corresponding to 0.62 mg/kg bw DMT, 6.6 mg/kg bw harmine and 0.52 mg/kg bw harmaline. Additionally, a potential toxic effect of ayahuasca in male rats was observed at the 4× dose, with a non-monotonic dose-response.

A potential toxic effect of ayahuasca in male rats was observed at the 4× dose, with a non-monotonic dose-response.

Behavioral and neurotoxic effect evaluation

Ayahuasca doses of 30x and 50x the dose taken during a religious ritual were tested in animal model using female Wistar rat. Higher neuronal activation in all brain areas involved in serotoninergic neurotransmission were observed. Although this led to some brain injury, no permanent brain damage was detected at a 30X ayahuasca dose. This neuronal activation (c-fos marked neurons) and toxicity (Fluoro-Jade B and Nissl/Cresyl staining) were investigated in the dorsal raphe nuclei (DRN), amygdaloid nucleus, and hippocampal formation brain areas. A lethal oral dose higher than the 50X (which corresponds to 15.1 mg/kg bw DMT) was confirmed.

In another study a dose-dependent risk of maternal and developmental toxicity following ayahuasca exposure were also proved.

Adverse effects

Naturally, some naturally occurring adverse effects are to be expected, since one is ingesting chemical compounds existing in the plants. The most frequent are episodes of vomiting. These episodes are frequently called purges, in a double meaning, because it is said that these occur as real but also as an urge to vomit without material, meaning the cleansing of "something" that would be considered "dirty" (thoughts, deeds, etc.) by the person. Changes in body or visual perception also occur. These changes look like as if there is a disagreement between what one feels proprioceptive and a visualization of the movements. For example, the displacement of an arm does not correspond to what is seen and simultaneously felt, like there is a delay in the movement. Other mentioned adverse effects are diarrhea, tachycardia, nausea and, often related to the experienced content, also emerge episodes of crying.

Some authors consider that these disagreeable effects can be diminished if there is a previously preparation, summarized under the word "dieta". Not only the subject should abstain, in the previous 3-6 days before the intake of the brew, from ingesting meat, taking medicines, sexual activity or drinking alcohol, but also, on the day, it should be fastened at least a minimum of 6 hours before the administration.

Future research trends

Ayahuasca as a potential medicine

Throughout the preparation of the present work we have confirmed that some aspects are determinants of the development of ayahuasca as medicine. The first one is the use of different plant material, coming from different regions and from different species and the different ways of preparing the traditional recipe. This implies the existence of differentiated chemical profiles for each of the traditional preparations and consequently different content of the majority alkaloids identified, namely the DMT (5-HT receptor agonist) and the β-carbonile alkaloids (monoamine oxidase inhibitors). Consequently, different levels of pharmacological activity and of toxicological profiles are observed and no comparative data analysis could be made between samples from different origins, i.e. no conclusive data can be used to validate the ayahuasca usefulness. In fact, a study carried out in 2017 confirms the variability of the composition among 20 different samples of ayahuasca, prepared in the same way, in relation to the DMT, tryptamine, harmine, harmaline, harmalol, and tetrahydroharmine. As observed, concentrations of the target compounds ranged from 0.3 to 36.7 g/L because they were obtained from different samples.

Conclusions

Ayahuasca is deserving an increasingly interest from the scientific community. The scientific literature range has a broad spectrum from Anthropology, Sociology, Religion and Spirituality, Psychology and Medicine, namely Oncology, Psychiatry and Neurology. There is evidence and promising results concerning the following clinical entities: Addictions - Alcohol and "heavy drugs", anxiety, depression, PTSD, psychotherapy enhancer, Parkinson disease and Alzheimer / dementia.

More research is need at preclinical and after at clinical level, using:

- Well characterized raw material, according to International Quality Control Rules.
- Standardized formulations, according to International Quality Control Rules.

- *In vivo* Efficacy (mode of action) tests - Larger samples.
- *In vivo* Toxicity Evaluation – Including genotoxicity and repeated dose toxicity tests.
- Clinical assays with larger samples and randomized and blinded test designs.

References

Beyer, S. (2009). Singing to the plants: A guide to mestizo shamanism in the Upper Amazon. Albuquerque, NM: University of New Mexico Press.

Bouso J., Santos R., Grob C., Silveira D., McKenna D., Araujo D., Riba J., Barbosa P., Aviléz C., Labate B. (2017). Ayahuasca Technical Report. Barcelona: ICEERS.

Brierley D., Davidson C. (2012). Developments in harmine pharmacology - Implications for ayahuasca use and drug-dependence treatment. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 39: 2, 263-272.

Carbonaro, T. M., Gatch, M. B. (2016). Neuropharmacology of N,N-dimethyltryptamine. Brain Research Bulletin, 126: Part 1, 74-88.

De Mori, B. B., Labate, B. C., Jungaberle, H. (2011). The Internationalization of Ayahuasca. Zurich: Lit Verlag.

Dobkin de Rios M., Rumrrill. R. (2008). A Hallucinogenic Tea, Laced with Controversy: Ayahuasca in the Amazon and the United States. Westport, CT: Praeger Hardback.

Domínguez-Clavé, E., Soler, J., Elices, M., Pascual, J. C., Álvarez, E., Revenga, M. F., Friedlander, P., Feilding, A., Jordi Riba, J. (2016). Ayahuasca: Pharmacology, neuroscience and therapeutic potential, Brain Research Bulletin, 126: Part 1, 89-101.

Frecska E., Bokor P., Winkelman M. (2016). The Therapeutic Potentials of Ayahuasca: Possible Effects against Various Diseases of Civilization. Frontiers in Pharmacology, 7:35.

Gearin A. (2015). Whatever you want to believe: kaleidoscopic individualism and ayahuasca healing in Australia. The Australian Journal of Anthropology, 26, 442–455.

Kavenská V., Simonová H. (2015). Ayahuasca Tourism: Participants in Shamanic Rituals and their Personality Styles, Motivation, Benefits and Risks. Journal of Psychoactive Drugs, 47: 5, 351-359.

Labate B., Cavnar C. (2014). The Therapeutic Use of Ayahuasca, Berlin: Springer-Verlag.

Labate, B. C., Cavnar, C. (2013). The Therapeutic Use of Ayahuasca. Cham: Springer Science & Business Media.

Llamazares A. M., Sarasola C. M. (2004). El Lenguaje de los Dioses. Buenos Aires: Editorial Biblos.

Nunes A., Santos R., Osório F., Sanches R., Crippa J., Hallak J. (2016). Effects of Ayahuasca and its Alkaloids on Drug Dependence: A Systematic Literature Review of Quantitative Studies in Animals and Humans. Journal of Psychoactive Drugs, 48: 3, 195-205.

Osório F., Sanches R., Macedo L., Santos R., Maia-de-Oliveira J., Wichert-Ana D., Riba J., Crippa J., Hallak J. (2015). Antidepressant Effects of a Single Dose of Ayahuasca in Patients with Recurrent Depression: a Preliminary Report. Brazilian Journal of Psychiatry, 37: 1, 13-20.

Palhano-Fontes F., Barreto D., Onias H., Andrade K., Novaes M., Pessoa J., Araújo D. (2018). Rapid Antidepressant Effects of the Psychedelic Ayahuasca in Treatment of Resistant Depression: a Randomized Placebo-Controlled Trial. Psychological Medicine, 1-9.

Passos C., Simoes-Pires C., Henriques A. Cuendel, M., Carrupt, P. A., Christen, P. (2014). Alkaloids as Inhibitors of Monoamine Oxidases and Their Role in the Central Nervous System. Studies in Natural Products Chemistry, Atta-ur-Rahman editor, vol. 43, 123-143.

Pic-Taylor A, da Motta L. G., de Morais J. A. , Junior W. M., Santos A. de F., Campos L. A., Mortari M. R., von Zuben M. V., Caldas E. D. (2015), Behavioural and Neurotoxic Effects of Ayahuasca Infusion (Banisteriopsis caapi and Psychotria viridis) in Female Wistar rat. Behavioural Processes. 118, 102-10.

Ribeiro, D. (1977). Estudos de antropologia da civilização: As Américas e a civilização, processo de formação e causas do desenvolvimento desigual dos povos americanos. Petrópolis: Vozes.

Santos R., Bouso C., Hallak J. (2017). Ayahuasca: What mental Health Professionals need to know? Archives of Clinical Psychiatry, 44, 103-109.

Santos R., Osório F., Crippa J., Hallak J. (2016). Antidepressive and Anxiolytic Effects of Ayahuasca: a Systematic literature Review of Animal and Human Studies. Revista Brasileira de Psiquiatria, 38: 1, 65-72.

Santos, A. F., Vieira, A. L. S., Pic-Taylor, A., Caldas, E. D. (2017). Reproductive Effects of the Psychoactive Beverage Ayahuasca in Male Wistar Rats After Chronic Exposure, Revista Brasileira de Farmacognosia, 2017, 27, 353-360.

Santos, M. C., Navickiene, S., Gaujac, A. (2017). Determination of Tryptamines and β-Carbolines in Ayahuasca Beverage Consumed During Brazilian Religious Ceremonies. Journal of AOAC International, 100: 3, 1-4.

Tupper K., Wood E., Yensen R., Johnson M. (2015). Psychedelic Medicine: a Re-emerging Therapeutic paradigm. CMAJ, 187: 14, 1054-1059.

ENHANCING THE MIND IN ANCIENT GREECE

***Yulia Ustinova* ***

Introduction[1]

Both the ancient Greek term *epipnoia* and the Latin *inspiratio*, from which the English word 'inspiration' derives, convey the idea of breath, an airy invisible flow, entering a person from the outside, temporarily elevating him or her to an extraordinary level – of creativity, vision, knowledge, physical force or courage. This flow was perceived as invading from the outside. The late antique lexicon of Suda explains the notion *epipnoia* very simply: *epipnoia* is *enthousiasmos*, inspiration is engoddedness, that is, possession, seizure by a deity (Suda, s.v. *epipnoia*).[2]

In this paper, I'll discuss methods employed by some famous Greek philosophers, traditional sages and prophetic priests, with the purpose of attaining the state of inspiration. My aim is not only to describe ancient Greek practices, but also to use Greece as an example illustrating the antiquity of the aspiration for mind enhancement, and to underscore the interaction between this cross-cultural proclivity and the historically conditioned environment of a particular culture.

The Greeks perceived mental experiences of exceptional intensity as stemming from divine intervention: the general belief was that poets were inspired by the Muses, the visions of prophets were imparted by gods and sages received from them revelatory dreams. However, there always were mortals who tried to rid themselves of human imperfection and initiate communication with the divine in order to be enlightened. Several ways to manipulate consciousness in order to attain insights were

* Department of General History, Ben-Gurion University, Neguev, Israel.

[1] This and related subjects are treated in detail in my book on alteration of consciousness in ancient Greece: Ustinova 2018. The research was supported by the Israel Science Foundation (Grant No. 1077/12).

[2] Ancient sources cited in this paper can be consulted online at the *Perseus Collection of Greek and Roman Materials:* http://www.perseus.tufts.edu/hopper/collection?collection=Perseus:collection:Greco-Roman.

known. Some individuals claimed that they could release their souls at will; independent of the body, the soul could achieve superhuman knowledge. Others attained states of intense concentration by means of meditation-like techniques. The state construed in antiquity as possession by a deity, divinely inspired madness, enabled temporary abandonment of the human self and transformed an individual into a medium. The words uttered by such people were considered as coming from the deity, rather than from the mortal mind. All these techniques were known to Plato (*Timaeus* 71 E-72 B).

Plato on his revelations

On several occasions Plato (427–347 BC) associates philosophical doctrines with ecstatic revelation, thus suggesting that human inquiry derives from a superhuman source (Morgan 1990: 22-24, 64, 195). Plato's writings suggest that he knew mystical experiences himself. In his *Seventh Letter* Plato gives precious details regarding his views. This remarkable, perhaps autobiographic, document is considered by the majority of experts as authentic.[3] Referring to his most important tenets, Plato writes:

> "There does not exist, nor will ever exist, any treatise of mine dealing with these subjects. For it does not at all admit of verbal expression like other studies, but, as a result of continued application to the subject itself and communion therewith, it is brought to birth in the soul of a sudden, as light that is kindled by a leaping spark, and thereafter it nourishes itself" (*Epistle* 7. 341C, translation R. G. Bury).

Plato does not say much about the nature of the ineffable things, but for two observations: they result from a long pondering on the subject ('communion' with it) and appear in sudden flashes. The instantaneousness of the revelation is especially noteworthy. 'The communion' may perhaps allude to the erotic passion of the soul for the ideas, which leads to the painful but exhilarating birth of the true knowledge, as described in the undoubtedly authentic *Republic* (490AB). This illumination is the state

[3] Brisson 1987: 72; Sayre 1988: 94; Knab 2006: 50; Liatzi 2008: 10-14; the *Seventh Letter* as Plato's autobiography: Brisson 2000: 15-14. However, Byrnyeat and Frede 2015 regard it as a later forgery.

of enhanced sensibility which brings about sensations of elation and heavenly joy, an ineffable experience that even *post factum* cannot be adequately put into words.

In Plato's opinion, prolonged absorption into enquiry is conductive to the ultimate knowledge, which bursts out as a revelation. Indeed, true knowledge requires deliberation, but these states are separated by a gap, and their nature is different. This position is reminiscent of the accounts of modern thinkers and scientists who arrived at their seminal ideas as a result of illumination. For instance, C. F. Gauss (1777-1855), one of the most influential mathematicians in history, gave an account of his years of unsuccessful attempts at proving a theorem, and then described 'the eureka moment':

> "Finally, two days ago, I succeeded, not on account on my painful efforts, but by the grace of God. Like a sudden flash of lightning, the riddle happened to be solved. I myself cannot say what was the conducting thread which connected what I previously knew with what made my success possible" (Hadamard 1945: 15).

This spark of truth, discussed by Plato, is possible only after a prolonged contemplation of a problem, culminating in the realization of the solution, that can subsequently be developed by reasoning and accepted or rejected as a result of further deliberation. This position is congruent with the viewpoint of C. G. Hempel who argues that even in modern science, a hypothesis may be freely invented and can come from the most unexpected sources, including mystical inspiration; scientific objectivity is safeguarded by subsequent scrutiny of the proposed ideas (Hempel 1966: 3-18). The distinction between 'context of discovery' and 'context of justification' profoundly influenced the discussion of discovery in the 20th century. This distinction is quite complex, and the emphasis is put on the instant when an idea or theory is conceived – 'the eureka moment' – and the long process of validation of the idea and its logical and experimental support (Schickore and Steinle 2006). Plato's 'context of discovery' comprised therefore mystical insights that are plainly referred to in the *Seventh Letter* and hinted to in several dialogues:[4] these

[4] Which are undeniably the philosopher's own work. Particularly interesting are such passages as *Phaedrus* 247 CE, *Symposium* 210D, 212 A; *Theaetetus* 173E-174A; *Republic* 490AB; cf. Bussanich 2006: 211; Robinson 1995: 56. For a detailed discussion see Ustinova 2018: 324-328.

texts constitute 'the context of justification.' Thus, states of revelation or illumination that we label as alteration of consciousness were probably experienced by Plato and played an important role in his search for the ultimate truth.

Socrates' enlightening experiences

Plato also mentions Socrates' (470–399 BC) trance-like meditations, out-of-body experiences and feeling of divine intrusion. In the *Phaedo* (66 DE), Plato has Socrates argue that the sustenance of the body and its desires hinders the pursuit of the truth: in order to reach the ultimate truth, the mind of a mortal must cease to be merely human, and come together with the divine. To attain the superhuman wisdom, the soul must be liberated from its connection with the body (Cornford 1952: 58; Morgan 1990: 55-79; Detienne 1963: 78). Socrates expertly describes out-of-body ecstatic experiences that involve the sensation of one's mind leaving the body and mingling with the eternal reality:

> "And does not the purification consist in this which has been mentioned long ago in our discourse, in separating, as far as possible, the soul from the body and teaching the soul the habit of collecting and bringing itself together from all the parts of the body, and living, so far as it can, both now and hereafter, alone by itself, freed from the body as from fetters?" (*Phaedo* 67C, translation H. N. Fowler).

Learning the technique of separation from the body and concentration of the soul is a long process that requires practice and is acquired by training. Socrates was probably referring to an ancient tradition of attaining out-of-body experiences, known to some Archaic sages (Bussanich 2006: 200); we will shortly return to them.

Another unusual trait of Socrates was his claim of communicating with a supernatural being. Plato' Socrates freely talked of his *daimonion,* the sign which prevented him from actions he was about to take, and assumed it to be god-sent. This sign was auditory: on multiple occasions Socrates heard 'a voice' (Plato *Phaedrus* 242BC). Visitation by the *daimonion* is experienced by Socrates as something foreign to himself, a divine intrusion (Destrée and Smith 2005; Lampe 2013: 405-406;

Brisson 2005: 3). In its essence, Socrates' *daimonion* appears to have been a sudden experience of 'indisputable truth, which is itself in no way either a product or qualified by ratiocination' (Brickhouse and Smith 2000: 86). Even nowadays, unexpected striking enlightening experiences are sometimes perceived, even by scientists, as stemming from an outer source, a deity or its intermediary (Hadamard 1945: 122). It may be surmised that Socrates' *daimonion,* that visited him usually at critical, dangerous or intellectually challenging junctures in his life, belonged to this kind of real-life psychological experiences.

Socratic 'practice of mental withdrawal and concentration' (Dodds 1945: 22) is mentioned by Plato on several occasions. For instance, during the siege of Potidaea in 432 BC, Socrates became immersed in resolving some problem, and remained motionless on the same spot in the camp during a day and a night (*Symposium* 220D). It was common knowledge that he prevailed over strongest erotic temptations, and when on a military campaign, endured hunger and many other hardships. In the words of B. Russel, Socrates 'had achieved the complete mastery of the soul over the body' (Russel 1961: 109). The altered state of Socrates' mind and body may be compared with radical detachment attested in mystical traditions worldwide, from India to mediaeval Europe, which comprises disregard of bodily needs, self-sufficiency and enhanced awareness (Bussanich 1999: 45-46). Socrates' 'mental tightness' (Montiglio 2005: 172) was required for the intense concentration, intellectual discipline referred to by his disciple Plato as necessary for proper philosophizing, which has already been discussed.

Archaic Greek sages and their way to ultimate truth: Pythagoras

These practices are reminiscent of the tradition of self-cultivation and manipulation of consciousness, practiced by many quasi-historical sages of the Archaic period (mid-eighth – sixth centuries BC), who in the opinion of later generations 'acquired their knowledge of the divine by means of ecstatic and initiatory wisdom' (Plutarch, *Solon* 12). Philosophizing of some predecessors of Socrates and Plato, such as Pythagoras and Parmenides, probably also included meditation, sensory deprivation, and complex preparations leading to illumination, subsequently re-considered my means of rational judgement.

The evidence on these philosophers, usually dubbed as the Presocratics, is scarce and difficult to interpret. Pythagoras is perhaps the most famous and the most controversial among them. The dispute as to whether Pythagoras was a natural philosopher and mathematician, founder of a sect and expert on the fate of the soul after death, or both, still continues (Barnes 1979: 100-114; Zhmud 2012: 148; 207-220). It is noteworthy that the early tradition, including Plato and Aristotle, hardly mentions Pythagoras' own achievements in natural philosophy, but rather pictures him as a charismatic teacher who formulated a new way of life for himself and his followers (for instance, Plato *Republic* 600 AB; Burkert 1972: 215-217; Huffman 2003: 404; Riedweg 2005: 1). The teacher's life was the ultimate proof of the truth of his tenets (Burkert 1972: 147). Extraordinary traits and abilities attributed to Pythagoras[5] belong to the sphere in which the earlier Greek sages and ritual purifiers were prominent and which is connected by many modern scholars with shamanic experiences.[6]

Pythagoras' descents into secret chambers and caves were well-known, and his legend contains several reiterations of this motif. In these secluded places, Pythagoras learnt to remain quiet. Pythagoras is credited with consuming special foods that freed him of hunger and thirst, or even with abstaining from food and drink entirely during his sojourns in sacred precincts. This tradition indicates awareness of the fact that fasting enhanced the mind-changing effect of subterranean sojourns, and enabled the sojourner to remain silent and motionless in the darkness of the isolated chamber: an ascetic technique of manipulation of consciousness was familiar to the Greeks (Ustinova 2009: 186-191).

Pythagoras' writings did not survive - to the extent that they ever existed, since the great master supposedly deliberately refrained from writing (Riedweg 2005: 43). His disciples, organized in a brotherhood which shared common secrets and required elaborate initiations, were to live through various trials, including prolonged silence, and unequivocally accept a set of orally transmitted precepts: in a word, they formed a sect

[5] Such as his golden thigh, as well as the ability to bilocate, employ magical healing skills and chase away pestilences. For an analysis of the ancient tradition see Detienne 1963: 69-70; Burkert 1972: 141-143, 160; Kingsley 1995: 291, 327.

[6] Kahn 1960: 32; Detienne 1963: 82; Dodds 1973: 144; Burkert 1972: 140-165; West 1983: 149; Brisson 1987: 95; for a denial of such association see Zhmud 2012: 221-230.

(Burkert 1972: 166-192; Brisson 1987; Kingsley 1995: 319; Riedweg 2005: 98-104; Kahn 2001: 11).

The early Pythagoreans placed an emphasis on revealed wisdom and on dreams as a direct way of contact with the divine and a prominent means of divination (Diogenes Laertius 8. 32). In addition, the Pythagoreans appear to have mastered methods of yoga-like breath control and used them for manipulation of consciousness. The philosopher Empedocles (405-444 BC) admired Pythagoras as

> "a man of outstanding knowledge, who possessed the greatest wealth of *prapides* and became especially capable of all wise deeds. For whenever he stretched his *prapides*, easily he contemplated each of the things existing in the tenth and twentieth generation of men.[7]"

These verses clearly attest to the alleged ability of Pythagoras to embrace in his thought aeons of time and the wholeness of reality, reminiscent of the talents of the Archaic ecstatics. Empedocles appears to have considered the *prapides* as the organ that had to be employed in order to achieve the separation of the soul from the body, probably by means of breath control, which is an essential technique of attaining out-of-body states (Delatte 1934: 26-27; Detienne 1963: 79-81; Vernant 1983: 86-87; 110-111; Kingsley 2002: 401). It is plausible that the same technique was used by several other early Greek sages.

In sum, the ascetic practices of Pythagoras and his disciples, including sensory deprivation and fasting, along with the emphasis on ineffability of the resulting knowledge indicate that manipulation of consciousness held a place of honour in their methods of philosophizing. Other customs and beliefs of the Pythagoreans, such as the attribution of magical skills and divine traits to Pythagoras, the rigid master-disciple relationship, the complex system of initiations – all point in the same direction, of the connection of Pythagoras and his school or sect to ancient cults. As already observed, Pythagoras was not alone, and continued the tradition of the Archaic sages called by the scholars 'impresarios of gods' (La Barre 1980: 50), 'mediators of the divine' (Berchman 1998), or 'masters of truth' (Detienne 1996).

[7] Diels and Kranz 1951: fragment B129. Iamblicus (*Life of Pythagoras* 15) and Porphyrius (*Life of Pythagoras* 30) cite these words as referring to Pythagoras, while Diogenes Laertius (8. 54) explains that Empedocles' praise was associated with either Pythagoras or Parmenides.

Enlightened individuals and traditional practices of attaining superhuman knowledge: Claros

The common derivation of the poet, the seer and the sage from the undifferentiated ecstatic ritual practitioner of the past, was noticed more than fifty years ago (Cornford 1952: 88-106). The last decades witnessed intensive studies of traces of common origin still discernible in the activities of Greek poets, prophets and philosophers of the Archaic and Classical ages, especially their conscious attribution of knowledge to divine inspiration, in particular by Apollo, the divine patron of healing, prophecy and poetry. Thus, in ancient Greece, the cradle of Western rationality, prominent intellectuals not only made deliberate efforts to manipulate their consciousness with the aim of attaining states of mind favourable for getting inspiration, but employed traditional age-old practices for this purpose.

A brief look Greek oracular technique is now in place. In many Greek oracular sanctuaries, a common prerequisite was a solitary way of life. Immediately preceding oracle-giving, the prophetic person performed a set of ritual actions, often including sensory deprivation, in order to attain the state of revelation construed as divine possession (Ustinova 2018: 58-67). I will briefly discuss one example only, of an oracular centre at Claros, near the city of Colophon in Asia Minor (modern Turkey). The sanctuary of Apollo at Claros was very famous throughout antiquity, and have yielded a compact corpus of evidence that is convenient to present.[8]

The mantic session was held in an artificial grotto with a well in its innermost part (Robert 1967: 309-310; Moretti, Bresch et al. 2014). The procedure took place at night and included, according to Iamblichus, 'numerous ceremonies' (*On the Mysteries* 3. 11).[9] A few enquirers were honoured and allowed to enter the grotto together with the medium and the cult officials. In the underground darkness, an intricate passage to the prophetic vault, with no less than seven turns, must have given the impression of a maze (Robert 1967: 311). The inspired medium was

[8] For details see Ustinova 2009: 109-112.

[9] A reconstruction of the procedure in its development from the Hellenistic to Roman period: Parke 1985: 222-223.

called *thespiôdos* ('inspired singer'), and this function demanded special personality traits (Robert 1967: 310, Moretti, Bresch et al. 2014: 41).

The *thespiôdos* alone entered the innermost sanctum (Iamblichus *On the Mysteries* 3. 11; Parke 1985: 219-220). Influenced by his faith, the long passage through the maze, and by purification ceremonies undergone before entering the grotto, he drank the sacred water. He sang his response in verse which was probably revised by another temple official, responsible for the recording of the prophecy; many of these oracles were carved on stelae and are still in existence today. The prophetic séance was an ordeal for the medium, who while in the grip of the god was 'neither himself nor has any consciousness of what he says and where on earth he is, so that even after prophesying, he sometimes scarcely gets control of himself' (Iamblichus *On the Mysteries* 3. 11, translation E. C. Clarke, J. M. Dillon, and J. P. Hershbell).

The diviner had to abstain from food for a day and a night before descending into the underground chamber, where he drank from the sacred source. This man, who possessed no special education, distanced himself from ordinary mortals. He withdrew from human affairs, lived in an inaccessible place, and prepared for possession by the god with a day and night of fasting (Iamblichus *On the Mysteries* 3. 11; Tacitus *Annals* 3. 54; Robert 1967; Parke 1985: 219-224). The strain of prophesying was considerable: Pliny notes that drinking from the sacred pool inspired wonderful oracles, but shortened the life of the drinker (Pliny *Natural History* 2. 232).[10] Drinking the sacred water was certainly not a life-shortening factor on its own, but was only a part of the strenuous lifestyle of the medium, comprised of seclusion, purifications, fasting and other austerities, and indeed the strain of possession by the god.

In modern terms, the medium at Claros, an individual endowed with a proclivity for alteration of consciousness, attained this state due to the effect of his descent into the underground grotto, enhanced by earlier preparations. Drinking of the water could have served as an immediate 'driving factor,' triggering prophetic singing. For the Greeks, this prophetic *mania* was Apollo's gift, transmitted by the water and bestowed upon the selected few, carefully safeguarding their purity.

[10] On prophetic qualities attributed to water by the Greeks and Romans, see Ustinova 2009: 131-132.

Conclusions

Seers, poets, and enlightened thinkers see and hear what others do not. These individuals perceive their inside and outside world in a manner different from the usual, which in Greece was construed as divine inspiration. When the Greeks witnessed a state of mind that was beyond comprehension in terms of regular experiences, they thought of engoddedness – in their language, *enthousiasmos*: such phenomena were ascribed either to pure divine intervention or to an interaction of human and divine forces. In order to attain this state, philosophers used methods comparable with the techniques applied in vision quest by traditional sages and in oracular practices.

The study of history, including that of mind enhancement, is important because of three main reasons. The first one is obvious: it is useful to have an idea of the chronological depth of any phenomenon, rather than limit the study to the evidence on modern humans only. Practices of mind enhancement retain some universal characteristics. Thus, rational thinkers and spiritual seekers, in the past and nowadays, use similar methods and report some congruent experiences that they regard as salient. Finally, we learn that human behaviour is shaped, *inter alia*, by cultural, that is, historical situation. For instance, while the intake of substances other than wine in Greece is attested to unequivocally in separated cases only,[11] we have seen that the Greeks influenced their internal chemistry by fasting, and used meditation, isolation, breathing exercises, concentration 'designer environments,' innocent substances which served as triggers releasing mental imagery, and other non-chemical methods of mind enhancement. Furthermore, while in the majority of ancient and modern complex societies manipulation of consciousness

[11] Naturally emitted poisonous gases were used in rituals in caves along the Meander valley and in Hierapolis in Asia Minor (modern Turkey; Ustinova 2009), and intoxicating gases probably served as a trigger of the oracular trance of Apollo's priestesses at Delphi (for a discussion of the evidence see Ustinova 2018: 59-62). The recipe of the sacred beverage drunk by the participants in the Eleusinian mysteries, remains controversial: Delatte 1954: 710-726 thinks that it was prepared from ground barley cooked with some innocent herbs. It has been suggested that the sacred beverage was prepared from barley contaminated with ergot (*Claviceps purpurea*), the common grain fungus containing potent hallucinogenic alkaloids similar to LSD (Wasson, Hofmann and Ruch 1998; Ott 1993: 141-144), but this theory has been rejected as unfeasible by most Classical scholars (Burkert 1987: 108-109; Bowden 2010: 37, 43).

remained a fringe socio-religious activity, in the Greek city-states ecstatic practices belonged to the mainstream (Ustinova 2018: 372-375). Thus, mind enhancement and its techniques are conditioned to a significant extent by culture, and this facet deserves careful consideration.

References

Barnes, J. (1979). *The Presocratic Philosophers*. London, Routledge & Kegan Paul.

Berchman, R. M., ed. (1998). *Mediators of the Divine. Horizons of Prophecy, Divination, Dreams and Theurgy in Mediterranean Antiquity*. Atlanta.

Bowden, H. (2010). *Mystery Cults of the Ancient World*. Princeton, Princeton University Press.

Brickhouse, T. C. and N. D. Smith (2000). Socrates' gods and his *daimonion*. *Reason and Religion in Socratic Philosophy*. N. D. Smith and P. B. Woodruff, eds. Oxford, Oxford University Press: 74-88.

Brisson, L. (1987). *Platon. Lettres*. Paris, Flammarion.

Brisson, L. (1987). Usages et fonctions du secret dans le pythagorisme ancien. *Le secret*. P. Dujardin, ed. Lyon, C.N.R.S. et Presses universitaires de Lyon: 87-101.

Brisson, L. (2000). *Lectures de Platon*. Paris, J. Vrin.

Brisson, L. (2005). Socrates and the divine sign according to Plato's testimony: Philosophical practice as rooted in religious tradition. *Socrates' Divine Sign: Religion, Practice and Value in Socratic Philosophy*. P. Destrée and N. D. Smith, eds. Kelowna, Academic Printing and Publishing: 1-12.

Burkert, W. (1972). *Lore and Science in Ancient Pythagoreanism*. Cambridge, Mass., Harvard University Press.

Burkert, W. (1987). *Ancient Mystery Cults*. Cambridge, Mass., Harvard University Press.

Bussanich, J. (1999). Socrates the mystic. *Traditions of Platonism: Essays Presented to John Dillon*. J. Cleary, ed. Alsershot-Brookfield, Ashgate: 29-51.

Bussanich, J. (2006). Socrates and religious experience. *The Blackwell Companion to Socrates*. S. Ahbel-Rappe and R. Kamtekar, eds. Oxford, Wiley-Blackwell: 200-213.

Byrnyeat, M. and M. Frede (2015). *The Pseudo-Platonic Seventh Letter*. Oxford.

Cornford, F. M. (1952). *Principium Sapientiae. The Origins of Greek Philosophical Thought*. Cambridge, Cambridge University Press.

Delatte, A. (1934). *Les conceptions de l'enthousiasme chez les philosophes présocratiques*. Paris, Les Belles Lettres.

Delatte, A. (1954). «Le cycéon, breuvage rituel des mystères d'Éleusis.» *Bulletin de la Classe des Lettres de l' Académie royale de Belgique* 40: 690-752.

Destrée, P. and N. D. Smith, eds. (2005). *Socrates' Divine Signe: Religion, Practice and Value in Socratic Philosophy*. Apeiron.

Detienne, M. (1963). *La notion de daïmôn dans le pythagorisme ancien*. Paris, Les Belles Lettres.

Detienne, M. (1996). *The Masters of Truth in Archaic Greece*. New York, Zone Books.

Diels, H. and W. Kranz (1951). *Die Fragmente der Vorsokratiker. 6th revised edition.* Berlin, Weidmann.

Dodds, E. R. (1945). "Plato and the Irrational." *Journal of Hellenic Studies* 65: 16-25.

Dodds, E. R. (1973). *The Greeks and the Irrational*. Berkeley-Los Angeles, University of California Press.

Hadamard, J. (1945). *The Psychology of Invention in the Mathematical Field*. Princeton, Princeton University Press.

Hempel, C. G. (1966). *Philosophy of Natural Science*. Princeton, Princeton University Press.

Huffman, C. (2003). Pythagoreanism. *A Guide to Greek Thought*. J. Brunschwig and G. E. R. Lloyd, eds. Cambridge, Mass., Harvard University Press: 396-414.

Kahn, C. H. (1960). "Religion and natural philosophy in Empedocles' doctrine of the soul." *Archiv für Geschichte der Philosophie* 42: 3-35.

Kahn, C. H. (2001). *Pythagoras and the Pythagoreans. A Brief History*. Indianopolis, Hackett.

Kingsley, P. (1995). *Ancient Philosophy, Mystery, and Magic. Empedocles and Pythagorean Tradition*. Oxford, Oxford University Press.

Kingsley, P. (2002). "Empedocles for the new millennium." *Ancient Philosophy* 22: 333-413.

Knab, R. (2006). *Platons Siebter Brief. Einleitung, Text, Übersetzung, Kommentar*. Hildesheim, Olms.

La Barre, W. (1980). *Culture in Context*. Durham N.C., Duke University Press.

Lampe, K. (2013). "Rationality, eros, and daemonic influence in the Platonic *Theages* and the Academy of Polemo and Crates." *American Journal of Philology* 134(3): 383-424.

Liatzi, M. (2008). *Die semiotische Erkenntnistheorie Platons im Siebten Brief*. Munich, C. H. Beck.

Montiglio, S. (2005). *Wandering in Ancient Greek Culture*. Chicago, The University of Chicago Press.

Moretti, J.-C., N. Bresch, et al. (2014). Le temple d'Apollon et le fonctionnement de l'oracle. *Le sanctuaire de Claros et son oracle*. J.-C. Moretti and L. Rabatel, eds. Lyon, Maison de l'Orient et de la Méditerranée-Jean Pouilloux: 33-50.

Morgan, M. L. (1990). *Platonic Piety. Philosophy and Ritual in Fourth-Century Athens*. New Haven, Yale University Press.

Ott, J. (1993). *Pharmacotheon. Entheogenic Drugs, Their Plant Sources and History*. Kennewick, Natural Products Co.

Parke, H. W. (1985). *The Oracles of Apollo in Asia Minor*. London, Croom Helm.

Riedweg, C. (2005). *Pythagoras. His Life, Teaching, and Influence*. Ithaca, Cornell University Press.

Robert, L. (1967). L'oracle de Claros. *La civilisation grecque*. C. Delvoye and G. Roux, eds. Brussels, La Renaissance du livre: 305-312.

Robinson, T. M. (1995). *Plato's Psychology*. Toronto, University of Toronto Press.

Russel, B. (1961). *History of Western Philosophy*. London, Allen & Unwin.

Sayre, K. M. (1988). Plato's dialogues in the light of the *Seventh Letter*. *Platonic Writings/Platonic Readings*. C. L. Griswold, ed. London-New York, Routledge: 93-109.

Schickore, J. and F. Steinle, eds. (2006). *Revisiting Discovery and Justification. Historical and Philosophical Perspectives on the Context Distinction*. Dordrecht, Springer.

Ustinova, Y. (2009). *Caves and the Ancient Greek Mind. Descending Underground in the Search for Ultimate Truth*. Oxford, Oxford University Press.

Ustinova, Y. (2009). "Caves and the ancient Greek oracles." *Time and Mind* 2(3): 265-286.

Ustinova, Y. (2018). *Divine Mania. Alteration of Consciousness in Ancient Greece*. London, Routledge.

Vernant, J.-P. (1983). *Myth and Thought among the Greeks*. London, Routledge & Kegan Paul.

Wasson, R. G., A. Hofmann, et al. (1998). *The Road to Eleusis: Unveiling the Secret of the Mysteries*. Los Angeles, William Dailey Rare Books Ltd.

West, M. L. (1983). *The Orphic Poems*. Oxford, Oxford University Press.

Zhmud, L. (2012). *Pythagoras and the Early Pythagoreans*. Oxford, Oxford University Press.

REGULATION OF ATTENTION AND EMOTIONS BY MEDITATION: NEUROPHYSIOLOGICAL BASIS AND IMPLICATIONS FOR MENTAL AND PHYSICAL HEALTH

Antoine Lutz *

Abstract

This present proceedings summarizes our lecture at the conference "Enhancing the Mind" organized by the Bial foundation in April 2018 in Porto, Portugal. This lecture presented a recent typology of meditation that we recently proposed (Dahl, Lutz, and Davidson 2015). This proceedings is a shorten version of this manuscript which resulted from a collaboration with Dr. Cortland Dahl and Pr. Richard Davidson at the University of Wisconsin-Madison. Dr. Cortland Dahl was the driving force of this typology, which was developed during his graduate work.

Scientific research highlights the central role of specific psychological processes, in particular those related to the self, in various forms of human suffering and flourishing. This view is shared by Buddhism and other contemplative and humanistic traditions, which have developed meditation practices to regulate these processes. Building on a previous paper in, we proposed a novel classification system that categorizes specific styles of meditation into attentional, constructive, and deconstructive families based on their primary cognitive mechanisms (Dahl, Lutz, and Davidson 2015). We suggest that meta-awareness, perspective taking and cognitive reappraisal, and cognitive insight may be important mechanisms in specific families of meditation and that alterations in these processes may be used to target states of experiential fusion, maladaptive self-schema, and cognitive reification.

* Lyon Neuroscience Research Centre, INSERM U1028, CNRS UMR5292, Lyon 1 University, Lyon, France.

Cognitive Mechanisms of Meditation Practice

Well-being is a complex phenomenon that is related to a variety of factors, including cultural differences, socio-economic status, health, the quality of interpersonal relationships, and specific psychological processes (Diener et al. 1999; Ryff 2014). While mindfulness (see Glossary), compassion, and other forms of meditation are increasingly being studied as interventions to alleviate suffering and promote well-being (Leiberg, Klimecki, and Singer 2011; Hoge et al. 2013; Goyal et al. 2014; J D Teasdale et al. 2000; MacLean et al. 2010; Davidson et al. 2003; Tang, Holzel, and Posner 2015; Sedlmeier et al. 2012), it is not yet clear how different styles of meditation affect specific cognitive processes, nor how alterations in these processes might impact well-being. Here, we address this question from the perspective of psychology and cognitive neuroscience to better understand how changes in well-being during meditation are mediated by alterations in distinct cognitive processes and in the structure and functioning of corresponding brain networks.

How does one define meditation? How does contemplative neuroscience contribute to the study of consciousness? These questions are not easily answered, in part because the term "meditation" encompasses many activities and in part because of the paucity of empirical data currently available in this field. In order to narrow the explanadum to a more tractable scope, this article uses Buddhist contemplative traditions as a paradigmatic framework. The reason, in brief, is that unlike many contemplative traditions, Buddhist traditions tend to offer extensive, precisely descriptive and highly detailed theories about their practices in a manner that lends itself readily to appropriation into a neuroscientific context. Despite the variety of contemplative practices encompassed by the term meditation within Buddhism, most Buddhist traditions use a term for meditation that correlates with the Sanskrit term bhāvanā, literally, "causing to become." In Tibetan traditions, the usual translation for bhāvanā is gôm (sgom), which roughly means "to become habituated to" or "to become familiar with." These Buddhist traditions share two axioms articulated in highly detailed scholastic texts such as the Abhidharma: 1) that a central goal of Buddhist practice is the elimination of suffering, where "suffering" coarsely refers to the negative affects associated with

physical pain, aging, neurosis or social stress; and 2) that any effective method to eliminate suffering must involve changes in one's cognitive and emotional states, in particular one's self-centered habits (Gethin 2011) (Gethin, 1998). Meditation in that view can be conceptualized as a family of complex i) attentional, ii) emotional and iii) conceptual training regimes developed for the cultivation of well-being and emotional balance.

In a previous article in this journal, we proposed a preliminary framework to discuss commonly practiced forms of mindfulness meditation (Lutz et al. 2008). Recent theoretical models have advanced our understanding further by attempting to identify potential cognitive and neural mechanisms in specific forms of meditation and to classify different forms of contemplative practice (Holzel et al. 2011; Vago and Silbersweig 2012; Austin 2013; Frederick Travis 2014; Josipovic 2013; Kozhevnikov et al. 2009; Nash and Newberg 2013; Fred Travis and Shear 2010). While these efforts provide crucial insights for the scientific study of meditation, further work is needed to identify core cognitive mechanisms across different families of meditation.

In Dahl, Lutz, and Davidson 2015 we expand our original framework to accommodate a broader range of traditional and contemporary meditation practices, grouping them into attentional, constructive, and deconstructive families. According to this model, the primary cognitive mechanisms in these three families are (1) attention regulation and meta-awareness, (2) perspective taking and reappraisal, and (3) cognitive insight, respectively. To illustrate the role of these processes in different forms of meditation, we discuss how experiential fusion, maladaptive self-schema, and cognitive reification are differentially targeted by these processes in the context of Buddhist meditation, integrating the perspectives of other contemplative, philosophical, and clinical perspectives when relevant. The mechanisms and targets we proposed in Dahl et al. 2015 are drawn from cognitive science and clinical psychology. Although these psychological processes are theoretically complex, as are the meditation practices that target them, we proposed this novel framework as a first step in identifying specific cognitive mechanisms to aid in the scientific study of different families of meditation and the impact of these practices on well-being.

The Attentional Family: Meta-awareness and Experiential Fusion

The group of meditative practices that we refer to here as the *attentional family* trains a variety of processes related to the regulation of attention. These include the capacities to manipulate the orientation and aperture of attention, to monitor, detect and disengage from distractors, and to re-orient attention toward a chosen object (Lutz et al. 2015; Jha, Krompinger, and Baime 2007; Hasenkamp et al. 2012; Tang et al. 2007). In Dahl et al. 2015, we proposed that a shared characteristic of all meditation practices in this family is the systematic training of the capacity to intentionally initiate, direct, and/or sustain these attentional processes while the strengthening the capacity to be aware of the processes of thinking, feeling, and perceiving.

In scientific literature, the term *meta-awareness* has been used to describe the cognitive process of being aware of the contents of consciousness (Smallwood, McSpadden, and Schooler 2007). In the absence of meta-awareness, we become experientially "fused" with what we experience. We may be aware of the objects of attention, yet unaware of the processes of thinking, feeling, and perceiving. This state of experiential fusion has been referred to using a variety terms in the study of meta-cognition, including "cognitive fusion," "identification," and "object mode" (Bernstein et al., n.d.).

To illustrate the difference between meta-awareness and experiential fusion, let us consider an example. Imagine that you are watching an enthralling movie. In one moment, you might be experientially fused with the movie, to the point when you are no longer consciously aware that you are sitting in a movie theater. In the next moment, you might suddenly become aware of your surroundings and the fact that you are viewing images on a screen. In both moments you may be attentive to the movie, but only in the second moment are you also aware of the process of watching the movie.

In this example, paying attention to the images and sounds that constitute the movie is a form of awareness. If someone tapped you on the shoulder and asked you what just happened in the movie, you could answer. However, if you were asked whether or not you were conscious of sitting in a movie theater in the moment before being asked, you would

probably answer no. The awareness that you were watching a movie, in this case, would only be retrospective. Across a range of traditional and contemporary contemplative traditions, the absence of meta-awareness is viewed as an impediment to various forms of self-monitoring, self-regulation, and self-inquiry (Hadot 1995; Gethin 2011; McCracken, Barker, and Chilcot 2014).

Forms of Attentional Meditation

In both traditional and clinical contexts, the capacity to sustain a heightened awareness of thoughts, behaviors, emotions, and perceptions is thought to be a central feature of mindfulness meditation. Though there is considerable discussion concerning the exact nature of mindfulness practice and its relationship to the construct of mindfulness in traditional Buddhist frameworks, there is general agreement that the cognitive process that we refer to here as meta-awareness plays a central role across a broad spectrum of meditation practices. Following our prior categorization, we proposed in Dahl et al. 2015 two main categories of attentional meditation, along with two new subcategories that allow for a more nuanced discussion of different styles of practice in this family.

Focused attention (FA) practices involve a narrowing of attentional scope and the cultivation of one-pointed concentration on a single object. The presence of meta-awareness distinguishes the attentional stability achieved through this form of meditation from other forms of absorption, such as the stable attentiveness that occurs when one is engaged in an engrossing conversation or playing an interesting game. *Open monitoring* (OM) practices similarly involve the cultivation of meta-awareness, but they do not involve selecting a specific object to orient one's attention. Rather, attentional scope is expanded to incorporate the flow of perceptions, thoughts, emotional content, and/or subjective awareness. OM meditation can be further divided into *object-oriented open monitoring*, which involves directing one's attention to whatever thoughts, percepts, and sensations enter the field of awareness, and *awareness-oriented open monitoring*, referring to the sustained recognition of the knowing quality of awareness itself. Both forms of open monitoring meditation are similar in many ways to practices discussed below in the

context of the deconstructive family. What distinguishes them from deconstructive forms of meditation is that their primary objective is the stabilization of meta-awareness in relation to a particular attentional configuration. As we will see below, in the deconstructive family a similar configuration of attention may be employed, but for different purposes (such as the cultivation of insight into the nature of sensory experience, for example).

Experiential Fusion and the Training of Attention

The inability to regulate attentional processes has been linked to ADHD (Castellanos et al. 2006), addiction (Waters, Marhe, and Franken 2012), and other forms of psychopathology (Van Bockstaele et al. 2014; Cohen et al. 2001), as well as to abnormalities in brain structure and function (Castellanos and Proal 2012). Experiential fusion in particular has received a great deal of attention in a number of contemporary therapeutic interventions. Although associated with overlapping constructs, such as "cognitive distancing," "cognitive defusion," and "decentering," reversing states of experiential fusion through the cultivation of meta-awareness terms is viewed as being especially important in the cultivation of mental health (Linehan et al. 1999; Segal, Williams, and Teasdale 2012; Hayes 2004; Kabat-Zinn 2013; Butler et al. 2006).

Clinical studies have shown that a diminished ability to step back and observe one's thoughts and feelings plays an important role in a variety of psychiatric conditions, including depression (Lo et al. 2014) and anxiety (Hoge et al. 2014). In one recent study, authors found that decreases in psychological processes related to experiential fusion were found in patients undergoing treatment for depression who received training in mindfulness-based cognitive therapy but not in control groups, and that these changes were associated with positive changes in depressive symptomology (Bieling et al. 2012). Similar findings have been found in relation to the treatment of addiction (J. A. Brewer, Elwafi, and Davis 2012). A study on smoking cessation, for example, demonstrated that mindfulness practice attenuated cigarette smoking, in particular by altering the relationship between addictive craving and the behavior of smoking (Elwafi et al. 2013).

As recently reviewed, mindfulness-related practices have been shown to train many of the attentional processes described above and to induce functional and structural changes in attention-related networks in the brain (Tang, Holzel, and Posner 2015; Fox et al. 2014). For instance, there is growing evidence that attentional stability increases with mindfulness training, as measured by reduced response time variability and EEG brain response variability during a continuous performance task (Lutz et al. 2009; MacLean et al. 2010). Similarly, intensive meditation training has also been shown to reduce both behavioral and EEG markers of attentional blink, a phenomena that reflects the propensity for attention to become fused with a perceptual target (Slagter et al. 2007). This effect is also modulated by different forms of meditation, with enhanced reductions in attentional blink in relation to open monitoring meditation (see below) relative to focused attention practices (Van Vugt and Slagter 2014). Reducing fusion with an emotional experience should facilitate emotional regulation by decreasing its lingering or stickiness. This prediction is in line with findings showing that expert meditators exhibited less amygdala activity in responses to negative emotional stimuli than controls (Brefzinscky Lewis, PNAS). A similar effect was found when patients with anxiety disorders entered a state of mindfulness meditation (Goldin and gross 2010).

One avenue through which meta-awareness might impact well-being lies in its relationship to mind wandering. Mind wandering has been found to consume as much as 50% of our waking life and is tied to our sense of well-being (Killingsworth and Gilbert 2010). If training in attentional forms of meditation does strengthen meta-awareness, we might expect this to impact both the incidence and impact of mind wandering. Recent studies have indeed found that meditation training alters patterns of task-unrelated thought, showing that even a brief training in mindfulness meditation decreases the behavioral indicators of mind wandering (Mrazek, Smallwood, and Schooler 2012; Levinson et al. 2014). Although meta-awareness and self-referential processes like mind wandering are difficult to operationalize, a few recent studies seem to indicate that brain regions associated with self-referential processing (Mason et al. 2007; Fox et al. 2015; Christoff et al. 2009), such as the medial prefrontal cortex and the posterior cingulate cortex, may be

down-regulated by mindfulness-related practices (Farb et al. 2007; J. A. Brewer et al. 2011). In one of these studies, this pattern was linked to enhanced coupling between these midline regions and attentional brain networks associated with executive function, such as the dorsolateral prefrontal cortex and the dorsal anterior cingulate cortex (J. A Brewer et al. 2011). In the other, this pattern was linked to a decreased coupling between the medial prefrontal cortex and an interoceptive region, the insular cortex (Farb et al. 2007). It was speculated that these patterns reflected decreased self-referential thought and enhanced present-centered awareness (Farb et al. 2007; J. A. Brewer et al. 2011). These interpretations require further investigation, particularly because mind-wandering recruits multiple brain regions, some of which may also play roles in attention and interoception (Fox et al. 2015). What is also unclear is how meta-awareness affects one's ability to use the constructive aspects of mind wandering more effectively, and how activation patterns in brain regions associated with self-referential thought change when periods of mind wandering coincide with meta-awareness.

The Constructive Family: Reappraisal, Perspective Taking, and Self-Schema

The style of practice that we refer to as the constructive family includes a variety of meditation practices that strengthen psychological patterns that foster well-being. In Dahl et al. 2015, we proposed that one avenue through which these practices may affect well-being is by targeting maladaptive self-schema and replacing them with more adaptive conceptions of self. In cognitive psychology, latent beliefs and conceptions about the self, referred to as self-schema, are thought to underlie and inform thoughts and emotions (Beck 2005) and to impact patterns of brain function (Disner et al. 2011). In contrast to attentional practices, which often focus on simply monitoring cognitive and affective patterns, constructive meditations involve systematically altering the content of thoughts and emotions. Some constructive practices are designed to cultivate qualities like patience and equanimity that safeguard the mind from the stressors of daily life. Others aim to bring about a restructuring of priorities and values and a reorienting of the mind toward what is

truly meaningful in life. Still more address interpersonal relationships by nurturing pro-social qualities like empathy and compassion.

The wide variety of practices in this family, as well as their individual complexity, makes identifying core cognitive mechanisms challenging. Nevertheless, a number of processes appear to be central to a broad spectrum of constructive meditations. We proposed that cognitive reappraisal and perspective taking are of particular importance in this style of practice. Cognitive reappraisal refers to the process of changing how we think about situations and events in such a way that our response to them is altered (Gross 2001). Reappraisal is an important strategy in the regulation of emotion (Webb, Miles, and Sheeran 2012) and recruits brain regions related to cognitive control, including the dorsomedial, dorsolateral, and ventrolateral prefrontal cortex, as well as the posterior parietal cortex (Buhle et al. 2013). In a study of reappraisal in those with social anxiety disorder (SAD), for example, results showed that the use of reappraisal reduced negative affect in both patients with SAD and healthy controls, but that in healthy controls different patterns of activity in regulatory brain regions were associated with reduced amygdala activity compared to SAD patients (Goldin et al. 2009).

The second core process that we proposed to be central in many constructive meditations is that of perspective taking, the act of considering how oneself or another would feel in a particular situation (Lamm, Batson, and Decety 2007). Perspective taking is especially important as a contributor to the experience of social emotions (Ruby and Decety 2004). As a critical component of healthy interpersonal relationships, it is found to be diminished in psychopaths (Decety et al. 2013) and also a central mediator in reducing intergroup prejudice (Pettigrew and Tropp 2008). Imaging studies indicate that there is no single neural mechanism related to perspective taking, but rather that differences in perspective (imagining oneself experiencing pain versus another experiencing pain, for example) recruit different brain networks (Ruby and Decety 2004).

To date, constructive meditation practices have received less attention than other forms of meditation in scientific research. A few studies have begun to explore practices related to this family, including prayer (Newberg et al. 2003), the cultivation of compassion (Mascaro

et al. 2013; Klimecki et al. 2014), and imagination-based meditations (Kozhevnikov et al. 2009). Nevertheless, the precise role that reappraisal and perspective taking play in constructive styles of meditation is not yet known, nor is it clear how these processes relate to the recruitment of specific brain networks. Nevertheless, investigations of the cultivation of compassion, a widely practiced style of meditation in this family, provide useful information regarding the cognitive and neural mechanisms of constructive meditations. Preliminary findings indicate that this practice may affect the regulation of emotion and corresponding brain networks. Though further work is needed to clarify the role of reappraisal and perspective taking in other forms of constructive meditation, these data suggest one possible mechanism through which specific forms of meditation may impact well-being.

Deconstructive Family: Self-inquiry and Cognitive Insight

The group of meditations that we refer to as the deconstructive family aims to undo maladaptive cognitive patterns by exploring the dynamics of perception, emotion, and cognition and generating insights into one's internal models of the self, others, and the world. Deconstructive meditations may involve logical analysis or direct, experiential inquiry, and often involve explorations of various self-related processes. This process of inquiry can similarly be applied to the nature and dynamics of perception, to the unfolding of thoughts and emotions, or to the nature of awareness.

In Dahl et al, we proposed that a central mechanism in the deconstructive family is *cognitive insight*, the capacity to recognize and evaluate distorted beliefs and opinions and to remain open to corrective information from the environment (Beck et al. 2004). Data suggests that low levels of cognitive insight are related to diminished working memory and executive function, a tendency to be over-confident regarding one's views and opinions, and resistance to modifying existing beliefs (Orfei et al. 2013). In clinical populations, gains in cognitive insight are associated with better treatment outcomes and improvements in adaptive functioning (Riggs et al. 2012). Though no extant data exists studying cognitive

insight in healthy populations, these data indicate that insight may play an important role in well-being, especially in relation to the role that implicit and explicit beliefs play in shaping subjective experience.

Future Directions for the Study of Meditation

Scientific research on the effects of meditation is in the very early stages. Though preliminary findings suggest that meditation and other forms of mental training may produce demonstrable changes in subjective experience, behavior, patterns of neural activity, and peripheral biology, rigorous studies are still needed to uncover the precise mechanisms that underlie these changes. In particular, randomized trials, active control groups, and longitudinal studies that examine within- and across-subject changes over time, as well as across-practice comparisons, will be especially important in determining the efficacy of meditation training paradigms. In addition, subjective, behavioral, and clinical correlates of meditation-related neural changes are needed to assess the impact of different styles of meditation.

The framework presented by Dahl et al 2015 and presented at this conference highlights the need to expand the scope of scientific research to include a broad range of meditation practices. In the same way that the study of mindfulness meditation has provided a unique window into the training of specific forms of attention, and the impact of attentional training on emotion regulation, learning and memory, and various forms of psychopathology, other forms of meditation may similarly yield important insights into the regulation of self-related processes and their import for well-being, health, and peripheral biology.

It is important to note that here we have explored these families through the lens of cognitive neuroscience and clinical psychology, focusing our attention on the primary cognitive mechanisms and phenomenological targets of specific forms of meditation. If, however, we are to fully understand these practices, it will also be important to study the wider context within which these practices are engaged. This context includes, but is certainly not limited to, issues of ethics embodiment, inter-personal dynamics, cultural setting, and the role that belief and expectation play in shaping subjective experience. In providing this framework, inadequate

though it may be, we hope to spur further discussion about the nature of contemplative practice and how scientific study of meditation may help us better understand the causes and conditions of human flourishing.

Glossary of Terms

Attentional Family: A class of meditation practices that strengthen the self-regulation of various attentional processes, especially the ability to initiate and sustain meta-awareness. Some forms of meditation in this family involve a narrowing of attentional scope, while others involve releasing attentional control and bringing awareness to whatever enters the field of consciousness.

Cognitive Insight: The capacity to recognize and evaluate distorted beliefs and opinions and to remain open to corrective information from the environment. This capacity is a central mechanism in the deconstructive family of meditation.

Cognitive Reification: The experience of thoughts, emotions, and perceptions as being accurate depictions of reality, and in particular the implicit belief that the self and objects of consciousness are inherently enduring, unitary, and independent of their surrounding conditions and circumstances. In the Buddhist tradition, this cognitive process is targeted by deconstructive styles of meditation.

Constructive Family: A family of meditation practices that allow one to cultivate, nurture, or strengthen cognitive and affective patterns that foster well-being. Practices in this family may aim to promote healthy interpersonal dynamics, to strengthen a commitment to ethical values, or to nurture habits of perception that lead to enhanced well-being. Perspective taking and cognitive reappraisal are important mechanisms in this style of meditation.

*Experiential Fusion***:** An automatic process whereby one becomes absorbed in the contents of consciousness, leading to a diminished capacity to monitor and/or regulate psychological processes. In attentional styles of meditation this process is systematically undermined through the cultivation of meta-awareness and the regulation of attention.

Deconstructive Family: A family of meditation practices that foster

cognitive insight into the nature of perception, emotion, and cognition. Deconstructive meditation practices may be oriented toward the objects of consciousness or toward consciousness itself.

Meta-awareness: Heightened awareness of the contents of consciousness, including thoughts, behaviors, emotions, and perceptions, as they occur in real time. Along with the regulation of the scope and stability of attention, the cultivation of meta-awareness is an important objective in attentional styles of meditation practice.

Mindfulness: A term that is defined differently in Buddhist and contemporary contexts, but which often refers to a self-regulated attentional stance oriented toward present-moment experience that is characterized by curiosity, openness, and acceptance.

Perspective Taking: The process of considering how one or another would think or feel in a particular situation.

Re-appraisal: The process of changing how we think or feel about situations and events in such a way that our response to them is altered.

Self-schema: Mental representations of the self that synthesize information from sensory, affective and/or cognitive domains. Constructive styles of meditation often involve developing and/or strengthening adaptive self-schema.

References

Austin, James H. 2013. "Zen and the Brain: Mutually Illuminating Topics." *Frontiers in Psychology* 4 (October): 784. https://doi.org/10.3389/fpsyg.2013.00784.

Beck, Aaron T. 2005. "The Current State of Cognitive Therapy." *Archives of General Psychiatry* 62: 953-59.

Beck, Aaron T., Edward Baruch, Jordan M. Balter, Robert A. Steer, and Debbie M. Warman. 2004. "A New Instrument for Measuring Insight: The Beck Cognitive Insight Scale." *Schizophrenia Research* 68: 319-29. https://doi.org/10.1016/S0920-9964(03)00189-0.

Bernstein Amit, Yuval Hadash, Yael Lichtash, Galia Tanay, Kathrine Shepherd, and David M. Fresco. n.d. "Decentering and Related Constructs: A Critical Review and Meta-Cognitive Processes."

Bieling, Peter J, Lance L Hawley, Richard T Bloch, Kathleen M Corcoran, Robert D Levitan, L Trevor Young, Glenda M. MacQueen, and Zindel V. Segal. 2012. "Treatment-Specific Changes in Decentering Following Mindfulness-Based Cognitive

Therapy versus Antidepressant Medication or Placebo for Prevention of Depressive Relapse." *Journal of Consulting and Clinical Psychology* 80 (3): 365-72. https://doi.org/10.1037/a0028245.

Blanke, Olaf, and Thomas Metzinger. 2009. "Full-Body Illusions and Minimal Phenomenal Selfhood." *Trends in Cognitive Sciences* 13 (1): 7-13. https://doi.org/10.1016/j.tics.2008.10.003.

Bockstaele, Bram Van, Bruno Verschuere, Helen Tibboel, Jan De Houwer, Geert Crombez, and Ernst H W Koster. 2014. "A Review of Current Evidence for the Causal Impact of Attentional Bias on Fear and Anxiety." *Psychological Bulletin* 140 (3): 682-721. https://doi.org/10.1037/a0034834.

Brewer, Judson A., Hani M. Elwafi, and Jake H. Davis. 2012. "Craving to Quit: Psychological Models and Neurobiological Mechanisms of Mindfulness Training as Treatment for Addictions." *Psychology of Addictive Behaviors* 27 (2): 366-79. https://doi.org/10.1037/a0028490.

Brewer, Judson A., Kathleen A Garrison, and Susan Whitfield-Gabrieli. 2013. "What about the 'Self' Is Processed in the Posterior Cingulate Cortex?" *Frontiers in Human Neuroscience* 7 (October): 647. https://doi.org/10.3389/fnhum.2013.00647.

Brewer, Judson A, Patrick D Worhunsky, Jeremy R Gray, Yi-Yuan Tang, Jochen Weber, and Hedy Kober. 2011. "Meditation Experience Is Associated with Differences in Default Mode Network Activity and Connectivity." *Proceedings of the National Academy of Sciences of the United States of America* 108 (50): 20254-59. https://doi.org/10.1073/pnas.1112029108.

Buhle, Jason T, Jennifer A Silvers, Tor D Wager, Richard Lopez, Chukwudi Onyemekwu, Hedy Kober, Jochen Weber, and Kevin N Ochsner. 2013. "Cognitive Reappraisal of Emotion: A Meta-Analysis of Human Neuroimaging Studies," no. Gross 1998: 1-10. https://doi.org/10.1093/cercor/bht154.

Butler, Andrew C, Jason E Chapman, Evan M Forman, and Aaron T Beck. 2006. "The Empirical Status of Cognitive-Behavioral Therapy: A Review of Meta-Analyses." *Clinical Psychology Review* 26 (1): 17-31. https://doi.org/10.1016/j.cpr.2005.07.003.

Castellanos, F. Xavier, and Erika Proal. 2012. "Large-Scale Brain Systems in ADHD: Beyond the Prefrontal-Striatal Model." *Trends in Cognitive Sciences* 16 (1): 17-26. https://doi.org/10.1016/j.tics.2011.11.007.

Castellanos, F. Xavier, E. J S Sonuga-Barke, Michael P. Milham, and Rosemary Tannock. 2006. "Characterizing Cognition in ADHD: Beyond Executive Dysfunction." *Trends in Cognitive Sciences* 10 (3): 117-24. https://doi.org/10.1016/j.tics.2006.01.011.

Christoff, Kalina, Alan M Gordon, Jonathan Smallwood, Rachelle Smith, and Jonathan W Schooler. 2009. "Experience Sampling during FMRI Reveals Default Network and Executive System Contributions to Mind Wandering." *Proceedings of the*

National Academy of Sciences of the United States of America 106 (21): 8719-24. https://doi.org/10.1073/pnas.0900234106.

Cohen, R, I Lohr, R Paul, and R Boland. 2001. "Impairments of Attention and Effort among Patients with Major Affective Disorders." *The Journal of Neuropsychiatry and Clinical Neurosciences* 13 (3): 385-95. https://doi.org/10.1176/appi.neuropsych.13.3.385.

Craig, A D Bud. 2009. "How Do You Feel-Now? The Anterior Insula and Human Awareness." *Nature Reviews. Neuroscience* 10 (1): 59-70. https://doi.org/10.1038/nrn2555.

Critchley, Hugo, and Anil Seth. 2012. "Will Studies of Macaque Insula Reveal the Neural Mechanisms of Self-Awareness?" *Neuron* 74 (3): 423-26. https://doi.org/10.1016/j.neuron.2012.04.012.

Dahl, Cortland J., Antoine Lutz, and Richard J. Davidson. 2015. "Reconstructing and Deconstructing the Self: Cognitive Mechanisms in Meditation Practice." *Trends in Cognitive Sciences* 19 (9): 515-23. https://doi.org/10.1016/j.tics.2015.07.001.

Damasio, Antonio. 2012. *Self Comes to Mind: Constructing the Conscious Brain*. Random House.

Davidson, Richard J., Jon Kabat-Zinn, Jessica Schumacher, Melissa Rosenkranz, Daniel Muller, Saki F Santorelli, Ferris Urbanowski, Anne Harrington, Katherine Bonus, and John F Sheridan. 2003. "Alterations in Brain and Immune Function Produced by Mindfulness Meditation." *Psychosomatic Medicine* 65 (4): 564-70. https://doi.org/10.1097/01.PSY.0000077505.67574.E3.

Decety, Jean, Chenyi Chen, Carla Harenski, and Kent A Kiehl. 2013. "An FMRI Study of Affective Perspective Taking in Individuals with Psychopathy: Imagining Another in Pain Does Not Evoke Empathy." *Frontiers in Human Neuroscience* 7 (September): 489. https://doi.org/10.3389/fnhum.2013.00489.

Denny, Bryan T, Hedy Kober, Tor D Wager, and Kevin N Ochsner. 2012. "A Meta-Analysis of Functional Neuroimaging Studies of Self- and Other Judgments Reveals a Spatial Gradient for Mentalizing in Medial Prefrontal Cortex." *Journal of Cognitive Neuroscience* 24 (8): 1742-52. https://doi.org/10.1162/jocn_a_00233.

Diener, Ed, Eunkook M. Suh, Richard E. Lucas, and Heidi L. Smith. 1999. "Subjective Well-Being: Three Decades of Progress." *Psychological Bulletin* 125 (2): 276-302. https://doi.org/10.1037/0033-2909.125.2.276.

Disner, Seth G, Christopher G Beevers, Emily a P Haigh, and Aaron T Beck. 2011. "Neural Mechanisms of the Cognitive Model of Depression." *Nature Reviews. Neuroscience* 12 (8): 467-77. https://doi.org/10.1038/nrn3027.

Elwafi, Hani M., Katie Witkiewitz, Sarah Mallik, Thomas A Thornhill Iv, and Judson A Brewer. 2013. "Mindfulness Training for Smoking Cessation: Moderation

of the Relationship between Craving and Cigarette Use." *Drug and Alcohol Dependence* 130 (1-3): 222-29. https://doi.org/10.1016/j.drugalcdep.2012.11.015.

Farb, Norman A S, Zindel V Segal, Helen Mayberg, Jim Bean, Deborah McKeon, Zainab Fatima, and Adam K Anderson. 2007. "Attending to the Present: Mindfulness Meditation Reveals Distinct Neural Modes of Self-Reference." *Social Cognitive and Affective Neuroscience* 2 (4): 313-22. https://doi.org/10.1093/scan/nsm030.

Fox, Kieran C R, Savannah Nijeboer, Matthew L Dixon, James L Floman, Melissa Ellamil, Samuel P Rumak, Peter Sedlmeier, and Kalina Christoff. 2014. "Is Meditation Associated with Altered Brain Structure? A Systematic Review and Meta-Analysis of Morphometric Neuroimaging in Meditation Practitioners." *Neuroscience and Biobehavioral Reviews*, April. https://doi.org/10.1016/j.neubiorev.2014.03.016.

Fox, Kieran C.R., R. Nathan Spreng, Melissa Ellamil, Jessica R. Andrews-Hanna, and Kalina Christoff. 2015. "The Wandering Brain: Meta-Analysis of Functional Neuroimaging Studies of Mind-Wandering and Related Spontaneous Thought Processes." *NeuroImage*.

Gallagher, Shaun. 2000. "Philosophical Conceptions of the Self: Implications for Cognitive Science." *Trends in Cognitive Sciences* 4 (1): 14-21.

Gazzaniga, Michael S. 2005. "Forty-Five Years of Split-Brain Research and Still Going Strong." *Nature Reviews Neuroscience* 6 (August): 653-59.

Gethin, Rupert. 1998. *The Foundations of Buddhism*. Oxford University Press.

———. 2011. "On Some Definitions of Mindfulness." *Contemporary Buddhism* 12 (1): 263-79. https://doi.org/10.1080/14639947.2011.564843.

Gillihan, Seth J, and Martha J Farah. 2005. "Is Self Special? A Critical Review of Evidence from Experimental Psychology and Cognitive Neuroscience." *Psychological Bulletin* 131 (1): 76-97. https://doi.org/10.1037/0033-2909.131.1.76.

Goldin, Philippe R., Tali Manber-Ball, Kelly Werner, Richard Heimberg, and James J. Gross. 2009. "Neural Mechanisms of Cognitive Reappraisal of Negative Self-Beliefs in Social Anxiety Disorder." *Biological Psychiatry* 66 (12): 1091-99. https://doi.org/10.1016/j.biopsych.2009.07.014.

Goyal, Madhav, Sonal Singh, Erica M S Sibinga, Neda F Gould, Anastasia Rowland-Seymour, Ritu Sharma, Zackary Berger, et al. 2014. "Meditation Programs for Psychological Stress and Well-Being: A Systematic Review and Meta-Analysis." *JAMA Internal Medicine* 174 (3): 357-68. https://doi.org/10.1001/jamainternmed.2013.13018.

Gross, James J. 2001. "Emotion Regulation in Adulthood: Timing Is Everything." *Current Directions in Psychological Science* 10 (6): 214-19.

Hadot, P. 1995. *Philosophy as a Way of Life: Spiritual Exercises from Socrates to Foucault*. Oxford: Blackwell.

Hasenkamp, Wendy, Christine D Wilson-Mendenhall, Erica Duncan, and Lawrence W Barsalou. 2012. "Mind Wandering and Attention during Focused

Meditation: A Fine-Grained Temporal Analysis of Fluctuating Cognitive States." *Neuroimage* 59 (1): 750-60. https://doi.org/10.1016/j.neuroimage.2011.07.008.

Hayes, Steven C. 2004. "Acceptance and Commitment Therapy, Relational Frame Theory, and the Third Wave of Behavioral and Cognitive Therapies." *Behavior Therapy* 35: 639-65. https://doi.org/dx.doi.org/10.1016/S0005-7894(04)80013-3.

Hoge, Elizabeth A., Eric Bui, Elizabeth Goetter, Donald J. Robinaugh, Rebecca A. Ojserkis, David M. Fresco, and Naomi M. Simon. 2014. "Change in Decentering Mediates Improvement in Anxiety in Mindfulness-Based Stress Reduction for Generalized Anxiety Disorder." *Cognitive Therapy and Research*, October.

Hoge, Elizabeth A., Maxine M Chen, Esther Orr, Christina A Metcalf, Laura E Fischer, Mark H Pollack, Immaculata De Vivo, and Naomi M Simon. 2013. "Loving-Kindness Meditation Practice Associated with Longer Telomeres in Women." *Brain, Behavior, and Immunity* 32 (August): 159-63. https://doi.org/10.1016/j.bbi.2013.04.005.

Holzel, B. K., S. W. Lazar, T. Gard, Z. Schuman-Olivier, D. R. Vago, and U. Ott. 2011. "How Does Mindfulness Meditation Work? Proposing Mechanisms of Action From a Conceptual and Neural Perspective." *Perspectives on Psychological Science* 6 (6): 537-59. https://doi.org/10.1177/1745691611419671.

Ionta, Silvio, Lukas Heydrich, Bigna Lenggenhager, Michael Mouthon, Eleonora Fornari, Dominique Chapuis, Roger Gassert, and Olaf Blanke. 2011. "Multisensory Mechanisms in Temporo-Parietal Cortex Support Self-Location and First-Person Perspective." *Neuron* 70 (2): 363-74. https://doi.org/10.1016/j.neuron.2011.03.009.

Jha, Amishi, J Krompinger, and MJ Baime. 2007. "Mindfulness Training Modifies Subsystems of Attention." *Cognitive, Affective, & Behavioral Neuroscience* 7 (2): 109-19.

Josipovic, Zoran. 2013. "Neural Correlates of Nondual Awareness in Meditation." *Annals of the New York Academy of Sciences*, September, 1-10. https://doi.org/10.1111/nyas.12261.

Kabat-Zinn, Jon. 2013. *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness*. Bantam.

Killingsworth, Matthew A, and Daniel T Gilbert. 2010. "A Wandering Mind Is an Unhappy Mind." *Science (New York, N.Y.)* 330 (6006): 932. https://doi.org/10.1126/science.1192439.

Klimecki, Olga M, Susanne Leiberg, Matthieu Ricard, and Tania Singer. 2014. "Differential Pattern of Functional Brain Plasticity after Compassion and Empathy Training." *Social Cognitive and Affective Neuroscience* 9 (May): 873-79.

Kozhevnikov, Maria, Olga Louchakova, Zoran Josipovic, and Michael A Motes. 2009. "The Enhancement of Visuospatial Processing Efficiency through Buddhist Deity Meditation: Research Article." *Psychological Science* 20 (5): 645-53. https://doi.org/10.1111/j.1467-9280.2009.02345.x.

Lamm, Claus, C Daniel Batson, and Jean Decety. 2007. "The Neural Substrate of Human Empathy: Effects of Perspective-Taking and Cognitive Appraisal." *Journal of Cognitive Neuroscience* 19 (1): 42-58. https://doi.org/10.1162/jocn.2007.19.1.42.

Legrand, Dorothée, and Perrine Ruby. 2009. "What Is Self-Specific? Theoretical Investigation and Critical Review of Neuroimaging Results." *Psychological Review* 116 (1): 252-82. https://doi.org/10.1037/a0014172.

Leiberg, Susanne, Olga Klimecki, and Tania Singer. 2011. "Short-Term Compassion Training Increases Prosocial Behavior in a Newly Developed Prosocial Game." *PloS One* 6 (3): e17798. https://doi.org/10.1371/journal.pone.0017798.

Lemogne, Cédric, Philip Gorwood, Loretxu Bergouignan, Antoine Pélissolo, Stéphane Lehéricy, and Philippe Fossati. 2011. "Negative Affectivity, Self-Referential Processing and the Cortical Midline Structures." *Social Cognitive and Affective Neuroscience* 6 (4): 426-33. https://doi.org/10.1093/scan/nsq049.

Levinson, Daniel B., Eli L. Stoll, Sonam D. Kindy, Hillary L. Merry, and Richard J. Davidson. 2014. "A Mind You Can Count on: Validating Breath Counting as a Behavioral Measure of Mindfulness." *Frontiers in Psychology* 5 (October): 1-10. https://doi.org/10.3389/fpsyg.2014.01202.

Linehan, MM, H Schmidt, LA Dimeff, JC Craft, J Kanter, and KA Comtois. 1999. "Dialectical Behavior Therapy for Patients with Borderline Personality Disorder and Drug-Dependence." *American Journal on Addictions* 8 (4): 279-92.

Lo, Cola S. L., Samuel M. Y. Ho, Nicky K. K. Yu, and Bowie P. Y. Siu. 2014. "Decentering Mediates the Effect of Ruminative and Experiential Self-Focus on Negative Thinking in Depression." *Cognitive Therapy and Research* 38 (4): 389-96. https://doi.org/10.1007/s10608-014-9603-2.

Lutz, Antoine, Amishi Jha, John D Dunne, and Clifford D Saron. 2015. "Investigating the Phenomenological and Neurocognitive Matrix of Mindfulness-Related Practices from a Cognitive Neuroscience Perspective." *American Psychologist*.

Lutz, Antoine, Heleen A Slagter, John D Dunne, and Richard J Davidson. 2008. "Attention Regulation and Monitoring in Meditation." *Trends in Cognitive Sciences* 12 (4): 163-69. https://doi.org/10.1016/j.tics.2008.01.005.

Lutz, Antoine, Heleen A Slagter, Nancy B Rawlings, Andrew D Francis, Lawrence L Greischar, and Richard J Davidson. 2009. "Mental Training Enhances Attentional Stability: Neural and Behavioral Evidence." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 29 (42): 13418-27. https://doi.org/10.1523/JNEUROSCI.1614-09.2009.

MacLean, Katherine A, Emilio Ferrer, Stephen R Aichele, David A Bridwell, Anthony P Zanesco, Tonya L Jacobs, Brandon G King, et al. 2010. "Intensive Meditation Training Improves Perceptual Discrimination and Sustained Attention." *Psychological Science* 21: 829-39. https://doi.org/10.1177/0956797610371339.

Mascaro, Jennifer S, James K Rilling, Lobsang Tenzin Negi, and Charles L Raison. 2013. "Compassion Meditation Enhances Empathic Accuracy and Related Neural Activity." *Social Cognitive and Affective Neuroscience* 8 (1): 48-55. https://doi.org/10.1093/scan/nss095.

Mason, Malia F, Michael I Norton, John D Van Horn, Daniel M Wegner, Scott T Grafton, and C Neil Macrae. 2007. "Wandering Minds: The Default Network and Stimulus-Independent Thought." *Science (New York, N.Y.)* 315 (5810): 393-95. https://doi.org/10.1126/science.1131295.

McCracken, Lance M, Estelle Barker, and Joseph Chilcot. 2014. "Decentering, Rumination, Cognitive Defusion, and Psychological Flexibility in People with Chronic Pain." *Journal of Behavioral Medicine* 37 (6): 1215-25. https://doi.org/10.1007/s10865-014-9570-9.

Mrazek, Michael D, Jonathan Smallwood, and Jonathan W Schooler. 2012. "Mindfulness and Mind-Wandering: Finding Convergence through Opposing Constructs." *Emotion (Washington, D.C.)* 12 (3): 442-48. https://doi.org/10.1037/a0026678.

Nash, Jonathan D., and Andrew Newberg. 2013. "Toward a Unifying Taxonomy and Definition for Meditation." *Frontiers in Psychology* 4 (NOV): 1-18. https://doi.org/10.3389/fpsyg.2013.00806.

Newberg, Andrew, Michael Pourdehnad, Abass Alavi, and Eugene G d'Aquili. 2003. "Cerebral Blood Flow during Meditative Prayer: Preliminary Findings and Methodological Issues." *Perceptual and Motor Skills* 97 (2): 625-30. https://doi.org/10.2466/pms.2003.97.2.625.

Orfei, Maria Donata, Fabrizio Piras, Enrica Macci, Carlo Caltagirone, and Gianfranco Spalletta. 2013. "The Neuroanatomical Correlates of Cognitive Insight in Schizophrenia." *Social Cognitive and Affective Neuroscience* 8: 418-23. https://doi.org/10.1093/scan/nss016.

Pettigrew, Thomas F., and Linda R. Tropp. 2008. "How Does Intergroup Contact Reduce Prejudice? Meta-Analytic Tests of Three Mediatorsy." *European Journal of Social Psychology* 38 (6): 922-34. https://doi.org/10.1002/ejsp.504.

Riggs, Sally E., Paul M. Grant, Dimitri Perivoliotis, and Aaron T. Beck. 2012. "Assessment of Cognitive Insight: A Qualitative Review." *Schizophrenia Bulletin* 38 (2): 338-50. https://doi.org/10.1093/schbul/sbq085.

Ruby, Perrine, and Jean Decety. 2004. "How Would You Feel versus How Do You Think She Would Feel ? A Neuroimaging Study of Perspective-Taking with Social Emotions." *Journal of Cognitive Neuroscience* 16 (6): 988-99.

Ryff, Carol D. 2014. "Psychological Well-Being Revisited: Advances in the Science and Practice of Eudaimonia." *Psychotherapy and Psychosomatics* 83 (1): 10-28. https://doi.org/10.1159/000353263.

Sedlmeier, Peter, Juliane Eberth, Marcus Schwarz, Doreen Zimmermann, Frederik Haarig, Sonia Jaeger, and Sonja Kunze. 2012. "The Psychological Effects of Meditation: A Meta-Analysis." *Psychological Bulletin* 138 (6): 1139-71. https://doi.org/10.1037/a0028168.

Segal, Z. V., J. M. G. Williams, and J. D. Teasdale. 2012. *Mindfulness-Based Cognitive Therapy for Depression*. Guilford Press.

Seth, Anil K. 2013. "Interoceptive Inference, Emotion, and the Embodied Self." *Trends in Cognitive Sciences* 17 (11): 565-73. https://doi.org/10.1016/j.tics.2013.09.007.

Slagter, Heleen A., Antoine Lutz, Lawrence L. Greischar, Andrew D. Francis, Sander Nieuwenhuis, James M. Davis, and Richard J. Davidson. 2007. "Mental Training Affects Distribution of Limited Brain Resources." *PLoS Biology* 5 (6): 1228-35. https://doi.org/10.1371/journal.pbio.0050138.

Smallwood, Jonathan, Merrill McSpadden, and Jonathan W. Schooler. 2007. "The Lights Are on but No One's Home: Meta-Awareness and the Decoupling of Attention When the Mind Wanders." *Psychonomic Bulletin & Review* 14 (3): 527-33. https://doi.org/10.3758/BF03194102.

Tang, Yi-Yuan, B. K. Holzel, and Michael I Posner. 2015. "The Neuroscience of Mindfulness Meditation." *Neuroscience* 16 (4): 213-25. https://doi.org/10.1038/nrn3916.

Tang, Yi-Yuan, Yinghua Ma, Junhong Wang, Yaxin Fan, Shigang Feng, Qilin Lu, Qingbao Yu, et al. 2007. "Short-Term Meditation Training Improves Attention and Self-Regulation." *Proceedings of the National Academy of Sciences of the United States of America* 104 (43): 17152-56. https://doi.org/10.1073/pnas.0707678104.

Teasdale, J D, Z V Segal, J M Williams, V A Ridgeway, J M Soulsby, and M A Lau. 2000. "Prevention of Relapse/Recurrence in Major Depression by Mindfulness-Based Cognitive Therapy." *Journal of Consulting and Clinical Psychology* 68 (4): 615-23. https://doi.org/10.1037/0022-006X.68.4.615.

Teasdale, John D., Richard G. Moore, Hazel Hayhurst, Marie Pope, Susan Williams, and Zindel V. Segal. 2002. "Metacognitive Awareness and Prevention of Relapse in Depression: Empirical Evidence." *Journal of Consulting and Clinical Psychology* 70 (2): 275-87. https://doi.org/10.1037//0022-006X.70.2.275.

Travis, Fred, and Jonathan Shear. 2010. "Focused Attention, Open Monitoring and Automatic Self-Transcending: Categories to Organize Meditations from Vedic, Buddhist and Chinese Traditions." *Consciousness and Cognition* 19 (4): 1110-18. https://doi.org/10.1016/j.concog.2010.01.007.

Travis, Frederick. 2014. "Transcendental Experiences during Meditation Practice." *Annals of the New York Academy of Sciences* 1307 (1): 1-8. https://doi.org/10.1111/nyas.12316.

Vago, David R, and David A Silbersweig. 2012. "Self-Awareness, Self-Regulation, and Self-Transcendence (S-ART): A Framework for Understanding the Neurobiological

Mechanisms of Mindfulness." *Frontiers in Human Neuroscience* 6 (October): 296. https://doi.org/10.3389/fnhum.2012.00296.

Vugt, Marieke K. Van, and Heleen A. Slagter. 2014. "Control over Experience? Magnitude of the Attentional Blink Depends on Meditative State." *Consciousness and Cognition* 23 (1): 32-39. https://doi.org/10.1016/j.concog.2013.11.001.

Waters, Andrew J., Reshmi Marhe, and Ingmar H A Franken. 2012. "Attentional Bias to Drug Cues Is Elevated before and during Temptations to Use Heroin and Cocaine." *Psychopharmacology* 219 (3): 909-21. https://doi.org/10.1007/s00213-011-2424-z.

Webb, Thomas L., Eleanor Miles, and Paschal Sheeran. 2012. "Dealing with Feeling: A Meta-Analysis of the Effectiveness of Strategies Derived from the Process Model of Emotion Regulation." *Psychological Bulletin* 138 (4): 775-808. https://doi.org/10.1037/a0027600.

UNDERSTANDING THE WORLD COLLECTIVELY

Gonzalo de Polavieja *

Abstract

Some simple rules like performing and average or majority-voting have been proposed as methods to extract the knowledge that a collective contains. We review the arguments made in the literature in favor of these simple rules (see also our more complete discussion [1]). Two theorems, Condorcet's theorem and Jenses's inequality, have been used almost as proofs that collective intelligence in unavoidable. Instead, we argue that the conditions under which they apply are very restrictive. Experimental demonstrations, like Galton's ox weight estimation, is also argued to be of limited validity in other scenarios. We then discuss how animals and how AI methods can help to understand how knowledge can be extracted from a collective.

Collective Intelligence is not guaranteed: why Condorcet, Jensen and Galton fail in practice

Condorcet considered a group of N people voting on whether or not a particular proposition is true [2, 3]. Each individual had a probability p of getting the answer right, so if p is greater than 0.5 and all individuals vote independently, then the probability that the majority get the answer correct is higher than p, and approaches 1 for large enough N. However, humans cannot vote with statistical independence because of common information sources and common cognitive apparatus. Thus, Condorcet result is not guaranteed. The majority vote can be worse than using the opinion of a single randomly selected individual.

Averaging opinions can also improve estimations by cancellation of independent errors [4, 5, 6, 7]. Probably the more famous case is the ox-

* Champalimaud Neuroscience Programme, Champalimaud Center for the Unknown, Lisbon, Portugal.

weighting competition reported by Galton [8]. In a county fair, visitors gave their estimation of the weight of a slaughtered ox. Galton found that the average estimation was only 1% of the true value despite the large variance of individual estimations. Other studies have reported similar effects [9, 10, 11, 12]. However, the result is not guaranteed as the group can show strong biases [13].

Another way to measure how well one solves a task is using a cost function. If we measure our cost using convex mathematical functions, as in the standard case of quadratic cost, then, according to Jensen's inequality [14, 15], the crowd mean outperforms a randomly selected individual. In real-world scenarios, however, the cost function need not be convex and the result does not hold.

Looking at animal Collectives for inspiration

As these simple aggregation rules are not guaranteed to work, researchers have developed new methods to extract knowledge from a crowd [16, 17, 18, 19, 20]. These methods attempt at weighting individuals differently depending on previous history, knowledge in related areas or confidence measures.

Some of these methods can look at animal collectives for inspiration. Animal collectives seem capable of behaviors of this type of weighting procedure. While it has been commonly assumed that animals aggregate information from other using an average, a better explanation of the data is given by a weighted average [21]. These weights are dynamical, allowing animals to perform an average or focus on one of several individuals. Animals can, in principle, match their aggregation to the distribution of knowledge in the group.

How AI can help to aggregate knowledge

Large datasets [22] and state-of-the-art AI methods allow the development of domain-specific methods that take into account history, confidence, correlations and costs. A simple application for knowledge aggregation in doctors show that this methodology can outperform simpler methods [1].

Funding

I acknowledge funding from the Champalimaud Foundation.

References

[1] Laan A, Madirolas G, de Polavieja GG. Front Robot AI. 2017 ;10(4:56):doi: 10.3389/frobt.2017.00056.

[2] Condorcet Md. Essai sur l'application de l'analyse la probabilité des décisions rendues la pluralité des voix. Paris; 1785.

[3] Boland PJ. Majority Systems and the Condorcet Jury Theorem. The Statistician. 1989;38(3):181.

[4] Sumpter DJT. Collective animal behavior. Princeton University Press; 2010.

[5] Surowiecki J. The wisdom of crowds: why the many are smarter than

the few and how collective wisdom shapes business, economies, societies, and nations. Doubleday; 2004.

[6] Hong L, Page SE. Some Microfoundations of Collective Wisdom. Collective Wisdom. 2008; p. 56-71.

[7] Watts DJ. Everything is obvious: once you know the answer. Crown Business; 2011.

[8] Galton F. Vox Populi (The Wisdom of Crowds). Nature. 1907; 75:450-451.

[9] Jack L Treynor. Market Efficiency and the Bean Jar Experiment. Financial Analysts Journal. 1987;43(3):50-53.

[10] Krause S, James R, Faria JJ, Ruxton GD, Krause J. Swarm intelligence in humans: diversity can trump ability. Animal Behaviour. 2011;81(5):941-948.

[11] Lorge DDJBM I Fox. A survey of studies contrasting the quality of group performance and individual performance, 1920-1957. Psychological bulletin. 1958 nov;55(6):337-72.

[12] Clemen RT. Combining forecasts: A review and annotated bibliography. International Journal of Forecasting. 1989;5(4):559-583.

[13] Lorenz J, Rauhut H, Schweitzer F, Helbing D. How social influence can undermine the wisdom of crowd effect. Proceedings of the National Academy of Sciences of the United States of America. 2011 may;108(22):9020-5.

[14] Kuczma M, Gilanyi A. An introduction to the theory of functional equations and inequalities: Cauchy's equation and Jensen's inequality. Birkhauser; 2009.

[15] Richard P Larrick JBS Albert E Mannes. The Social Psychology of the Wisdom of Crowds. In: Frontiers in Social Psychology: Social Judgment and Decision Making. vol. 6. New York: Psychology Press; 2003. p. 227-242.

[16] Madirolas G, de Polavieja GG. Improving Collective Estimations Using Resistance to Social Influence. PLOS Computational Biology. 2015 nov;11(11):e1004594.

[17] Ward AJW, Herbert-Read JE, Sumpter DJT, Krause J. Fast and accurate decisions through collective vigilance in fish shoals. Proceedings of the National Academy of Sciences of the United States of America. 2011 feb;108(6):2312-5.

[18] Soll JB, Larrick RP. Strategies for revising judgment: How (and how well) people use others' opinions. Journal of Experimental Psychology: Learning, Memory, and Cognition. 2009 may;35(3):780-805.

[19] Mannes AE, Soll JB, Larrick RP. The wisdom of select crowds. Journal of Personality and Social Psychology. 2014 aug;107(2):276-299.

[20] Whalen A, Yeung S. Using Ground Truths to Improve Wisdom of the Crowd Estimates. CogSci conference. 2015;.

[21] Heras F, Romero-Ferrero F, HInz R, de Polavieja GG. Aggregation rule in animal collectives dynamically changes between majority and minority influence. bioarxiv. 2018;10: doi: http://sci{hub.tw/10.1101/400747.

[22] Sun C, Shrivastava A, Singh S, Gupta A. Revisiting unreasonable effectiveness of data in deep learning era. arXiv preprint arXiv:170702968. 2017;.

SIMPLE MINDS LIVING IN COMPLEX SOCIAL WORLDS

***Rui Oliveira** **

Introduction

Social interactions are a complex phenomenon that is present in the life of most organisms, from those with more complex brains to those with simpler nervous systems. On the other hand social interactions have a major impact on health, which has not been acknowledged as much as other factors that affect our health. In a meta-analysis of the impact of different mortality risks on Humans social factors emerged among the major risks together with the classically named ones such as smoking, alcohol consumption, lack of physical activity and obesity (1). Interestingly, social factors, such as the perceived quality of social relationships and social support, have quite significant effect sizes and people in general are not as aware of their impact on health (1). So, there is a need to understand the mechanisms underlying this relationship between our social lives and our health. Social organisms with simpler nervous systems offer an opportunity to study such mechanisms. Within this framework our lab has been using zebrafish to study social behavior and to understand how the social environment is modulating biological systems and therefore impacting on health (2). We started by characterizing the cognitive adaptations for social group living in zebrafish and so far we have demonstrated the occurrence of: experience-driven changes in social behavior (3), ability to discriminate between different individuals in a social group (i.e. social recognition, 4), social attention (i.e. paying attention to interactions between others, (5), eavesdropping on third party interactions to collect social information that is used in subsequent interactions with the observed individuals (6), and audience effects in which individuals change their social behavior when interacting in the presence of third parties (i.e. audience, 7). Together these results suggest

* Integrative Behavioural Biology Research Group, Gulbenkian Institute of Science; ISPA - University Institute, Lisbon, Portugal.

that zebrafish have a number of cognitive adaptations for living in social networks and so they are a suitable model to study social phenomena and their impact on health.

Social buffering in zebrafish

In our lab we have recently validated a behavioral paradigm to study the impact of social factors on health in zebrafish. This paradigm is based in the fact that zebrafish exhibit a very stereotypic fear response when they are exposed to skin extracts from conspecifics than contain an alarm substance (8). When there are skin extracts from conspecifics in the water it indicates that a conspecific is wounded, most probably it has been beaten by a predator, and so it is a sign of danger to which they react very strongly. Thus, we have used this "alarm substance" to elicit a stereotypic alarm response that has two phases: first, the fish increases its swimming speed and assumes an erratic trajectory (zig-zag), which is an active response to threat; subsequently, they descend to the bottom where they remain motionless in a freezing posture, which resembles the freezing fear response in mammals. So, this paradigm provides us with a very stereotypic and robust behavior that is easy to quantify in an objective manner.

Using this behavioral paradigm we have studied the effect of the presence of conspecifics in the fear response to the "alarm substance" (9). It was shown that when exposed to the alarm substance by themselves zebrafish exhibited more freezing, indicating higher levels of fear, than when exposed to the alarm substance in the presence of conspecifics. This effect was present both with visual or chemical only access to the conspecifics indicating that is a multimodal social signal that is involved (9). So apparently, we also observe social buffering in zebrafish such that the presence of others functions as some kind of social support that reduces the fear response to a stressor. Since living in groups serves the adaptive function of reducing exposure to predators, it is expected that the larger the group more protected an individual is. Based on this rational one can predict that larger groups would be more efficient in making an individual feel safer, and so individuals exposed to the alarm substance should stress less in the presence of larger groups than in the presence of

smaller groups. However, we found no differences in the social buffering provided by shoals between 2 and 8 individuals (9).

Social decision-making about threat detection

The above mentioned result, led us to think that it was the behavioral state of the conspecifics in the companion shoal rather than their numbers that was being used by our focal fish to moderate their fear response. So we started thinking about this effect in terms of social decision-making rather than in terms of an social support / empathy construct. According to this view, what zebrafish are doing is basically to monitor the environment for the presence of threats, and to make a decision to flee or to keep with their current behavior based on the cues they can collect for the presence of a potential predator given background noise. In terms of signal detection theory, zebrafish have to make decisions if a predator is present with a certain degree of uncertainty and so there are four possible outcomes - 2 correct decisions (decided predator is present and it is really present; decided that predator was absent and it was really absent); and two types of errors: (1) false alarms, when they decide to activate an alarm response in the absence of the predator; and (2) misses, when they decide not to flee but there was a predator present (10). According to this framework animals should establish a threshold of response that balances the relative costs of false alarms and misses. Thus, depending on some factors, individuals can shift their threat detection threshold either to decrease the number of false alarms, if, for example, they live in more dangerous environments or they can relax it and decrease the cost associated with misses. In social species, public information can also help to set a threat detection threshold, such that animals can integrate both the cues from the predator and the background noise together with cues from other individuals, and so this becomes a social decision-making problem (10).

In zebrafish there are two cues from conspecifics that can be integrated to make such decisions: (1) chemical cues, such as the "alarm substance"; and (2) visual cues, such as the sight of alarmed/ relaxed conspecifics. So if zebrafish sees a conspecific expressing an alarm response, they may activate an alarm response themselves even if they do not smell the "alarm

substance". According to this view one we can think of social buffering as just one component of a wide range of phenomena one can observe in groups if animals are using social information to make decisions about the presence of threats in the environment.

Following this rational we have also investigated the occurrence of social contagion of fear (i.e. we stressed the conspecifics without stressing our focal fish to see if there is a social contagion of fear coming from the conspecifics to our individual), and of social facilitation (i.e. enhanced fear response in individuals exposed to the alarm substance by the presence of other alarmed conspecifics) of the fear response in zebrafish. Preliminary results confirm the occurrence of all these phenomena in zebrafish, suggesting they are indeed using social information to decide if threat is present in the environment or not.

Neuromolecular mechanisms of social information use

Nonapeptides of the vasotocin family (oxytocin and vasopressin in mammals and similar peptides in other taxa) have been consistently implicated in the regulation the social behavior across vertebrates (11). Hence, we have focused on these nonapeptides as candidates for the regulation of the neural mechanisms involved in the use of social information.

Preliminary data from our lab using a zebrafish mutant line that lacks a functional oxytocin receptor (OTR -/-) suggests that both social buffering and social contagion of fear are not present in OTR -/- fish. If confirmed these results will implicate oxytocin signaling in the use of social information in zebrafish.

In summary, zebrafish uses social information to adjust their response to the presence of threats in the environment and therefore, given the genetic toolbox available for this species it can be used to dissect the neural circuits involved in social-decision-making.

Acknowledgements

I thank the lab members that conducted the original research described here, in particular Ana Faustino and Ibukun Akinrinade. Part

of the work reported here is funded by Fundação para a Ciência e a Tecnologia (grant Lisboa-01-0145-FEDER-030627).

References

(1) Holt-Lunstad J., Smith T.B., Layton J.B. 2010. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 7(7): e1000316.

(2) Oliveira, R.F. 2013. Mind the fish: zebrafish as a model in cognitive social neuroscience. Frontiers in Neural Circuits 7: e131.

(3) Oliveira, R.F., Silva, J.F., Simões, J.M. 2011. Fighting zebrafish: characterization of aggressive behavior and winner-loser effects. Zebrafish 8: 73-81.

(4) Madeira N., Oliveira R.F. 2017. Long-Term Social Recognition Memory in Zebrafish. Zebrafish.

(5) Abril-de-Abreu, R., Cruz, J., Oliveira, R.F. 2015. Social Eavesdropping in Zebrafish: Tuning of Attention to Social Interactions. Scientific Reports 5: 12678.

(6) Abril-de-Abreu, R., Cruz, A.S., Oliveira, R.F. 2015. Social dominance modulates eavesdropping in zebrafish. Royal Society Open Science 2: 150220.

(7) Cruz, A.S., Oliveira, R.F. 2015. Audience effects and aggressive priming in agonistic behaviour of male zebrafish, Danio rerio. Animal Behaviour 107: 269–276.

(8) Speedie, N., Gerlai, R. 2008. Alarm substance induced behavioral responses in zebra sh (*Danio rerio*). Behav. Brain Res. 188: 168–177.

(9) Faustino A.I., Tacão-Monteiro A., Oliveira R.F. 2017. Mechanisms of social buffering of fear in zebrafish. Scientific Reports 7: 44329.

(10) Oliveira R. F. and Faustino A. I. 2017. Social information use in threat perception: Social buffering, contagion and facilitation of alarm responses. Communicative and Integrative Biology 10: e1325049.

(11) Donaldson Z.R., Young L.J. 2008. Oxytocin, vasopressin, and the neurogenetics of sociality. Science 322: 900-904.

BRAIN VS. MACHINE CONTROL, WHICH ONE GETS THE POWER?

Jose Carmena *

Brain-Machine Interfaces (BMIs) and neuroprostheses include a plethora of techniques, encompassing both invasive and noninvasive approaches acting at the central or peripheral level, with the common aim of improving or restoring function, such as communication, and lower or upper limb control. Among the number of options, the choice will be established based on the single patient and his personal needs. A common underlying requirement for the success of these techniques is the fact that the brain should be at least partially aware of the device.

The first studies on BMIs date back in the early 2000s. Such works showed that, in the absence of task-relevant movement, primates could modulate neural activity to control external devices and, most importantly, they were able to improve with training [**1**]. After fifteen years of intensive research, a number of techniques have been designed and tested on different species all the way to humans.

However, BMIs are not yet a clinically viable solution to help patients and the gap between academic and industry state of the art is significant. To bridge this gap, future research should address two main metacategories that run in parallel. The first challenge consists in the optimization of the neural interface, which should ideally be small, long-lasting and allow efficient bidirectional communication. The optimization of the design encompasses many sub-challenges, such as the optimization of the biophysical interface, the choice of the proper material to avoid the degradation process, and the improvement of the communication modalities. The second metacategory concerns the scaling up in functionality with the aim of allowing patients to gain back independence and easily perform daily-living tasks. This category includes several fields, such as the optimization of control strategy and sensory feedback.

* Department of Electrical Engineering and Computer Sciences, Helen Wills Neuroscience Institute, University of California, Berkeley, USA.

In the framework of BMI, our group tackles mainly three points. The first important line of research investigates neuroprosthetic skills, meaning the proficient, readily-recalled control of artificial actuators irrespective of natural physical movements. The main hypothesis underlying BMIs is that neuroprosthetic learning occurs through the selection of specific neural patterns via feedback and reinforcement. Neuroprosthetic skills are typically investigated through center-out reaching tasks, where a cursor on the screen is a simple, yet efficient actuator to investigate the principles of how brain learns. More generally, the working loop consists in the recording of volitional control signals as spike trains of neurons which are then input to a decoder that controls a N-Degree of Freedom (DOF) virtual or physical actuator. The decoder achieves a dimensionality reduction from many inputs to a lower number of outputs and does not have to meet excessive biomimetic requirements. A crucial point in the design of the system is to leverage the brain's ability to learn something about the BMI. We demonstrated such brain's capacity when training animals over multiple days [**2**]. Once accomplished the necessary requirement of obtaining stable neural recordings, animals underwent multiple BMI sessions and their performance improved with time, reaching a plateau after an average of 6-7 days. The key finding of the experiment was that the tuning of neurons changed with learning. Indeed, as performance improved, the patterns of neuron activity became more stable and remained constant once the animal reached the plateau.

This finding indicates that the animal can learn and use this piece of knowledge day after day, at the beginning of each session, showing that the brain can consolidate neuroprosthetic motor skills to be readily-recalled, stable over time and robust to interferences as for natural learning.

Another important observation of our work is that learning is state-dependent. More specifically, we showed that cortical neurons can flexibly switch between manual and brain control modes after learning and that the brain learns to specifically modulate task-relevant units [**3**].

Gaining insights into the dynamics of neural exploration is a key requirement to optimize BMI design. To deal with high variability, the brain has two options: either learning how to control each single neuron independently, or reduce the dimensionality of the problem and achieve shared layered control. To address this question, in collaboration with Rui

Costa, we used factor analysis to decompose variability during learning into two sources: shared and private. Our results suggest that brain starts exploring the high-dimensional space through private inputs and, as it learns and achieves better control, it switches to co-modulated activity. In other words, private signals are noisier and results in low-quality performance but are useful for the fundamental initial space exploration [**4**].

BMI can be interpreted as a two-learner system consisting of brain and decoder. Ideally, the system should simultaneously harness the brain's ability to learn from the decoder and the benefits of machine learning to optimally choose when and how update the decoder's parameters.

Therefore, to improve performance, our group achieved closed-loop decoder adaptation using a SmoothBatch algorithm that updated decoder parameters on a 1-2 min time-scale [**5**]. The algorithm was successfully tested on one nonhuman primate, suggesting that closed-loop decoder adaptation involves a co-adaptation process between the subject and the decoder. Notwithstanding these positive results, decoders based on Kalman filters do not model the spikes directly, and therefore may limit the processing time-scale of BMI control and adaptation. Thus, a new promising method applies point process filtering to allow for neural processing, control and decoder adaptation with every spike event and at a faster time-scale with respect to previous decoders [**6**]. Our results shows that the high control rate results in a significant improvement in performance (up to 30%) [**7**].

To date, BMI learning and control have primarily been studied in laboratory-controlled settings where users control a BMI isolated from other tasks. However, real world is noisy and neuroprostheses will ultimately be used for a number of behaviors in coordination with existing motor and cognitive functions. Consequently, tasks that activate brain areas near (or overlapping) with those used for BMI control may cause degradation of performance. In this framework, we claim that neuroplasticity and skill formation are critical for reducing disruptions from native motor networks. To prove this hypothesis, our group developed a behavioral paradigm that required a non-human primate to simultaneously control arm and BMI cursor [**8**]. The subject simultaneously performed an isometric force task with the arm contralateral to the units used for BMI decoding and a center-out task with the BMI cursor. Results showed that

the isometric force task significantly disrupted BMI performance but, most importantly, did not alter skilled control of the BMI. This finding supports the hypothesis that neuroplasticity and skill formation are key requirements for the robustness of the BMI system.

All the BMI principles described above can also be leveraged with a rehabilitation purpose. A clinical trial targeting chronic stroke is about to start with the aim of helping patients to rewire movements through exploitation of the natural afferent feedback provided by BMI systems. Another possibility is represented by neurofeedback studies targeting Parkinson's (PD) patients implanted with Deep Brain Stimulation (DBS). Our group is currently carrying out the first home-based electrocorticographic (ECoG) neurofeedback study that exploits DBS electrodes to record cortical activity and train patients to modulate it. Preliminary results on three PD patients show that they could gain control over β-power activity with practice.

The second line of research tackles mental health and aims at providing alternative treatment to pharmacotherapy which presents side effects and shows unsatisfying mixed results. This innovative treatment program exploits BMI technology to develop system-based closed-loop therapy to gain insights into the underlying physiology of a variety of mental disorders and to investigate the anxiolytic effect reported for stimulation of specific loci [**9**].

The protocol consists of an engaging free-choice probabilistic reward task during which task difficulty is modulated to induce emotional stress in macaques and simulate pathological conditions. The protocol is divided into three blocks, namely regular, stress and stress with stimulation. Preliminary results show that the stress level, assessed through heart rate and pupil dilatation, can be modulated through stimulation. Importantly, we have been able to accomplish an additional step by closing the control loop and stimulate the animal only when the recorded variables revealed a stressed emotional state.

The third line of research addresses the lack of implantable, life-lasting, untethered neural interface systems. In this framework, while radio frequency attenuates very quickly with distance in tissue, meaning that communicating with devices deep in the body would be difficult without using potentially damaging high-intensity radiation, leveraging

ultrasonic transmission provides us with the potential of shrinking down the size of the sensors to 10s of micrometers.

To this end, over the last few years, our group has been working with Michel Maharbiz's group on the development of ultrasonic neural dust [**10**] which allows wireless recording in the peripheral nervous system and uses ultrasound both to power and read out the measurements. The system contains a piezoelectric crystal that converts ultrasound vibrations from outside the body into electricity to power a tiny transistor that is in contact with a nerve (or muscle fiber). A voltage spike in the fiber alters the crystal vibration, which changes the echo detected by the ultrasound receiver. While the experiments so far have involved the peripheral nervous system and muscles [**11**], our group is currently working with the Maharbiz group to miniaturize the device further and shrink down the sensors to the 100s-micron target size, which we would need for the central nervous system.

In summary, we have discussed three points about the science and technology of BMI, namely neuroplasticity, machine learning and neurotechnology, that are important for the adoption of this technology by society and its evolution [**12**].

References

[**1**] Carmena J.M., Lebedev M.A., Crist R.E., O'Doherty J.E., Santucci D.M., Dimitrov D.F., Patil P.G., Henriquez C.S. and Nicolelis M.A.L. (2003) *Learning to control a brain-machine interface for reaching and grasping by primates.* PLoS Biology 1(2), pp. 193-208.

[**2**] *Ganguly K and Carmena JM. (2009) Emergence of a cortical map for neuroprosthetic control.* PLoS Biology 7(7):e1000153.

[**3**] Ganguly K, Dimitrov DF, Wallis JD and Carmena JM. (2011) *Reversible large-scale modification of cortical networks during neuroprosthetic control.* Nature Neuroscience 14, pp. 662-667, 2011.

[**4**] Athalye V.R., Ganguly K., Costa R.M.*, and Carmena J.M.* (2017) *Emergence of coordinated neural dynamics underlies neuroprosthetic learning and skillful control.* Neuron 93(4):955-970.e5. doi: 10.1016/j.neuron.2017.01.016.

[**5**] Orsborn AL, Dangi S, Moorman HG, Carmena JM. *Closed-loop decoder adaptation on intermediate time-scales facilitates rapid BMI Performance improvements independent of decoder initialization conditions.* IEEE Trans Neural Syst Rehabil Eng 2012 Jul;20(4):468-77.

[**6**] Shanechi MM, Orsborn AL, Carmena JM. *Robust Brain-Machine Interface design using optimal feedback control modeling and adaptive point process filtering.* PLoS Comput Biol 2016 Apr 1;12(4):e1004730.

[**7**] Shanechi M.M.*, Orsborn A.L.*, Moorman H.G.*, Gowda S.*, Dangi S, and Carmena J.M. (2016) *Rapid control and feedback rates in the sensorimotor pathway enhance neuroprosthetic control*. Nature Communications, 2017.

[**8**] Orsborn AL, Moorman HG, Overduin SA, Shanechi MM, Dimitrov DF, Carmena JM. *Closed-loop decoder adaptation shapes neural plasticity for skillful neuroprosthetic control.* Neuron 2014 Jun 18;82(6):1380-93.

[**9**] Santacruz S.R., Rich E.L., Wallis J.D., and Carmena J.M. (2017) *Caudate microstimulation increases value of specific choices.* Current Biology DOI: http://dx.doi.org/ 10.1016/j.cub.2017.09.051.

[**10**] Seo D.J., Carmena J.M., Rabaey J.M., Alon E. and Maharbiz M.M. (2013) *Neural Dust: an ultrasonic, low power solution for chronic brain-machine interfaces*. arXiv:1307.2196

[**11**] Seo D, Neely RM, Shen K, Singhal U, Alon E, Rabaey JM *et al. Wireless recording in the peripheral nervous system with ultrasonic neural dust.* Neuron 2016 Aug 3;91(3):529-39.

[**12**] Yuste R., Goering S., Agüera y Arcas B., Bi G., Carmena J.M., et al. (2017) *Four ethical priorities for neurotechnologies and AI.* Nature 551(7679), pp. 159-163.

COLLECTIVE INTELLIGENCE AS A CENTRAL CHARACTERISTIC OF SMALL GROUPS

Christopher Chabris *

Abstract

Much important work is performed by small groups of people who collaborate. This is increasingly true in scientific and academic disciplines, as well as in business and government. Borrowing from the long tradition of research on individual cognitive ability, which has found that people who perform well on one cognitive task tend to perform well on other tasks - the basis of the phenomenon known as "general intelligence", which is measured by IQ tests - we looked for the same phenomenon in small teams.

Over several studies involving hundreds of teams and thousands of individuals, my colleagues and I have found that task performance is indeed correlated across teams, with a general factor explaining about as much of the variance in team performance as it does in individual performance of cognitive tasks. We label this factor "collective intelligence". We also found that teams with more evenly distributed member contributions, with members who score higher in social intelligence, and with more women, tend to exhibit greater collective intelligence. The collective intelligence of a team predicts how well it will perform over extended periods in complex tasks.

In this talk I will review research on the collective intelligence of small groups and discuss some current and future research directions in this area. I will also distinguish between this form of collective intelligence and other ways in which the same term is used to describe different (but related) concepts. The main conclusion will be that just as we cannot fully understand individual differences in behavior without accounting for differences in individual intelligence, we must consider the collective intelligence of small groups to understand why groups differ so much in their performance and outcomes.

* Geisinger Health System, Lewisburg, Pennsylvania, USA; Union College, Schenectady, New York, USA; Institute for Advanced Study in Toulouse, France.

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

HOW WELL DOES THE RESEARCH SUPPORTED BY THE BIAL FOUNDATION PERFORM? A BIBLIOMETRIC ASSESSMENT

Marinho, S.*, Guedes, P.*, & Sousa, N.*

Background

Created in 2014, the BIAL Foundation's online database, which gathers all funded projects' scientific publications, has enabled a more systematic and quantitative assessment of the projects' productivity over the years. Bibliometric indicators have been widely used and proven to be useful tools in the assessment of the research performance, provided that their pitfalls are taken into consideration and they are combined with more qualitative knowledge about the projects to be assessed.

Aims

To analyse and to monitor the research productivity and impact of projects supported by the BIAL Foundation by using bibliometric indicators.

Method

The research projects' productivity was assessed by counting the number of papers published in academic journals indexed by Scopus or Web of Science (WoS). The publications' impact was assessed by the number of citations per item retrieved from WoS Core Collection in March 2018. This information was used to manually calculate the total number of times cited and the average citations per item. Combining the productivity (total number of papers published) and the impact (number of citations for each paper) the BIAL Foundation's *h*-index was calculated,

* BIAL Foundation, Portugal.

where *h* equalled the number of publications for which it received at least *h* citations each. For papers published from 2007 to 2017, the number of citations were compared with the expected number of citations for papers in the same research field and publication year, based on field baselines percentiles dataset of Essential Science Indicators (ESI), updated on January 1st, 2018. The Highly Cited Papers, featuring those that ranked in the top 1% by citations for field and publication year in WoS, were also retrieved. The quality of journals was assessed by their impact factor and mainly by their quartile score (provided by Journal Citation Reports) in order to mitigate differences between research fields. When a journal occupied different positions in the quartile ranking (Q1, Q2, Q3 or Q4) depending on the subject category with which it was associated, the best one was chosen. These results were compared with the previous assessment made in March 2016 to pinpoint the major improvements achieved in these last 2 years.

Results

Since 1994, the BIAL Foundation has supported 610 research projects through its grants programme, in the areas of Psychophysiology (307 grants, 50%), Parapsychology (206 grants, 34%) and Interdisciplinary – a combination of Psychophysiology and Parapsychology (97 grants, 16%). The BIAL Foundation has also supported four additional projects focused on specific topics of research interest. Overall, 910 indexed papers (journal article, review, conference paper, letter, book and book chapter) were published from 1995 to 2018. Excluding the last two grant editions (2014/15 and 2016/17), in which most projects are still ongoing or starting, a ratio of 1.76 indexed papers per project was obtained (806 papers per 459 projects).

Currently, the BIAL Foundation has 136 ongoing projects. It is worth noting that some projects of the last grant edition, which started during 2017, have already a substantial number of published papers. In 2016, 91 indexed papers were published, representing an increase of 26% when compared to 2015.

Overall, a total of 12.737 citations were counted, with 756 papers being cited on average 17 times (M = 16.85), ranging from 0 to 353 citations. The BIAL Foundation *h*-index was 52. In the last 10 years,

almost 20% of the papers ranked in the top 10% by citations for field and publication year.

749 papers were published in journals with an average impact factor of 3.5. In comparison with the previous analyses made in 2016, an additional 210 papers were published. This represents an increase of 39%. The majority of papers were published in journals of quartile 1 (n = 360; 48%) and quartile 2 (n = 183; 24%).

Conclusion

The systematic qualitative analyses of scientific reports alongside the use of conventional and up-to-date bibliometric indicators provide a reliable assessment of the quality, quantity and impact of the scientific research supported by the BIAL Foundation. When comparing the present results with the previous assessment conducted in 2016, the steady increase of indexed papers and higher number of citations is noteworthy. This improvement aligns with BIAL Foundation's primary goal: to promote research of excellence.

Keywords

BIAL Foundation grants, Indexed publications, Citations, Impact factor, Quartiles.

LISTA DE POSTERS
POSTERS

Posters com resultados finais apresentados pelos investigadores apoiados pela Fundação Bial e/ou disponíveis em www.fundacaobial.com

Posters with final results presented by the Bial Foundation grant holders and/or available at www.fundacaobial.com

Resumos dos posters disponíveis em / *Posters' abstracts available at www. fundacaobial.com*

2010

128/10 - "Extending the spiritual healing paradigm to explore distant mental interaction effects with Wiccan healers"
Investigadores/*Researchers*: Chris Roe, Charmaine Marie Sonnex
Instituição/*Institution*: Centre for the Study of Anomalous Psychological Processes (CSAPP), University of Northampton, Psychology Division, Northampton (UK)
Duração estimada/*Estimated duration*: 2014/10 – 2018/04

2012

51/12 - "The interpretation and evaluation of meaningful coincidences suggestive of psi communication in everyday life"
Investigadores/*Researchers*: Robin Wooffitt, Germaine Gunther
Instituição/*Institution*: Anomalous Experiences Research Unit, Dep. of Sociology, University of York (UK)
Duração/*Duration*: 2013/09 – 2018/01

87/12 - "Neurobiological correlates of empathy in couples: A study of central and peripheral measures"
Investigadores/*Researchers*: Joana Fernandes Pereira Coutinho, Cledna Patricía de Oliveira Silva, Jean Decety, Kristin Perrone McGovern, Óscar Filipe Coelho Neves Gonçalves, Vânia Andrea Sousa Gonçalves Moreira de Lima
Instituição/*Institution*: Centro de Investigação em Psicologia, Escola de Psicologia, Universidade do Minho, Braga (Portugal)
Duração/*Duration*: 2013/05 – 2017/07

98/12 - "Eye-brain dynamics during the emergence of three-dimensional perceptual awareness in Humans" - only abstract available
Investigadores/Researchers: Rafael Malach, Amos Arieli
Instituição/Institution: Department of Neurobiology - The Weizmann Institute of Science, Rehovot (Israel)
Duração estimada/*Estimated duration*: 2013/07 - 2018/04

130/12 - "Neural mechanisms of cognitive bias"
Investigadores/*Researchers*: Rui Filipe Nunes Pais de Oliveira, Ana Félix, Sara Cardoso
Instituição/*Institution*: ISPA, CRL, Lisbon and Instituto Gulbenkian de Ciência, Oeiras (Portugal)
Duração estimada/*Estimated duration*: 2013/09 – 2018/04

157/12 - "Contributions of parent-infant psychophysiology during dyadic interactions to child development"
Investigadores/*Researchers*: Raquel Alexandra Gonçalves Costa, Iva Tendais, Ana Conde, Catarina Tojal
Instituição/*Institution*: ISLA Campus Lisboa, Laureate International Universities, Lisboa (Portugal)
Duração/*Duration*: 2013/10 – 2016/11

178/12 - "How collaboration in psychotherapy becomes therapeutic: A study of interactive and psychophysiological processes in good and poor outcome cases"
Investigadores/*Researchers*: Eugénia Maria Ribeiro Pereira, Adriana Sampaio, Cledna Patrícia Silva, António P. Ribeiro, Adam O. Horvath, William B. Stiles, Inês Sousa, Joana Mourão, Dulce Pinto, Zita Sousa
Instituição/*Institution*: Centro de Investigação em Psicologia (CIPsi/UM), Escola de Psicologia, Universidade do Minho, Braga (Portugal)
Duração/*Duration*: 2013/06 – 2017/01

185/12 - "Circuit mechanisms of spatial attention in the zebrafish midbrain"
Investigadores/*Researchers*: Michael Brian Orger, Sabine L. Renninger
Instituição/*Institution*: Fundação Champalimaud, Lisboa (Portugal)
Duração/*Duration*: 2013/06 – 2017/07

192/12 - "Effects of conditional foxp2 deletion on motor-sequence learning"
Investigador/*Researcher*: Catherine Ann French
Instituição/*Institution*: Fundação Champalimaud, Lisboa (Portugal)
Duração/*Duration*: 2013/06 – 2016/07

253/12 – "REM-sleep, the regulation of self-conscious emotion and hyperarousal in psychophysiological insomnia" - only abstract available
Investigadores/*Researchers*: Lucia Talamini, Ekaterini Georgopoulou, Eus Van Someren
Instituição/*Institution*: University of Amsterdam, Psychology, Dept. Brain and Cognition (The Netherlands) and Netherlands Institute for Neuroscience, Dept. Sleep & Cognition, Amsterdam (The Netherlands)
Duração/*Duration*: 2015/11 – 2017/09

262/12 - "The neural basis of magical Ideation: A multimodal imaging study in twin subjects" - only abstract available
Investigadores/*Researchers*: Paolo Brambilla, Gioia Negri, Sara Piccin, Giuseppe Cabras, Corrado Fagnani
Instituição/*Institution*: Universitá delgi Studi di Milano and Unit of Epidemiology of the Italian Institute of Health, Rome (Italy)
Duração/*Duration*: 2014/01 – 2018/04

2014

51/14 - "The dissociated self: An investigation of emotional responses to a new body-threat task in those predisposed to anomalous body experiences, dissociation and disembodiment" - only abstract available
Investigador/*Researcher*: Jason John Braithwaite
Instituição/*Institution*: School of Psychology, University of Birmingham (UK)
Duração estimada/*Estimated duration*: 2015/09 – 2018/04

83/14 - "Electrophysiological correlates of the incorporation of recent memory sources into REM and non-REM dreams and of levels of insight following REM and non-REM dream interpretation"
Investigadores/*Researchers*: Mark Blagrove, Chris Edwards, Jean-Baptiste Eichenlaub, Perrine Ruby
Instituição/*Institution*: College of Human and Health Sciences, Department of Psychology, Swansea University (UK)
Duração/*Duration*: 2015/03 – 2017/11

118/14 - "Recursive consciousness training: Using neurofeedback to induce altered states"
Investigadores/*Researchers*: Amir Raz, Niels Birbaumer, Robert T Thibault
Instituição/*Institution*: Montreal Neurological Institute, McGill University (Canada); Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen (Germany)
Duração/*Duration*: 2015/09 – 2017/11

121/14 – "Maternal brain gain: Changes in neural representations and body perception during pregnancy" - only abstract available
Investigadores/*Researchers*: Jane Aspell, Flavia Cardini
Instituição/*Institution*: Anglia Ruskin University, Cambridge (UK)
Duração estimada/*Estimated duration*: 2015/11 - 2018/04

122/14 - "Internal and external world in parietal cortex" - only abstract available
Investigador/*Researcher*: Paolo Capotosto
Instituição/*Institution*: Department of Neuroscience, Imaging and Clinical Science, University "G. D'Annunzio", Chieti (Italy)
Duração/*Duration*: 2015/02 – 2016/09

128/14 - "Autonomic nerve recordings applied as a novel psychophysiological tool for Consciousness Science"
Investigadores/*Researchers*: Hugo Dyfrig Critchley, Peter Taggart, Yrsa Sverrisdottir
Instituição/*Institution*: Brighton and Sussex Medical School, University of Sussex (UK); Department of Physiology, Anatomy and Genetics, University of Oxford (UK)
Duração estimada/*Estimated duration*: 2015/09 - 2018/04

143/14 - "From audio-visual perception to action: The processing of spatio-temporal components"
Investigadores/*Researchers*: Sandra Mouta, Joana Vieira, Mariana Silva
Instituição/*Institution*: Association/ZGDV-Centro de Computação Gráfica, Guimarães (Portugal)
Duração/*Duration*: 2015/10 – 2018/04

150/14 - "Measuring the self: Behavioural and neural correlates of bodily awareness" - only abstract available
Investigadores/*Researchers*: Emmanuele Tidoni, Gaetano Tieri, Matteo Candidi, Salvatore Maria Aglioti
Instituição/*Institution*: Social Cognitive Neuroscience Laboratory, Department of Psychology, University of Rome "La Sapienza" (Italy)
Duração/*Duration*: 2015/02 – 2017/03

163/14 - "Sacred values underlying conflict proneness: A neuroimaging study of religious and nationalist radicals"
Investigadores/*Researchers*: Adolf Tobena, Clara Pretus, Joseph Hilferty, Oscar Vilarroya, Scott Atran
Instituição/*Institution*: Department of Psychiatry and Forensic Medicine UAB, Bellaterra Campus (Spain)
Duração estimada/*Estimated duration*: 2015/02 – 2018/04

180/14 - "Neural mechanisms of word learning: Contributions from amnesic patients and fMRI on healthy ageing" - only abstract available
Investigadores/*Researchers*: Tânia Patrícia Gregório Fernandes, Ana Luísa Nunes Raposo, Maria Isabel Segurado Pavão Martins Catarino Petiz, Rita Isabel Saraiva Jerónimo
Instituição/*Institution*: Faculdade de Psicologia da Universidade de Lisboa - FP-ULisboa (Portugal)
Duração estimada/*Estimated duration*: 2016/02 - 2018/02

206/14 - "Examination of brain coordination dynamics underlying hypnosis and volitional acts using intracranial electroencephalography" - only abstract available
Investigadores/*Researchers*: Jose Luis Perez Velazquez, Navinder Persaud, Taufik A. Valiante
Instituição/*Institution*: Hospital for Sick Children, Neurology, University of Toronto (Canada); Toronto Western Hospital (Canada)
Duração/*Duration*: 2015/05 – 2017/11

228/14 - "Pushing consciousness and selfhood towards their boundaries - An EEG neurophenomenological study"
Investigadores/*Researchers*: Joseph Glicksohn, Aviva Berkovich-Ohana, Tal Dotan Ben-Soussan
Instituição/*Institution*: Bar-Ilan University, Ramat Gan (Israel); Fondazione Patrizio Paoletti, Assisi (Italy)
Duração estimada/*Estimated duration*: 2015/02 - 2018/04

233/14 - "Training anomalous cognition in a motor task with subliminal auditory feedback"
Investigador/*Researcher*: John Albert Palmer
Instituição/*Institution*: Rhine Research Center, Durham, NC (USA)
Duração/*Duration*: 2015/04 – 2018/02

244/14 - "Induced brain plasticity after perinatal stroke: Structural and functional connectivity"
Investigadores/*Researchers*: Antoni Rodriguez-Fornells, Alfredo García-Alix, Carme Fons, Clément François, Jordi Muchart, Laura Bosch, Mónica Rebollo, Pablo Ripollés
Instituição/*Institution*: Department of Basic Psychology, University of Barcelona (Spain); Hospital Sant Joan de Deu, Esplugues de Llobregat (Spain)
Duração/*Duration*: 2015/02 – 2017/09

246/14 - "Anomalous/paranormal experiences reported by nurses themselves and in relation with theirs patients in hospitals: Examining psychological, personality and phenomenological variables"
Investigador/*Researcher*: Alejandro Enrique Parra
Instituição/*Institution*: Instituto de Psicologia Paranormal, Buenos Aires (Argentina)
Duração/*Duration*: 2015/03 – 2017/03

253/14 - "The impact of lipid signaling modulation in cognition"
Investigadores/*Researchers*: Tiago Gil Rodrigues Oliveira, Isabel Maria Sousa Castanho, Neide Marina Vieira Pereira, Rita Catarina Ribeiro da Silva, Vítor Manuel da Silva Pinto
Instituição/*Institution*: Life and Health Sciences Institute - ICVS, School of Health Sciences, University of Minho, Braga (Portugal)
Duração estimada/*Estimated duration*: 2015/05 – 2018/04

257/14 - "Genetics of psychic ability" - only abstract available
Investigadores/*Researchers*: Dean Radin, Garret Yount, Garry Nolan
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA); Stanford University (USA)
Duração estimada/*Estimated duration*: 2015/07 - 2018/04

260/14 - "Psi-Q: A smartphone testing suite for psi ability" - only abstract available
Investigadores/*Researcher*s: Dean Radin, Arnaud Delorme
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA)
Duração/*Duration*: 2015/07 - 2017/07

279/14 - "Facial and bodily temperature maps of emotions"
Investigadores/*Researchers*: Maria Lucia Martins das Neves Garrido, Lisa Katharina Kuhn, Nicholas Pound
Instituição/*Institution*: Division of Psychology, Department of Life Sciences, Brunel University, Uxbridge (UK)
Duração estimada/*Estimated duration*: 2015/01 - 2018/04

282/14 - "The mindful eye: Smooth pursuit and saccadic eye movements in meditators and non-meditators"
Investigadores/*Researchers*: Veena Kumari, Elena Antonova
Instituição/*Institution*: Institute of Psychiatry, King's College London (UK)
Duração/*Duration*: 2015/04 - 2017/01

287/14 - "Cryptochrome (CRY) and Intention"
Investigadores/*Researchers*: Yung-Jong Shiah, Hsu-Liang Hsieh, Dean Radin
Instituição/*Institution*: Graduate Institute of Counseling Psychology and Rehabilitation Counseling of the National Kaohsiung Normal University, Kaohsiung (Taiwan); Photobiology Lab, Taipei (Taiwan)
Duração/*Duration*: 2015/09 – 2017/06

308/14 - "A study of heterogeneity in parapsychological databases" - only abstract available
Investigador/*Researcher*: Peter Amalric Bancel
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA); Institut Métapsychique International, Paris (France)
Duração estimada/*Estimated duration*: 2015/06 – 2018/04

318/14 - "Neural correlates of tracking changing positions of objects" - only abstract available
Investigadores/*Researchers*: Christina Jayne Howard, Matthew K Belmonte
Instituição/*Institution*: Division of Psychology, Nottingham Trent University (UK)
Duração/*Duration*: 2015/02 – 2017/07

340/14 - "A question of belief: An analysis of item content in paranormal belief questionnaires"
Investigadores/*Researchers*: Lance Storm, Ken Drinkwater, Tony Jinks
Instituição/*Institution*: Brain and Cognition Centre, School of Psychology, University of Adelaide (Australia); Department of Psychology, Faculty of Health, Psychology and Social Care, Manchester (UK)
Duração/*Duration*: 2015/04 – 2017/07

344/14 - "An integrative approach to the neural basis of hypnotic suggestibility"
Investigador/*Researcher*: Devin Blair Terhune
Instituição/*Institution*: Goldsmiths, University of London (UK)
Duração/*Duration*: 2015/04 – 2016/07

355/14 - "Cognitive and personality differences in supernatural belief"
Investigadores/*Researchers*: Ian Scott Baker, David Sheffield, Malcolm Schofield, Paul Staples
Instituição/*Institution*: College of Life and Natural Sciences, University of Derby (UK)
Duração/*Duration*: 2015/06 – 2017/09

366/14 - "Changes in subjective time as indication of increased mindfulness after meditation"
Investigador/*Researcher*: Marc Christoph Wittmann
Instituição/*Institution*: Institute for Frontier Areas of Psychology and Mental Health, Freiburg (Germany); Department of Psychosomatic Medicine, University Medical Center Freiburg (Germany)
Duração estimada/*Estimated duration*: 2015/04 – 2018/04

372/14 - "Development and implementation of a comprehensive survey of secular American mediums" - only abstract available
Investigadores/*Researchers*: Julie Beischel, Chad Mosher, Mark Boccuzzi
Instituição/*Institution*: The Windbridge Institute for Applied Research in Human Potential, Tucson (USA)
Duração estimada/*Estimated duration*: 2015/07 – 2018/04

373/14 - "Multimodal mapping of visual motion perceptual decision: Dissecting the role of different motion integration areas in visual surface reconstruction"
Investigadores/*Researchers*: Miguel de Sá e Sousa de Castelo Branco, Gabriel Nascimento Ferreira da Costa, Gilberto Silva, João Valente Duarte, Ricardo Martins
Instituição/*Institution*: ICNAS - Institute for Nuclear Sciences Applied to Health, Coimbra (Portugal); IBILI - Institute for Biomedical Imaging and Life Sciences, Coimbra (Portugal)
Duração/*Duration*: 2016/02 - 2017/10

380/14 - "Using neural stimulation to modulate paranormal beliefs"
Investigadores/*Researchers*: Miguel Farias, Ute Kreplin
Instituição/*Institution*: Centre for Research in Psychology, Behaviour and Achievement, Coventry University (UK)
Duração/*Duration*: 2015/12 – 2017/10

385/14 - "Affective and cognitive modulation of pain by using real-time fMRI neurofeedback"
Investigadores/*Researchers*: Pedro Jose Montoya Jimenez, Beatriz Rey Solaz, Inmaculada Riquelme, Miguel Angel Munoz Garcia, Niels Birbaumer
Instituição/*Institution*: Research Institute on Health Sciences, University of Balearic Islands, Palma (Spain)
Duração estimada/*Estimated duration*: 2015/03 – 2018/04

386/14 - "Remote meditation support - A multimodal distant intention experiment"
Investigadores/*Researchers*: Stefan Schmidt, Han-gue Jo, Marc Wittmann, Thilo Hinterberger, Wolfgang Ambach
Instituição/*Institution*: Department of Psychosomatic Medicine, University Medical Center Freiburg (Germany); Institut für Grenzgebiete der Psychologie und Psychohygiene, Freiburg (Germany)
Duração estimada/*Estimated duration*: 2015/05 - 2018/04

388/14 - "Are free will and moral responsibility real or illusory? On the causal role of consciousness in decision-making, a combined EEG and intracranial study" - only abstract available
Investigador/*Researcher*: Uri M. Maoz
Instituição/*Institution*: California Institute of Technology – Caltech, Pasadena (USA)
Duração estimada/*Estimated duration*: 2016/02 - 2018/04

400/14 - "Is the matrix-experiment really a robust and artifact free experimental model to demonstrate generalized entanglement effects?"
Investigador/*Researcher*: Harald Walach
Instituição/*Institution*: Institute of Transcultural Health Studies, European University Viadrina, Frankfurt Oder (Germany)
Duração estimada/*Estimated duration*: 2016/01 - 2018/06

402/14 - "Skin Conductance Feedback Meditation (SCFM) – Exploring the role of skin conductance in meditative practice"
Investigador/*Researcher*: Thilo Hinterberger
Instituição/*Institution*: Department of Psychosomatic Medicine, Clinic of the University of Regensburg (Germany)
Duração estimada/*Estimated duration*: 2016/03 - 2018/04

413/14 - "The role of dopamine in behavioral exploration and action selection"
Investigador/*Researcher*: Aaron Christopher Koralek
Instituição/*Institution*: Champalimaud Neuroscience Programme, Lisboa (Portugal)
Duração estimada/*Estimated duration*: 2015/03 – 2018/04

480/14 - "The role of experimenter and participant mindset in the replication of psi experiments: Phase II of a global initiative"
Investigador/*Researcher*: Marilyn Schlitz
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA)
Duração/*Duration*: 2015/07 - 2017/07

489/14 - "An examination of the effects of mood and emotion on a real-world computer system and networking environment"
Investigador/*Researcher*: John G. Kruth
Instituição/*Institution*: Rhine Research Center, Durham (USA)
Duração estimada/*Estimated duration*: 2015/05 - 2018/04

495/14 - "Episodic memory enhancement in aging: The role of cognitive training combined with (bilateral) tDCS in the medial-temporal cortex and cerebellum on episodic memory performance in the elderly"
Investigadores/*Researchers*: Mário Manuel Rodrigues Simões, Filipe Fernandes, Jorge Evandro de Araújo Alves, Marcel Simis, Ana Rita Simões Martins, Jorge Almeida
Instituição/*Institution*: CINEICC - Centro de Investigação do Núcleo de Estudos e Intervenção Cognitivo-Comportamental/Universidade de Coimbra (Portugal)
Duração estimada/*Estimated duration*: 2015/07 - 2018/04

506/14 - "The Selfield: Optimizing precognition research"
Investigadores/*Researchers*: Mario Varvoglis, Peter Bancel
Instituição/*Institution*: Institut Metapsychique International, Paris (France); Institute of Noetic Sciences, Petaluma, California (USA)
Duração estimada/*Estimated duration*: 2015/09 - 2018/04

534/14 - "Exploring unconscious knowledge: Individual differences in ideomotor response" - only abstract available
Investigadores/*Researchers*: Jeremy Olson, Amir Raz, Mathieu Landry
Instituição/I*nstitution*: Raz Cognitive Neuroscience Lab, McGill University, Montreal (Canada); Montreal Neurological Institute (Canada)
Duração/Duration: 2015/08 - 2017/06

"The Aging Social Brain - Neural and behavioral age-related changes in social cognition and decision-making"
Investigadores/*Researchers*: João Eduardo Marques Teixeira, Manuel Fernando Santos Barbosa, Fernando Ricardo Ferreira Santos, Pedro Manuel Rocha Almeida, Hugo Daniel Leão Sousa
Instituição/*Institution*: Faculdade de Psicologia e de Ciências da Educação, Universidade do Porto (Portugal)
Duração/*Duration*: 2014/11 – 2018/01

"Aware Mind-Brain: Bridging insights on the mechanisms and neural substrates of human awareness and meditation"
Investigadores/*Researchers*: Antonino Raffone, Salvatore Maria Aglioti, Henk P. Barendregt, Fabio M. Giommi, Juliana Jordanova, Peter Malinowski, Stephen Whitmarsh
Instituição/*Institution*: ECONA - Interuniversity Center for Cognitive Processing in Natural and Artificial Systems, Università degli Studi di Roma "La Sapienza" (Italy)
Duração estimada/*Estimated duration*: 2015/11 - 2018/04

2016

97/16 - "Reproductive hormonal status as a predictor of precognition"
Investigadores/Researchers: Julia Mossbridge, Daryl Bem
Instituição/Institution: Institute of Noetic Sciences, Petaluma, California (USA); Department of Psychology, Cornell University, Ithaca (USA)
Duração estimada/*Estimated duration*: 2017/02 – 2018/04

124/16 - "The missing photon experiment: Does focused attention employ matter as an agent for interacting with light?" - only abstract available
Investigador/*Researcher*: Loren Carpenter
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA)
Duração estimada/*Estimated duration*: 2017/02 – 2018/04

PALESTRANTES E MODERADORES
SPEAKERS AND MODERATORS

MATTIA BERGOMI Investigador no *Collective Behavior Lab*, *Champalimaud Centre for the Unknown,* Programa de Neurociências, Lisboa, Portugal. Interesses científicos: topologia algébrica - análise topológica de dados, variedades topológicas de dimensão superior, homologia persistente e persistência multidimensional, topologia de sistemas dinâmicos; aprendizagem de máquinas - redes de crenças profundas, memória e criatividade na inteligência artificial, aprendizagem por reforço, granularidade ótima para análise de séries temporais multivariadas.

Researcher at Collective Behavior Lab, Champalimaud Centre for the Unknown, Neuroscience Programme, Lisbon, Portugal. Scientific interests: algebraic topology - topological data analysis, topology of high-dimensional varieties, persistent homology and multi-dimensional persistence, topology of dynamical systems; machine learning - deep belief networks, memory and creativity in artificial intelligence, reinforcement learning, optimal granularity for multivariate time series analysis.

ETZEL CARDEÑA *Thorsen Professor* de Psicologia, Departamento de Psicologia, Universidade de Lund, Suécia. Interesses científicos: psicologia das experiências excecionais/estados não ordinários de consciência, fenómenos parapsicológicos, neurofenomenologia da hipnose, dissociação, perturbações dissociativas e divagação mental, estados alterados de consciência e parapsicologia.

Thorsen Professor of Psychology, Department of Psychology, Lund University, Sweden. Scientific interests: the psychology of anomalous experiences/non-ordinary mental expressions, parapsychological phenomena, neurophenomenology of hypnosis, dissociation, dissociative disorders and mind wandering, altered states of consciousness and parapsychology.

JOSE CARMENA Professor de Engenharia Elétrica e Neurociências, Departamento de Engenharia Elétrica e de Ciências da Computação, *Helen Wills Neuroscience Institute.* Universidade da Califórnia, Berkeley, EUA. Interesses científicos: dinâmica das redes neuronais de larga-escala envolvidas na aprendizagem, mecanismos neuronais da ação, controlo motor e neuroplasticidade. Interação mente-máquina, algoritmos para a adaptação da descodificação de um circuito fechado, sistema neuroprostético e computação de conjuntos de redes neuronais.

Professor of Electrical Engineering and Neuroscience, Department of Electrical Engineering and Computer Sciences, Helen Wills Neuroscience Institute, University of California, Berkeley, USA. Scientific interests: large-scale neural circuit dynamics during learning, neural mechanisms of action, motor control and neuroplasticity. Brain-machine interface, algorithms for closed circuit decoder adaptation, neuroprosthetic systems and sets of neural networks computation.

MIGUEL CASTELO-BRANCO Professor de Biofísica e Matemática e Ciências da Visão e Diretor do IBILI e ICNAS, Universidade de Coimbra, Portugal. 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, Portugal. Scientific interests: sensory and cognitive neuroscience in healthy and ill populations.

CHRISTOPHER CHABRIS Professor, *Geisinger Health System*, Lewisburg, Pensilvânia, EUA; Professor Associado de Psicologia, *Union College*, Schenectady, Nova Iorque, EUA. Interesses científicos: atenção, inteligência (individual, coletiva e social), genética comportamental, tomada de decisão, jogos de vídeo e ciência cognitiva.

Professor, Geisinger Health System, Lewisburg, Pennsylvania, USA; Associate Professor of Psychology, Union College, Schenectady, New York, USA. Scientific interests: attention, intelligence (individual, collective, and social), behavior genetics, decision-making and video games and cognitive science.

ANJAN CHATTERJEE *Elliot Professor* de Neurologia, Departamento de Neurologia, Escola de Medicina, Universidade de Pensilvânia, Filadélfia, EUA. Interesses científicos: ética da transformação tecnológica da experiência humana, neurologia cosmética e ética da neuropotencialização, neurociência da estética e da arte, abstração de formas e formas de abstração, linguagem figurativa em indivíduos saudáveis e afásicos, inteligência espacial e centro de aprendizagem.

Elliot Professor of Neurology, Department of Neurology, University of Pennsylvania School of Medicine, Philadelphia, USA. Scientific interests: ethics of technological transformation of human experience, cosmetic neurology and the ethics of neuroenhancement, the neuroscience of aesthetics and art, abstraction of forms and forms of abstraction, figurative language in aphasic and healthy individuals, spatial intelligence and learning center.

AXEL CLEEREMANS Diretor de Investigação, Grupo da Consciência, Cognição e Computação, Universidade Livre de Bruxelas, 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. Scientific interests: consciousness and implicit learning, models of conscious and unconscious cognition, neural network of cognitive processes.

LORENZA COLZATO Professora de Potencialização Cognitiva, Departamento de Psicologia Cognitiva, Instituto de Neurociência Cognitiva, Faculdade de Psicologia, *Ruhr-University Bochum*, Alemanha; Investigadora Principal, Unidade de Psicologia Cognitiva, *Leiden University*, Holanda. Interesses científicos: potencialização cognitiva e cerebral visando melhorar o desempenho de indivíduos saudáveis, mediante intervenção nutricional (tirosina, triptofano, gaba, colina, probióticos) e estimulação transcutânea do nervo vago.

Professor of Cognitive Enhancement, Department of Cognitive Psychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr-University Bochum, Germany; Principal Investigator, Cognitive Psychology Unit, Leiden University, The Netherlands. Scientific interests: brain and cognitive enhancement aimed at improving performance in healthy individuals, through nutritional interventions (thyrosine, tryptophan, gaba, choline, probiotics) and transcutaneous vagus nerve stimulation.

RUI COSTA Professor de Neurociências e Neurologia, Universidade Columbia, e Investigador Principal no *Columbia's Zuckerman Institute,* Nova Iorque, EUA. Co-diretor do *Champalimaud Research* e Investigador Principal do *Neurobiology of Action Lab., Champalimaud Centre for the Unknown,* Programa de Neurociências, Lisboa, Portugal. 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).

Professor of Neuroscience and Neurology, Columbia University and Principal Investigator at Columbia's Zuckerman Institute, New York, USA. Co-director of Champalimaud Research and Principal Investigator of the Neurobiology of Action Lab., Champalimaud Centre for the Unknown, Neuroscience Programme. Lisbon, Portugal. Scientific 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).

GONZALO DE POLAVIEJA Investigador Principal do *Collective Behavior Lab*, *Champalimaud Centre for the Unknown,* Programa de Neurociências, Lisboa, Portugal. Interesses científicos: comportamento quantitativo, neurobiologia da tomada de decisão e da aprendizagem, comportamento coletivo, interações sociais e biologia matemática.

Principal Investigator of Collective Behavior Lab, Champalimaud Centre for the Unknown, Neuroscience Programme. Lisbon, Portugal. Scientific interests: quantitative behavior, neurobiology of decision-making and learning, collective behavior, social interactions and mathematical biology.

RAINER GOEBEL Professor de Neurociência Cognitiva, Faculdade de Psicologia e Neurociência, Universidade de Maastricht, Holanda. Diretor e fundador do *Maastricht Brain Imaging Centre* (M-BIC). Interesses científicos: representações neuronais no cérebro e o modo como estas são processadas para permitir funções percetivas e cognitivas específicas, correlatos neuronais da perceção visual, aplicações clínicas nas interfaces cérebro-computador (ICC) e estudos de *neurofeedback*.

Professor of Cognitive Neuroscience, Faculty of Psychology and Neuroscience, Maastricht University, The Netherlands. Founding director of the Maastricht Brain Imaging Centre (M-BIC). Scientific interests: neuronal representations in the brain and how they are processed

to enable specific perceptual and cognitive functions, neural correlates of visual awareness, clinical applications in brain computer interfaces (BCIs) and neurofeedback studies.

TORKEL KLINGBERG Professor de Neurociências Cognitiva, *Karolinska Institute,* Estocolmo, Suécia; Diretor do *CognitionMatters.org*. Interesses científicos: desenvolvimento do cérebro da criança e competências académicas, educação, treino cognitivo e treino da memória de trabalho.

Professor of Cognitive Neuroscience, Karolinska Institute, Stockholm, Sweden; Head of CognitionMatters.org. Scientific interests: child brain development and academic abilities, education and cognitive training and working memory training.

ANTOINE LUTZ Investigador Principal no INSERM, *Lyon Neuroscience Research Center*, no grupo de investigação *Cerebral Dynamic and Cognition*, Bron, França. Interesses científicos: estudos comportamentais e de neuroimagem da consciência, neurofenomenologia, relação entre a neuroplasticidade e o treino mental, bases neurobiológicas da meditação e o seu impacto em processos biológicos periféricos relevantes para a saúde física e mental, neuroimagem funcional, estudo do cérebro em estados de repouso para analisar diferenças individuais.

Tenured scientist at INSERM, Lyon Neuroscience Research Center, team Cerebral Dynamic and Cognition, Bron, France. Scientific interests: behavioral and brain imaging studies of consciousness, neurophenomenology, relation between neuroplasticity and mental training, neurobiological basis of meditation and their impact on peripheral biological processes relevant to physical and mental health, functional brain imaging, study of brain resting states to study individual differences.

JEAN-NOËL MISSA Diretor de Investigação do *National Fund for Scientific Research*, Bélgica; Professor de Filosofia e Ética, Universidade Livre de Bruxelas, Bélgica, e Diretor do *Center for Interdisciplinary Research in Bioethics.* Interesses científicos: história, filosofia e ética da biomedicina - neurociências e psiquiatria biológica -, ética e filosofia do "doping".

Research Director at the National Fund for Scientific Research, Belgium; Professor of Philosophy and Ethics, Université Libre de Bruxelles, Belgium, and Director of the Center for Interdisciplinary Research in Bioethics. Scientific interests: history, philosophy and ethics of biomedicine - neuroscience and biological psychiatry -, ethics and philosophy of doping.

RUI OLIVEIRA Investigador Principal do Grupo de Investigação em Biologia Integrativa do Comportamento, Instituto Gulbenkian de Ciência; Professor Catedrático e Reitor do ISPA - Instituto Universitário, Lisboa, Portugal. Interesses científicos: neurobiologia do comportamento social, modulação social do cérebro e do comportamento, evo-devo da cognição social, mecanismos genómicos e epigenéticos da plasticidade social, enviesamento cognitivo e suscetibilidade/resiliência à doença.

Principal Investigator of the Integrative Behavioural Biology Research Group, Gulbenkian Institute of Science; Professor of Psychobiology and Dean of ISPA - University Institute, Lisbon, Portugal. Scientific interests: neurobiology of social behavior, social modulation of brain and behavior, evo-devo of social cognition, genomic and epigenetic mechanisms of social plasticity, cognitive bias and susceptibility/resilience to disease.

TANIA RE Professora Assistente de Etnomedicina e Etnopsicologia. Psicóloga, Antropologista Médica, Fundadora e membro da Direção da *UNESCO Chair "Health Anthropology, Biosphere and Healing systems"*, Universidade de Génova, Itália. Investigadora e bolseira no *Regional Centre for Phytotherapy* (CERFIT), Hospital *Careggi*, Florença, Itália. Interesses científicos: antropologia médica, etnomedicina, fenomenologia dos estados alterados de consciência e medicina tradicional.

Assistant Professor of Ethnomedicine and Ethnopsychology. Psychologist, Medical Anthropologist, Founder and Board Member of the UNESCO Chair "Health Anthropology, Biosphere and Healing systems", University of Genoa, Italy. Researcher and fellow at the Regional Centre for Phytotherapy (CERFIT), Careggi Hospital, Florence, Italy. Scientific interests: medical anthropology, ethnomedicine, phenomenology of altered states of consciousness and traditional medicines.

ALEXANDER SACK Vice-Reitor e Diretor de Investigação, Faculdade de Psicologia e Neurociências, Departamento de Neurociências Cognitivas, Universidade de Maastrich, Holanda. Interesses científicos: mecanismos de comunicação para potenciar a cognição humana, ritmos cerebrais e perceção multissensorial, uso do equipamento necessário para medição simultânea de fMRI, TMS e EEG, modulação de redes não correlacionadas em fase precoce da doença de Alzheimer, predição de comportamento violento futuro de criminosos antissociais e recuperação do cérebro após um AVC.

Vice-Dean and Research Director, Faculty of Psychology and Neuroscience, Department of Cognitive Neuroscience, Maastricht University, The Netherlands. Scientific interests: communication mechanisms for enhancing human cognition, brain rhythms and multisensory perception, use of equipment required for simultaneous fMRI, TMS & EEG measurements, modulation of not correlated networks in early Alzheimer's disease, prediction of future violent behavior of antisocial offenders and brain recovery after stroke.

OLGA SILVA Professora Associada de Farmacognosia e de Plantas Medicinais e Fitoterapia, Departamento de Ciências Farmacológicas, Diretora do Laboratório de Farmacognosia, Faculdade de Farmácia da Universidade de Lisboa, Portugal. Interesses científicos: farmacognosia, etnofarmacologia, plantas medicinais e fitoterapia, qualidade, segurança e modo de ação de plantas usadas na Medicina Tradicional de países da Lusofonia.
Associate Professor of Pharmacognosy and Medicinal Plants and Phytotherapy, Department of Pharmacological Sciences, Director of the Laboratory of Pharmacognosy, Faculty of Pharmacy, University of Lisbon, Portugal. Scientific interests: pharmacognosy, ethnopharmacology,

medicinal plants and phytotherapy, quality, safety and mode of action of plants used in Traditional Medicine of Lusophony countries.

MÁRIO SIMÕES Professor de Psiquiatria e de Ciências da Consciência e Diretor do LIMMIT - Laboratório de Interação Mente-Matéria de Intenção Terapêutica, Faculdade de Medicina de Lisboa, Portugal. Interesses científicos: psicologia e psicofisiologia dos estados alterados de consciência, etnomedicina, experiências excecionais humanas e psicologia e espiritualidade.

Professor of Psychiatry and Consciousness Sciences and Director of LIMMIT - Laboratory of Interaction Mind-Matter with Therapeutic Intention, Faculty of Medicine of Lisbon, Portugal. Scientific interests: psychology and psychophysiology of altered states of consciousness, ethnomedicine, human exceptional experiences and psychology and spirituality.

NUNO SOUSA Professor e Presidente da Escola de Medicina da Universidade do Minho. Diretor do Centro Clínico Académico (2CA) - Braga e Investigador do ICVS, Universidade do Minho, Braga, Portugal. Interesses científicos: neurobiologia do stress e plasticidade das redes neuronais.

Professor and President at the School of Health Science, University of Minho. Director of the Clinical Academic Center (2CA) - Braga and Researcher at ICVS, University of Minho, Braga, Portugal. Scientific interests: neurobiology of stress and brain network plasticity.

YULIA USTINOVA Professora Associada, Departamento de História Geral, *Ben-Gurion University*, Negev, Israel. Interesses científicos: alteração da consciência e insanidade na cultura grega, harmonia cognitiva e pensamento enviesado na Grécia Antiga; religiões orientais no mundo grego e romano, práticas de alteração da consciência no Ocidente desde a Pré-História até à Antiguidade tardia, aspetos experienciais de rituais do mistério grego antigo.

Associate Professor, Department of General History, Ben-Gurion University, Neguev, Israel. Scientific interests: alteration of consciousness and insanity in Greek culture, cognitive harmony and biased thinking in ancient Greece; oriental religions in the Greek and Roman world, consciousness alteration practices in the West from Prehistory to Late Antiquity, experiential aspects of ancient Greek mystery rites.

CAROLINE WATT Professora titular da *Koestler Chair of Parapsychology* e membro fundador da *Koestler Parapsychology Unit,* Departamento de Psicologia, Universidade de Edimburgo, Escócia. Interesses científicos: questões metodológicas e de replicabilidade em parapsicologia.

Holder of the Koestler Chair of Parapsychology, and founder member of the Koestler Parapsychology Unit, Psychology Department, University of Edinburgh, Scotland. Scientific interests: replication and methodological issues in parapsychology.

Posters com resultados finais apresentados pelos investigadores apoiados pela Fundação Bial

Posters with final results presented by the Bial Foundation grant holders

2010

128/10 - "Extending the spiritual healing paradigm to explore distant mental interaction effects with Wiccan healers"

Investigadores/*Researchers*: Chris Roe, Charmaine Marie Sonnex

Instituição/*Institution*: Centre for the Study of Anomalous Psychological Processes (CSAPP), University of Northampton, Psychology Division, Northampton (UK)

Duração estimada/*Estimated duration*: 2014/10 – 2018/04

Background: Previous research investigating the efficacy of spiritual healing practices has been sufficiently successful to warrant further study. We argue that research designs could be improved by working with participant populations that are not critically ill so that we can have greater confidence that those in a control group are not receiving healing intentions from friends and family, by ensuring that the outcome parameters that are measured reflect the nature of the healing claim made by practitioners, and most importantly that healers are drawn from a homogenous group that come from a spiritual tradition that incorporates healing as part of its belief system and set of practices. We therefore proposed a study in which Wiccan practitioners are interviewed to generate an in-depth understanding of the effects that they aim to produce so that those insights can be used to inform a double-blind randomised control study of Wiccan healing.

Aims: To review the literature on spiritual healing so as to identify best practice in conducting an appropriately controlled experimental test and to identify those outcome markers that have been found to be most sensitive to noncontact healing effects. To interview practising Wiccan healers so as to develop an authentic account of the range of healing rituals practised, their claimed benefits, strengths and limitations; also to develop an understanding of practitioners' own perceptions of the mechanism by which healing is effected. Informed by objectives 1 & 2, to conduct a double-blind randomised control study to look for evidence of healing effects as a consequence of being treated by experienced Wiccan healers as they conduct healing rituals for specified persons. Participants will not be medically ill but rather the study will focus on changes in general wellbeing in a manner not dissimilar to the DMILS paradigm.

Method: Phase 1 consisted of a meta-analytic review of extant literature on noncontact healing and complementary therapies to identify possible mechanism. Phase 2 consisted of semi-structured interviews with eight practising Pagan spellcasters that were recorded and later transcribed. Phase 3 consisted of a double-blind randomised controlled study that adheres to design quality criteria outlined by phases 1 and 2. Using an interrupted time series design, 44 participants attended a 'baseline' session at time T0 at which they completed measures of wellbeing and participated in a group meditation exercise. All participants attended further group meditation sessions at time T1, T2, and T3 (spaced a week apart). After the first meeting they were randomly allocated to one of two groups, A or B, with participants in group A being the focus of noncontact healing efforts from a Pagan practitioner in the period from T0-T1 and group B in the period T1-T2. All participants and researchers who interact with them were blind to this allocation. Participants were run in small cohorts of between 6 and 8 persons.

Results: Interview material was analysed using thematic analysis, eliciting the primary themes: balance between adhering to tradition and personalising of practice; ethical considerations in what represents an appropriate outcome; the importance of belief and intention, and the role that ritual plays in maintaining that; and the relationship between practice and one's understanding of the nature of reality, particularly the energetic/spiritual nature of humankind and its implications for the causes of illness and wellbeing. Differences in scores on all subscales of the WHOQOL- BREF between T0 and T1 were calculated and compared between group A (the active condition) and group B (the wait list control condition) using MANOVA. No significant differences were found, suggesting no discernible healing effect in period 1. Scores were similarly compared for the period T1-T2 for which group A were the control group and group B the group receiving treatment, and again showed no evidence of a healing effect. However, participants did show an improvement across the length of the study in domains of the WHOQOL that were hypothesised *a priori* to be most directly related to their spell requests (that is, the psychological and physical rather than the social or environmental).

Conclusions: Findings suggests that there is some aspect of participating in this healing study that confers a positive effect upon wellbeing. The most likely explanation is that this represents a placebo expectancy effect, though one might argue that an effect due purely to suggestion would be reflected in all domains of the wellbeing measure. Participants' scepticism towards the efficacy of noncontact healing was measured before the study began but, contrary to the expectancy explanation, showed no relationship with changes in wellbeing scores across the duration of the study. One confounding factor was the inclusion of a meditation session to bring the group together and to provide a focal point for meetings that were primarily to allow participants to complete interim wellbeing measures; an extensive literature suggests that meditation can affect wellbeing, and in future designs an alternative activity might control this potential confound. Finally, it may be that the active period was too brief in duration to capture effects that may be slow acting but long lasting.

Keywords: Noncontact healing, Paganism, Thematic analysis, Randomized control trial

Publications:

Dieppe, P., & Roe, C., & Warber, S. (2015). Caring and healing in health care: The evidence base. *International Journal of Nursing Studies*, *52*, 1539–1541.

Dieppe, P., & Roe, C. (2015). Is healing an option to aid sustainable healthcare futures? *Journal of Holistic Healthcare*, *12*(1), 22-25. ISSN: 1743-9493

Roe, C.A., Sonnex, C., & Roxburgh, E.C. (2015). Two meta-analyses of noncontact healing studies. *Explore: The Journal of Science & Healing*, *11*(1), 11-23. ISSN: 1550-8307

Roe, C.A., Sonnex, C., & Roxburgh, E.C. (2015) Noncontact healing: What does the research tell us? *European Journal of Integral Medicine*, *7*(6), 687. ISSN: 1876-3820.

Sonnex, C.S. (2016) Psi healing research. *Psi Encyclopedia*, Society for Psychical research. Available at http://psi-encyclopedia.spr.ac.uk/articles/psi-healing-research

Sonnex, C.S. (2017). *Extending the non-contact healing paradigm to explore distant mental interaction effects of pagan healing spells*. Unpublished PhD thesis, University of Northampton.

Sonnex, C., Roe, C.A., & Roxburgh, E.C. (2015). Testing the Pagan prescription: Using a randomised controlled trial to investigate Pagan spellcasting as a form of distant spiritual healing. *Abstracts of presented papers: Parapsychological Association 58th Annual Convention, University of Greenwich, London, July 16-19, 2015*. (pp. 74-75)

E-mail contact: chris.roe@northampton.ac.uk

2012

51/12 - "The interpretation and evaluation of meaningful coincidences suggestive of psi communication in everyday life"

Investigadores/*Researchers*: Robin Wooffitt, Germaine Gunther
Instituição/*Institution*: Anomalous Experiences Research Unit, Dep. of Sociology, University of York (UK)
Duração/*Duration*: 2013/09 – 2018/01

Background: Meaningful coincidences can be strongly suggestive of psi processes. However, there has been little investigation of the ways coincidence experiencers describe their experiences. Analysis of coincidence accounts can provide understanding of the underlying tacit knowledge which people draw on in interpreting events as having a meaningful coincidental character. Similarly there has been little prior work on coincidences that occur in naturally occurring talk in social interaction.

Aims: First: to investigate the discourse of coincidence accounts to identify tacit normative and communicative practices. Second: to examine a particular class of coincidence that occurs in everyday interaction. This coincidence, called poetic confluence, takes the form of word selection that suggests telepathic communication with a co-interactant's unstated mental imagery or thoughts.

Method: For the analysis of coincidence accounts, an ethnomethodological discourse analysis was used. For the analysis of psi in word selection, we employed an interpretative method informed by the findings from Conversation Analytic studies of naturally occurring interaction.

Results: The analysis of accounts investigated: the rhetorical structure of coincidence accounts; the management of personal agency in coincidence experience; the design of coincidence account for specific audience, and the management of sceptical interpretations of coincidence claims. The analysis of poetic confluence found co-ordination of mutual attention; alignment and affiliation; and the normalisation of sensitive thoughts or imagery.

Conclusions: Coincidence accounts are rhetorically structured to manage a range of inferential issues arising from making claims of significant coincidental experiences. The phenomenon of poetic confluence suggests that psi in everyday life performs interpersonal tasks common to mundane social interaction.

Keywords: Coincidence, Accounts, Poetic confluence

Publications:

Stockbridge, G. (2017) *Crafting Coincidence: The Rhetoric of Improbable Events*. PhD, University of York.

Wooffitt, R. Relational psychoanalysis and anomalous communication: Continuities and discontinuities. *History of the Human Sciences*, *30*(1), 2017, 118-137.

E-mail contact: robin.wooffitt@york.ac.uk

87/12 - "Neurobiological correlates of empathy in couples: A study of central and peripheral measures"

Investigadores/*Researchers*: Joana Fernandes Pereira Coutinho, Cledna Patricía de Oliveira Silva, Jean Decety, Kristin Perrone McGovern, Óscar Filipe Coelho Neves Gonçalves, Vânia Andrea Sousa Gonçalves Moreira de Lima

Instituição/*Institution*: Centro de Investigação em Psicologia, Escola de Psicologia, Universidade do Minho, Braga (Portugal)

Duração/*Duration*: 2013/05 – 2017/07

Background: Empathy is one of the most studied constructs in psychology. An interpersonal context in which empathy appears to be critical is that of romantic relationships. Social neuroscience has clarified the neural basis of the different dimensions of empathy both at the central and pheripheral nervous system levels. For example previous evidence showed that not only the autonomic arousal per se but also the autonomic synchrony between spouses are markers of empathy. At the central level different brain areas have been linked with empathic processes.

Aims: This project aimed to explore the neural correlates of empathy in couples both at the peripheral and central nervous system level. Specific goals: 1) To characterize the autonomic (electrodermal (EDA) and cardiac activity) and neuroendocrine response (cortisol) in couples during an interactive task; 2) To test whether more empathic couples have higher levels of physiological synchrony; 3) To clarify the relationship between the patterns of connectivity of the Default Mode Network (DMN) and empathy 4) To analyse the brain areas involved in the self-other distinction during an empathy task.

Method: 32 couples (N = 64) in a committed relationship for at least one year performed a couple´s interaction task consisting in a structured discussion about the positive and problematic aspects of their relationship, while their cardiac and electrodermal activity was recorded using Biopac MP-150. Questionnaires of dyadic empathy and relationship satisfaction were administered to both spouses. The video-vignettes from this task were used to construct an fMRI paradigm in which each partner was asked to process his/her own feelings and those of his partner. A resting state acquisition was also performed.

Results: We found higher levels of heart rate and cortisol during the negative interaction condition whereas EDA was higher during the positive interactions. Physiological synchrony between spouses was higher in the negative interaction. At the central level we confirmed the association between both functional and effective connectivity of the DMN and dyadic empathy. Finally we found that brain areas such as insula and medial temporal regions were more active during the self condition whereas the supramarginal and fusiform gyrus were more active during the other condition.

Conclusions: Our results contributed for the understanding of the neural response during couple´s interactions and have important clinical implications.

Keywords: Empathy, Intimate relationships, Autonomic measures, Neuroimaging measures, Default Mode Network

Publications

Coutinho J., Oliveira-Silva P. & Decety J (2014) Neurosciences, Empathy, and Healthy Interpersonal Relationships: Recent Findings and Implications for Counseling Psychology". *Journal of Counseling Psychology.* doi.org/10.1037/cou0000021

Coutinho J., Beiramar A., Silva C., Calvo A., Lima V., Grace R., Oliveira-Silva P., Gonçalves O. & Sampaio A. (2015). Evidências de validade da Versão Portuguesa do Índice de Reatividade Interpessoal para Avaliação da Empatia em Casais". *Avaliação Psicológica. Vol* 14(3), pp.309-317. DOI: 10.15689/ap.2015.1403.02

Coutinho J., Patrícia Oliveira-Silva P., Mesquita A., Barbosa M., Perrone-McGovern K. & Gonçalves O. F., (2017) "Psychophysiological reactivity in couples during a marital interaction task", *Applied Psychophysiology and Biofeedback.* doi:10.1007/s10484-017-9380-2

Coutinho J., Perrone-McGovern K. M & Gonçalves O. F. (2017) "The Use of Neuroimaging in Clinical Psychological Science Research: Promises, Pitfalls and Recommendations*", Canadian Journal of Counselling and Psychotherapy*

Coutinho J, Oliveira-Silva P., Fernandes E., Correia D., Gonçalves O. F. & Tschacher W. (*in revision*) "Psychophysiological synchrony during verbal interaction in romantic relationships", *Family Process*

E-mail contact: joanafpc@gmail.com; joanacoutinho@psi.uminho.pt

98/12 - "Eye-brain dynamics during the emergence of three-dimensional perceptual awareness in Humans" - only abstract available
Investigadores/Researchers: Rafael Malach, Amos Arieli
Instituição/Institution: Department of Neurobiology - The Weizmann Institute of Science, Rehovot (Israel)
Duração estimada/*Estimated duration*: 2013/07 - 2018/04

Background: During 3D perception, vergence eye movements (VeyeM) play a significant role. The common view in binocular depth perception is that three dimensional (3D) objects identification occurs when the eyes are stably fixed at the right distance from an object. Our working hypothesis is that in addition to a pre-perception focusing process, VeyeM is part of a high-level object-oriented processing: The inter-ocular dynamical changes, occurring during VeyeM towards a new focal-point, guides the ongoing clustering of relevant (continuous) disparity information of the object's surface until a perception of the object in its spatial position and in the context of an action is obtained.

Aims: In the present research, we studied under slow dynamics - i.e. by generating conditions in which there is a substantial lag between the physical appearance of the stimulus, and the emergence of a reportable percept - the nature and function of VeyeM in visual perception of three dimensional (3D) objects.

Methods: In order to test our hypothesis, we used dynamic random dot stereograms (dRDS) to create an asymmetric Gaussian-like 3D object which, in a slowdown perceptual process, emerges out of the screen. The participants were asked to report which side of the object is perceived as further away. In some of the trials, the participants were asked to stably fixate on one out of two possible fixation points that were located at the center of the object at different depth planes. In a third condition, the participants were asked to move their eyes between this two fixation points during the presentation of the object. We call this condition the "vergence-path" condition (Vpath). Using precise measurement of binocular eye movements, we examined whether peripheral perception of a 3D object is improved by the transition of a stimulus on the retina during VeyeM: meaning that 3D vision of an object is improved while we move our gaze toward a new fixational point relative to a steady gaze in an optimal focal point.

Results: Our results show that when the shape has significant 3D curvatures in depth the participant's performance is better during VeyeM than at the stable fixation. When the shape was flattened the participants could detect which peripheral border is deeper either by their distances or by their curvature. Moreover, curvature discontinuities in the surface of a shape reduced performance to chance level.

Conclusion: These results are in agreement with the hypothesis that VeyeM dominates the ability of individuals to localize and orient themselves to visual objects in nearby space while acting in and on it, clarifying the perceived characteristics of the surrounding space, and offering insight into action-oriented or space-object oriented processing.

Keywords: Binocular depth perception; Three dimensional objects identification; Vergence eye movements.

E-mail contact: amos.arieli@weizmann.ac.il

130/12 - "Neural mechanisms of cognitive bias"
Investigadores/*Researchers*: Rui Filipe Nunes Pais de Oliveira, Ana Félix, Sara Cardoso
Instituição/*Institution*: ISPA, CRL, Lisbon and Instituto Gulbenkian de Ciência, Oeiras (Portugal)
Duração estimada/*Estimated duration*: 2013/09 – 2018/04

Background: The fact that cognitive appraisal is involved in the evaluation of stimuli creates the potential for cognitive biases that produce subjective evaluations (i.e., some individuals will consistently evaluate ambiguous stimuli as negative – aka pessimists, whereas others will perceive them as positive – aka optimists). Thus, cognitive biases may explain inter-individual variation in the response to stressors and concomitantly in the susceptibility to stress-related diseases.

Aims: In the present study we aim to investigate the occurrence of cognitive bias in zebrafish and to assess if optimistic and pessimistic differ in their susceptibility to detrimental effects of exposure to chronic stress.

Method: Zebrafish were tested in a cognitive bias paradigm and classified in an optimistic/pessimistic dimension. Afterwards, we used exposed the individuals to unpredictable chronic stress during 1 month, and the consequences of chronic social stress in pessimistic and optimistic zebrafish were assessed at multiple levels (behavior, functioning of the hypothalamic-pituitary-interrenal axis and cellular aging as measured by telomere shortening).

Results: First, we analyzed the differential responsiveness to stress by measuring whole-body cortisol and expression levels of stress-related genes in the brain. Our results show that optimistic and pessimistic individuals are characterized by different basal brain states, suggesting that cognitive bias towards optimistic/pessimistic judgments differentially activates a stress response. Secondly, we studied the impact of chronic stress on cellular aging by analyzing telomere dynamics. Our results suggest that cognitive bias towards pessimistic judgments could make individuals more susceptible to the detrimental effects of chronic stress, since telomere shortening seems to be associated to pessimistic individuals exposed to chronic stress.

Conclusions: Cognitive bias seems to play a major role in the inter-individual variation in the susceptibility / resilience to stress.

Keywords: Cognitive bias, Stress, Telomere, Cortisol, Zebrafish

E-mail contact: ruiol@ispa.pt

157/12 - "Contributions of parent-infant psychophysiology during dyadic interactions to child development"

Investigadores/*Researchers*: Raquel Alexandra Gonçalves Costa, Iva Tendais, Ana Conde, Catarina Tojal
Instituição/*Institution*: ISLA Campus Lisboa, Laureate International Universities, Lisboa (Portugal)
Duração/*Duration*: 2013/10 – 2016/11

Background: Parent-infant interactions characterized by mutual engagement difficulties and low parental sensitivity and responsiveness are associated with child developmental difficulties.

Aims: to understand what characterizes the behavioral and physiological point of view difficulties in situations of mutual engagement, low parental sensitivity and responsiveness.

Method: longitudinal study with 400 families from 6 weeks to 18 months of the child's life. At 6 weeks, a sociodemographic questionnaire will be conducted for both mothers and fathers. Parental mental health will be assessed using the World Health Organization Composite International Diagnostic Interview (CIDI) and perinatal health will also be assessed using the Optimality Index (OI). Separate face-to-face interactions between the infant and each parent will be video recorded for a 10-minute interval according to the protocol of the Global Rating Scales (GRS). This procedure will be followed by the face-to-face still-face paradigm. During these interactions parental respiratory sinus arrhythmia (RSA), heart rate (HR) and skin conductance (SC) will be monitored (VU-AMS). Measures of infant social withdrawal using the Alarm Distress Baby Scale (ADBB) were conducted.

Results: Maternal depression symptoms (DS) during pregnancy and at 2 months postpartum is associated with more rejecting behaviors toward the infant *(r* = -0,156, p = 0.044 and r = -0.211, p = 0.008, respectively) and less attentive infants (r = -0,156, p = 0.045 and r = -0.188, p = 0.017, respectively). Maternal DS at 2 months is associated with higher sadness in the interaction (r = -0.174, p = 0.028). Paternal antenatal DS is associated with more rejecting behaviors (r = -0.179, p = 0.032) while paternal DS at 2 months is associated with lower responsiveness and activity (r = -0.203, p = 0.18; r = -0.235, p = 0.006, respectively) and higher sadness (r = -.235, p = 0.006). Paternal DS at 2 months is also associated with infant's self-centered behavior (r = -.179, p = .039) and with less fun and enthusiastic involvement interactions (r = -.172, p = .048 and r = -.231, p = .007, respectively). Both maternal and paternal DS, before and after childbirth, are associated with lower quality of early interactions. Our findings also show that during normal interactions parental intrusive behavior is associated with lower respiratory sinus arrhythmia while parental non-remote behavior is associated with higher skin conductance during a still-face perturbation. Lower excited engagement is associated with higher skin conductance during recovery.

Conclusion: The physiological reactions during early interaction may be an important complementary tool for the psychological assessment of parental behaviors.

Keywords: Mother-infant interaction, Father-infant interaction, Depression, Respiratory sinus arrhythmia, Skin conductance

E-mail contact: raquel.costa@universidadeeuropeia.pt

178/12 - "How collaboration in psychotherapy becomes therapeutic: A study of interactive and psychophysiological processes in good and poor outcome cases"

Investigadores/*Researchers*: Eugénia Maria Ribeiro Pereira, Adriana Sampaio, Cledna Patrícia Silva, António P. Ribeiro, Adam O. Horvath, William B. Stiles, Inês Sousa, Joana Mourão, Dulce Pinto, Zita Sousa

Instituição/*Institution*: Centro de Investigação em Psicologia (CIPsi/UM), Escola de Psicologia, Universidade do Minho, Braga (Portugal)

Duração/*Duration*: 2013/06 – 2017/01

Background: Therapeutic alliance the strongest predictor of therapy outcomes and one of the most important therapeutic common factors. While there is a great deal of research available on what the alliance does, much less investigation has been done on how the alliance does what it does. Looking at this question, we will describe in detail the interactive and physiologic processes through which therapeutic collaboration (TC), the core dimension of alliance, is developed. We conceptualize TC has having two main components: 1) supporting and helping the patient to feel safe. This usually involves an expression of understanding the patient's experience within his or her usual perspective; and 2) challenging the maladaptive perspective by using strategies that stimulates change. This therapeutic interaction process implies self and other observations that will be further transformed into inferential processes and allow the empathic comprehension of the self and the other internal experience. These processes are modelled by several brain regions and are translated into psychophysiological signatures. Although there are some theoretical references regarding the neural substrates of therapeutic alliance correlates, empirical studies conducting within psychotherapy process and unravelling its underlying psychophysiological signatures are still rare.

Aims: This project aimed to explore the relationship between interactive and psychophysiological processes underlying the TC. Thus, the heart rate was used for a description of psychophysiological correlates of the therapeutic collaboration.

Method: We focused on the analysis of all sessions of 23 clinical cases treated with Cognitive Behaviour Therapy. The Therapeutic Collaboration Coding System was used to analyse the dyad's therapeutic collaboration within the sessions. The heart rate of both the therapist and the patient was measured using the BIOPAC System MP150.

Results: The results showed that the therapist and patient's psychophysiological synchrony differed according to the sessions and the therapeutic exchange types. Specifically, we found that, when the therapist and the patient were being collaborative the dyad showed physiological synchrony.

Conclusions: Collaboration between the therapeutic dyad appears to be particularly tied to the mutual influence of the cardiac responsivity pattern. The results are discussed in terms of the role of physiological reactivity for the therapeutic collaboration.

Keywords: Therapeutic collaboration, Heart rate, Physiological synchrony

Publications:

Ribeiro, E.*, Cruz, S.*, Sampaio, A., Oliveira-Silva, P. Pinto, D. & Sousa, I (2017, Submitted) Therapeutic collaboration and the dyad's physiological profile in the early phase of psychotherapy. *Psychotherapy*.

E-mail contact: eugenia@psi.uminho.pt

185/12 - "Circuit mechanisms of spatial attention in the zebrafish midbrain"
Investigadores/*Researchers*: Michael Brian Orger, Sabine L. Renninger
Instituição/*Institution*: Fundação Champalimaud, Lisboa (Portugal)
Duração/*Duration*: 2013/06 – 2017/07

Background: Faced with a continuous barrage of sensory stimuli, animals are able to reliably identify salient information and select appropriate behavioural responses. A central aim of neuroscience is to understand how such processes are implemented in neural circuits in the brain. However, such circuits typically consist of interconnected networks of neurons distributed across many brain areas. The small, transparent brain of zebrafish provides a powerful model system to address these questions, since every neuron is optically accessible using non-invasive methods.

Aims: The goal of this project was to understand how the brain selects the appropriate sensory information to guide behavior, particularly in the presence of multiple conflicting stimuli. Specifically we aimed to understand how the process of stimulus selection is mediated by the midbrain optic tectum, and different nuclei with which it makes reciprocal connections.

Method: Experiments used larval zebrafish aged 6-7 days post-fertilization. Transgenic driver and reporter lines were generating using the Tol2 transposase system. Behavior was tracked using infrared high-speed cameras and visual stimuli were displayed on a diffusing screen using digital projectors. For functional imaging, larvae were immobilized in low-melting temperature agarose gel, and imaged using custom-built two-photon microscope systems. Data were analysed using custom routines in Matlab.

Results: We generated a suite of transgenic lines, including panneural calcium indicator lines, reporter lines for analyzing anatomy, neural recording and optogenetics, and driver lines targeting GABAergic and cholinergic populations. We first identified, in behavioural experiments, what features of moving visual stimuli elicit different motor responses. We then mapped responses to these features throughout the larval midbrain, using 2-photon in vivo calcium imaging. We also made comprehensive maps of stimulus tuning properties in the retinal ganglion cell inputs to the optic tectum. To dissect out the role of specific circuit elements in processing these stimuli, we imaged different transgenic lines and registered each set of data to a reference brain anatomy, allowing the comparison of gene expression patterns and functional data across different individuals. Finally we developed systems to allow reversible manipulation of activity using optogenetics.

Conclusions: The larval zebrafish provides a powerful model to dissect the role of genetically identified neurons in behavioral choices.

Keywords
Vision, Calcium imaging, Zebrafish, Behaviour, Optogenetics

Publications:
Lu, R., Sun, W., Liang, Y., Kerlin, A., Bierfeld, J., Seelig, J. D., et al. (2017). Video-rate volumetric functional imaging of the brain at synaptic resolution. *Nature Neuroscience, 20*(4), 620–628.
Orger, M. B., & de Polavieja, G. G. (2017). Zebrafish Behavior: Opportunities and Challenges. *Annual Review of Neuroscience*.
Orger MB (2016) The cellular organization of zebrafish visuomotor circuits. *Current. Biology* 26:R377-385.
Manuscripts currently submitted:
Marques, J., Lackner, S., Felix, R. and Orger, MB. Hierarchical structure of the zebrafish locomotor repertoire revealed with unsupervised behavioural clustering. (currently in revision)
Marques, J. and Orger MB. Clustering by search of density valleys. (submitted)

E-mail contact: michael.orger@neuro.fchampalimaud.org

192/12 - "Effects of conditional foxp2 deletion on motor-sequence learning"
Investigador/*Researcher*: Catherine Ann French
Instituição/*Institution*: Fundação Champalimaud, Lisboa (Portugal)
Duração/*Duration*: 2013/06 – 2016/07

Background: Disruptions of the *FOXP2* gene cause a rare speech and language disorder, a core feature of which is problems in sequencing orofacial movements. The gene encodes a transcription factor which is expressed in cortico-striatal and cortico-cerebellar circuits required for sensorimotor integration and motor-skill learning, and imaging studies have identified structural abnormalities in these same regions in affected individuals. *FOXP2* is also highly conserved in several other vertebrate species, where expression is seen both during development and in adulthood.

Aims:
i) Investigate motor function in mice with brain-region/ cell-type specific disruptions of Foxp2.
ii) Determine if Foxp2 is required for motor function in adulthood.

Method: The Cre-*loxP* system was used to disrupt Foxp2 selectively in the cortex, striatum or cerebellar Purkinje cells of mice. Global Foxp2 disruption in adulthood was achieved using a tamoxifen-inducible Cre line. These genetic approaches were combined with a behavioural task where mice learned to execute sequences of lever presses. Activity in Purkinje cells was measured using *in vivo* and slice electrophysiology techniques.

Results: Loss of Foxp2 in specific brain regions/ cell types impacted motor-skill learning and performance differently, with Foxp2 disruption in cerebellar Purkinje cells and striatum affecting the speed and variability of lever-press sequences respectively. Mice lacking Foxp2 in Purkinje cells showed a prominent phenotype involving slowed lever pressing as well as deficits in skilled locomotion. *In vivo* recordings from Purkinje cells uncovered an increased simple spike firing rate and decreased modulation of firing during limb movements. This was caused by increased intrinsic excitability rather than changes in excitatory or inhibitory inputs. Disruption of Foxp2 in adulthood resulted in the death of around one third of mice. However, surviving animals were healthy and able to perform lever-press sequences normally despite appearing to be less motivated.

Conclusions:
i) Foxp2 expression in specific brain regions affects different aspects of motor behaviour.
ii) Foxp2 modulates Purkinje cell activity, a function which is important for skilled movements.
iii) Developmental expression of Foxp2 is required motor-skill learning and performance in adulthood.

Keywords: Speech and language, Foxp2, Motor-skill learning

Publications:
French C.A. & Fisher S.E. (2014) What can mice tell us about Foxp2 function? *Current Opinion in Neurobiology* 28:72-79.
French C.A.*, Vinueza Veloz M.F.*, Zhou K.*, Peter S.*, Fisher S.E., Costa R.M. & De Zeeuw C.I. Differential Effects of Foxp2 Disruption in Distinct Motor Circuits. *Under review, Molecular Psychiatry*. *equal contribution

E-mail contact: catherine.french@neuro.fchampalimaud.org

253/12 – "REM-sleep, the regulation of self-conscious emotion and hyperarousal in psychophysiological insomnia" - only abstract available

Investigadores/*Researchers*: Lucia Talamini, Ekaterini Georgopoulou, Eus Van Someren
Instituição/*Institution*: University of Amsterdam, Psychology, Dept. Brain and Cognition (The Netherlands) and Netherlands Institute for Neuroscience, Dept. Sleep & Cognition, Amsterdam (The Netherlands)
Duração/*Duration*: 2015/11 – 2017/09

Background: The mechanisms of hyperarousal, the key symptom of insomnia, have remained elusive. Recently, restless REM sleep emerged as a robust signature insomnia. Given the role of REM sleep in emotion regulation, we hypothesized that restless REM sleep could interfere with the overnight resolution of emotional distress, thus contributing to accumulation of arousal

Aims: We aimed to investigate whether restless REM sleep impedes overnight distress resolution, and accumulates as hyperarousal.

Method: Observational and experimental studies employed psychometrics, EEG and fMRI. We first validated a proxy measure for restless REM sleep, and assessed it in a large sample along with measures of distress dissolving and hyperarousal. We then implemented an internet-protocol to induce self-conscious distress and assessed distress dissipation across 5 consecutive days. The same distress-inducing protocol was used in a MRI scanner while conditioning it to a simultaneously provided odor. The odor was again given during part of the subsequent sleep period, to induce targeted memory reactivation. A second MRI scan of distress induction evaluated how neural correlates of its impact changed overnight.

Results: Of the association between restless REM sleep and hyperarousal, 62.4% was mediated specifically by reduced overnight resolution of emotional distress in insomnia. In people with insomnia, a night's sleep could even increase distress, rather than resolve it. MRI findings indicated activation of the salience network during the induction self-conscious emotions, that ameliorated with sleep but not with a similar interval of being awake.

Conclusions: Restless REM sleep interferes with overnight maintenance of balanced salience network activation.

Keywords: REM-sleep, Psychophysiological insomnia, Hyperarousal, Self-conscious emotion

Publications:

Wassing R, Benjamins JS, Dekker K, Moens S, Spiegelhalder K, Feige B, Riemann D, van der Sluis S, Van Der Werf YD, Talamini LM, Walker MP, Schalkwijk F and Van Someren EJW (2016) Slow dissolving of emotional distress contributes to hyperarousal. *PNAS 113*:2538-2543.

Wassing R. Insomnia: restless REM sleep promotes nocturnal mentation and hyperarousal by interfering with the resolution of emotional distress. Abstracts of the 23rd Congress of the European Sleep Research Society Meeting, Bologna, Italy, 13-16 September 2016.

Wassing R, Benjamins JS, Schalkwijk F et al. (in preparation) A bad night of sleep disrupts overnight downregulation of distress by self-conscious emotions: a Karaoke experiment.

Wassing R, Stoffers D, Ramautar J et al. (in preparation) Overnight changes in insula activation are involved in downregulation of distress by self-conscious emotions.

E-mails: rickwassing@gmail.com; eusvansomeren@gmail.com; L.M.Talamini@uva.nl

262/12 - "The neural basis of magical Ideation: A multimodal imaging study in twin subjects" - only abstract available

Investigadores/*Researchers*: Paolo Brambilla, Gioia Negri, Sara Piccin, Giuseppe Cabras, Corrado Fagnani

Instituição/*Institution*: Universitá delgi Studi di Milano and Unit of Epidemiology of the Italian Institute of Health, Rome (Italy)

Duração/*Duration*: 2014/01 – 2018/04

Background: Proneness to psychoses was widely investigated through self-report measures, showing moderate heritability in twin and family studies. It is unclear how life-events modulate it. In fact, distress is strongly associated to disorder onset.

Aims: To investigate effects of stressful events and familial relationship on proneness to psychosis.

Method: From *Italian Twin Registry*, 139 complete pairs (54% females) aged 8-32 (18±6.7) were assessed with scales for positive schizotypy (**MIS**, *Magical Ideation Scale* [1]; **PAS**, *Perceptual Aberration Scale* [2]) and for proneness to affective disorders (**HPS**, *Hypomanic Personality Scale* [3]), and sub-scales: **SV**, *Social Vitality*; **MV**, *Mood Volatility*; **Ex**, *Excitement* [4]. *Life-time stressful events* (**LEs**) were collected with an ad-hoc inventory. Quality of parents' relationship was assessed (**RQI**, *Relationship Quality Index* [5]). Univariate twin models for quantitative traits were fitted on proneness scales in monozygotic (N 104) and same-sex dizygotic (N 92) twins. Effects of introducing LEs (last-year and life-time) and RQI in selected models were evaluated.

Results: Age negatively correlated with HPS scales (r ranging from –0.34 to –0.22). Life-time LEs were negatively correlated with SV (–0.17) and HPS (–0.15), while recent LEs correlated with MIS (+0.18) and PAS (+0.15). RQI was negatively correlated with MV (–0.18), HPS (–0.17), and MIS (–0.15). An AE model best explained MIS and SV data, with heritability estimates of 42% and 61% respectively. Under a CE model, shared environment explained 53%, 47% and 27% of variance in Ex, HPS and MV scores respectively. Unique environment only affected PAS. Sex showed significant effects in MIS and PAS final models, age in all HPSs ones. Introducing recent LEs had a significant effect on MIS and PAS models; in MIS model, last-year LEs modified variance explained by A (–10%) and by E (+8%). Life-time LEs and RQI did not affect fitted models.

Conclusions: Recent stressful events resulted to increase positive schizotypy, affecting twin models. Life-time stressful events, instead, were negatively associated with extraversion (SV). Quality of parental relationship could protect against neuroticism (MV) and positive schizotypy (MIS). Moderate heritability resulted for extraversion (61%, SV) and positive schizotypy (42%, MIS).

Keywords: Twin, Schizotypy, Vulnerability, Stress, Family

E-mail contacts:

maria.nobile4@gmail.com; corrado.fagnani@iss.it; marcogarzitto@gmail.com; boniventocarolina@gmail.com; sara.piccin@gmail.com; maddamauri90@gmail.com; eleonora.maggioni@gmail.com; miriam.salemi@iss.it; antonio.arnofi@iss.it; virgilia.toccaceli@iss.it; monica.bellina@gmail.com; massimo.molteni@bp.lnf.it; antonia.stazi@iss.it; paolo.brambilla1@unimi.it

2014

51/14 - "The dissociated self: An investigation of emotional responses to a new body-threat task in those predisposed to anomalous body experiences, dissociation and disembodiment" - only abstract available

Investigador/*Researcher*: Jason John Braithwaite
Instituição/*Institution*: School of Psychology, University of Birmingham (UK)
Duração estimada/*Estimated duration*: 2015/09 – 2018/04

Background: Certain dissociative experiences associated with disorders in consciousness have been associated with suppressed autonomic responding – though this has not been examined for non-clinical groups predisposed to such anomalous experiences and the scientific tools to investigate such instances are limited.

Aims: This project sought to examine suppressed autonomic responses that are associated with disorders in self-consciousness. The project had a focus on devising new tools / methodologies for exploring dissociative experiences in non-clinical groups and establishing their utility.

Method: This project devised a new computer-based 'body-threat' task where high-definition movie clips depicting threats to a human body, and baseline non-body clips, were created (*The Body-Threat Assessment Battery: BTAB*). This project also devised a new physical body-threat task (the *Implied Body-Threat Task: IBT*). Psychophysiological responses (Skin Conductance responses: SCRs; and finger temperature) to such threats were quantified as a function of predisposition to dissociative experience.

Results: Aversive body-threat imagery (movie clips) elicited more SCRs and these were of significantly higher amplitude relative to baseline non-body threat imagery. Furthermore, suppression of autonomic responses increased as predisposition to aberrant dissociative experiences also increased.

Conclusions: Individuals predisposed to certain dissociative and depersonalization-like experiences showed a suppression of autonomic responses to aversive body-based stimuli. This was demonstrated for threats carried out on the observers own body, and a newly devised computer based body-threat task (BTAB). Both paradigms represent significant extensions in scientific methodologies to explore disorders in body and self-consciousness.

Keywords: Depersonalization, Dissociation, Consciousness, Autonomic suppression

Publications:

Braithwaite, J.J., Watson, D.G., & Dewe, H. (2017) Predisposition to out-of-body experiences (OBEs) is associated with aberrations in multisensory integration: Psychophysiological support from a "rubber-hand illusion" study. *Journal of experimental Psychology: Human Perception & Performance, 43*(6), 1125-1143.

Dewe, H., Watson, D.G., & Braithwaite (2016). Uncomfortably Numb: New evidence for suppressed emotional reactivity in response to body-threats in those predisposed to sub-clinical dissociative experiences. *Cognitive Neuropsychiatry, 21*(5)377-401.

Dewe, H., & Braithwaite, J.J. et al (submitted / under review). The Depersonalized Brain: New Evidence Supporting a Distinction between Depersonalization and Derealization from Discrete Patterns of Autonomic Suppression. *Consciousness & Cognition*.

Braithwaite et al (in preparation). The "Body-threat Assessment Battery" (BTAB): A new instrument for the measurement of affective autonomic responses in relation to aversive body-threats via dynamic movie clips.

Dewe et al (in preparation). Evidence for emotional suppression in non-clinical groups predisposed to depersonalization / dissociative experiences revealed by a new "body-threat" assessment battery.

E-mail contact: j.j.braithwaite@lancaster.ac.uk

83/14 - "Electrophysiological correlates of the incorporation of recent memory sources into REM and non-REM dreams and of levels of insight following REM and non-REM dream interpretation"
Investigadores/*Researchers*: Mark Blagrove, Chris Edwards, Jean-Baptiste Eichenlaub, Perrine Ruby
Instituição/*Institution*: College of Human and Health Sciences, Department of Psychology, Swansea University (UK)
Duração/*Duration*: 2015/03 – 2017/11

Background: Although current concerns and recent emotional events are known to be incorporated into daydreams, the timescale of their incorporation has not yet been studied.

Aims: To investigate the time course of incorporation of waking life experiences into daydreams using methods used to study such incorporations into dreams.

Method: Thirty-one participants kept a diary for 10 days, reporting major daily activities (MDAs), personally significant events (PSEs) and major concerns (MCs). They were then cued for daydream, Rapid Eye Movement (REM) and N2 dream reports in the sleep laboratory.

Results: There was a higher incorporation into daydreams of MCs from the previous two days (day-residue effect), but no day-residue effect for MDAs or PSEs, supporting a function for daydreams of processing current concerns. A day-residue effect for PSEs and the delayed incorporation of PSEs from 5-7 days before the dream (the dream-lag effect) have previously been found for REM dreams. Delayed incorporation was not found in this study for daydreams.

Conclusions: Daydreams differ in function from REM sleep dreams. However, the REM dream-lag effect was not replicated here, possibly due to design differences from previous studies.

Keywords: Daydreaming, Mind-wandering, Dreaming, Day-residue, Memory consolidation

Publications:
Elaine van Rijn, Alexander M. Reid, Christopher L. Edwards, Josie E. Malinowski, Perrine M. Ruby, Jean-Baptiste Eichenlaub and Mark T. Blagrove (2017). Daydreams incorporate recent waking life concerns but do not show delayed ('dream-lag') incorporations. *Consciousness and Cognition* (in press). doi.org/10.1016/j.concog.2017.10.011

E-mail contact: m.t.blagrove@swansea.ac.uk

118/14 - "Recursive consciousness training: Using neurofeedback to induce altered states"
Investigadores/*Researchers*: Amir Raz, Niels Birbaumer, Robert T Thibault
Instituição/*Institution*: Montreal Neurological Institute, McGill University (Canada); Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen (Germany)
Duração/*Duration*: 2015/09 – 2017/11

Background: Since 1958, researchers and practitioners have used neurofeedback to entrain brain activity and improve human functioning in health and disease. This procedure provides individuals with real-time depictions of their ongoing brain activity. With this information, they can learn to modulate specific brain activity in connection with related behavior. In 2003, the field of neurofeedback took a leap forward with the first fMRI-based neurofeedback protocol (fMRI-nf).

Aims: We aimed to explore whether real-time brain imaging can train individuals to actively modify their neural processes and, in turn, achieve specialized states of consciousness. With the variety of available brain imaging techniques, we first identified the most effective means to train neural self-regulation. Because specialized brain states pair with particular postures (e.g., sitting upright in meditation), we also conducted experiments to identify the body-position most advantageous to successful training.

Method: To find the top imaging modality for neurofeedback, we conducted a comprehensive literature search reviewing the most oft-cited and influential papers concerning various feedback methods (Thibault, Lifshitz, & Raz, 2016) We followed this up with a comprehensive literature review on fMRI-nf (Thibault, MacPherson, Lifshitz, Roth, & Raz, *under review*).
To uncover the most ideal posture for neurofeedback, we leveraged multi-postural magnetoencephalography to measure brain activity in three positions (i.e., lying supine, reclined at 45°, and sitting upright) conducting both sensor-level (Thibault, Lifshitz, & Raz, 2015) and source-level analyses (Lifshitz, Thibault, Roth, & Raz, 2017).

Results: Our survey of the literature suggests that training outcomes associated with electroencephalography neurofeedback are likely attributable to expectations and placebo-like effects (Thibault & Raz, 2017). FMRI-nf, alternatively, appears to help guide participants toward neural self-regulation (Thibault et al., *under review*).
Sitting upright, compared to sitting reclined or lying supine, increases left-hemisphere high-frequency neural activity over common speech areas (Thibault et al., 2015) and pairs with a more alert brain state (Lifshitz et al., 2017); thus, rendering upright postures more conducive to brain training.

Conclusions: With appropriate controls, fMRI-nf may help naïve individuals achieve expert brain states.

Keywords: Self-regulation, Neurofeedback, fMRI, Real-time, Neuroimaging

Publications:
Lifshitz, M., Thibault, R. T., Roth, R., & Raz, A. (2017). Source-localization of brain states associated with canonical neuroimaging postures. *Journal of Cognitive Neuroscience*, in press.
Thibault, R. T., Lifshitz, M., & Raz, A. (2015). Body position alters human resting-state: Insights from multi-postural magnetoencephalography. *Brain Imaging and Behavior, 10*(3), 772–780.
Thibault, R. T., Lifshitz, M., & Raz, A. (2016). The Self-Regulating Brain and Neurofeedback: Experimental Science and Clinical Vogue. *Cortex, 74*, 247–261.
Thibault, R. T., MacPherson, A., Lifshitz, M., Roth, R., & Raz, A. (n.d.). Neurofeedback with fMRI: A critical systematic review. *Under Review*.
Thibault, R. T., & Raz, A. (2017). The Psychology of Neurofeedback: Clinical Intervention even if Applied Placebo. *American Psychologist, 72*(7), 679–688.

E-mail contact: amir.raz@mcgill.ca

121/14 – "Maternal brain gain: Changes in neural representations and body perception during pregnancy" - only abstract available
Investigadores/*Researchers*: Jane Aspell, Flavia Cardini
Instituição/*Institution*: Anglia Ruskin University, Cambridge (UK)
Duração estimada/*Estimated duration*: 2015/11 - 2018/04

Background: The space immediately surrounding our body - referred to as 'peripersonal space' (PPS; Rizzolatti et al., 1997) - is important, as it is where we interact with stimuli in the external world. Recent studies have shown that the PPS boundaries are malleable. For example, it has been found that being in proximity to an individual we have previously co-operated with induces an expansion of our PPS towards that person.

Aims: With our study we aimed at investigating whether the PPS changes during pregnancy, a critical stage in life, when extremely rapid changes occur in the body size and shape. Given the rapidity of these bodily changes, we expected a likewise rapid plastic reorganization of the representation of the body and of the surrounding space. As pregnancy advances, the PPS should expand, reflecting an updated mental representation of one's body that, as the abdomen increases in size, makes external stimuli, initially perceived as being outside of the PPS, to be perceived closer, within the PPS.

Methods: To this aim, we tested 37 pregnant women and 19 non-pregnant women three times: at the 20th and at 34th week of the gestational period and 8 weeks postpartum (and at the same time intervals in the control group). To assess the PPS boundaries we used a well-established audiotactile task (Canzoneri et al., 2012) whereby participants' reaction times (RTs) to a tactile stimulus on the abdomen, were measured while listening to a dynamic sound that seems to start at a location far from the participant and progressively approach the participant's body. When touches occurred at short temporal delays the sound was perceived far and gradually closer to the participant's body as the delays increase. As sounds facilitate tactile RTs only when presented close to the body (Serino et al., 2007), we expected RTs to progressively decrease as the sound was approaching. The critical distance where the sound speeds up tactile RTs can be taken as a proxy of the PPS boundary.

Results: By comparing this critical distance across the three time periods we found that whereas at the first and the third testing period no differences in the PPS size were observed between the two groups, in the second period – i.e. at the advanced stage of pregnancy – the pregnant participants' PPS was larger than the controls'.

Conclusions: We conclude that during pregnancy our brain adapts to the sudden change in body size, by expanding the representation of the space around us, possibly in order to protect the vulnerable abdomen from bumping against objects.

Keywords: Peripersonal space, Pregnancy, Multisensory Integration, Body representation

E-mail contact: flavia.cardini@anglia.ac.uk; Jane.aspell@anglia.ac.uk

122/14 - "Internal and external world in parietal cortex" - only abstract available
Investigador/*Researcher*: Paolo Capotosto
Instituição/*Institution*: Department of Neuroscience, Imaging and Clinical Science, University "G. D'Annunzio", Chieti (Italy)
Duração/*Duration*: 2015/02 – 2016/09

Background: One robust electrophysiological correlate of anticipation is the modulation of posterior scalp electroencephalographic (EEG) alpha oscillations (8–12 Hz). Specifically, the pre-stimulus alpha power de-synchronization (ERD) is strongly associated to visual perception but has been observed in a large variety of tasks, indicating a general role in task anticipation. We previously reported that interference by repetitive trans-cranial magnetic stimulation (rTMS) of parietal regions of the dorsal attention network (DAN) disrupts both anticipatory alpha ERD and performance during a visuo-spatial attention task.

Aims: We tested the hypothesis of a causal role of left angular gyrus (AG) and left posterior intraparietal sulcus (IPS) (and by extension the role of the dorsal attention and default networks, i.e. DMN and DAN) in the regulation of cortical neural synchronization mechanisms (reflected by alpha rhythms) in two different cognitive domains. Moreover, we investigated the temporal dynamics of the anticipatory alpha ERD and tested whether the TMS produces either a general attenuation or an interruption of the typical development of alpha ERD.

Method: We contrast the effects of inhibitory rTMS (150 ms duration, 20-Hz frequency, and intensity set at 100% of the individual motor threshold) on alpha rhythms and behaviour on two different tasks: a visuo-spatial attention and a semantic decision task, by targeting either the IPS, a core region of the DAN, or the AG, a core region of the DMN.

Results: In the first study we reported that both performance and anticipatory alpha ERD were affected by stimulation of IPS only during visuo-spatial attention, and of AG only during semantic decisions. In the second study, we found that during a semantic decision task, rTMS over left AG shortened the peak latency and decreased the peak amplitude of the anticipatory alpha de-synchronization as compared to both active (left IPS) and non-active (Sham) TMS conditions.

Conclusions: Results of the first study indicate the existence of multiple dedicated parietal channels for the modulation of anticipatory alpha rhythms, which in turn reflect task-specific modulation of excitability in human parieto-occipital cortex. Results of the second study suggest that magnetic interference not simply reduces the mean amplitude of anticipatory alpha ERD but also interrupts its typical temporal evolution in paradigms employing fixed cue-target intervals.

Keywords: TMS, EEG, Parietal cortex, Attention, Semantic memory

Publications:
Capotosto P, Baldassarre A, Sestieri C, Spadone S, Romani GL and Corbetta M. "Task and regions specific top-down modulation of alpha rhythms in parietal cortex" *Cereb Cortex*. 2016 Sep 6
Spadone S, Sestieri C, Baldassarre A, Capotosto P. Temporal dynamics of TMS interference over preparatory alpha activity during semantic decisions. *Sci Rep*. 2017 May 24;7(1):2372.
Baldassarre A*, Capotosto P*, Committeri G, Corbetta M. "Magnetic stimulation of visual cortex impairs perceptual learning". *Neuroimage*. 2016 Dec;143:250-255.

E-mail contact: paolocapotosto@gmail.com

128/14 - "Autonomic nerve recordings applied as a novel psychophysiological tool for Consciousness Science"

Investigadores/*Researchers*: Hugo Dyfrig Critchley, Peter Taggart, Yrsa Sverrisdottir
Instituição/*Institution*: Brighton and Sussex Medical School, University of Sussex (UK); Department of Physiology, Anatomy and Genetics, University of Oxford (UK)
Duração estimada/*Estimated duration*: 2015/09 - 2018/04

Background: Recent theories in consciousness science embrace the notion of *interoceptive predictive coding* wherein the sense and integrity of 'self' depends upon control and representation of the physiological state of the body. In this model, selfhood is coupled to internal agency which arises from active inference, through the activity of efferent autonomic nerves and their predicted impact in visceral afferents. Correspondingly, change in conscious perception of the self is accompanied by autonomic responses and interoceptive signaling influences self-representation.

Aims: To test the hypothesis that peripheral autonomic (sympathetic) nerve traffic fine-grained will encode states of conscious (vs. subconscious perception, volitional action and, illusions of body ownership) consistent with interoceptive predictive coding models of conscious selfhood.

Method: We manipulated and tested conscious perceptual awareness using backward masked presentation of emotional face stimuli, sense of volitional action using Libet experiments, and the sense of body ownership using the Rubber Hand Illusion. Experiments were conducted using multiaxis autonomic recordings, including direct sympathetic nerve recordings (muscle and skin sympathetic nerve activity, recorded from common peroneal nerve) in three individuals and, in 20 individuals, a novel non-invasive measurement of skin sympathetic nerve traffic (chest SKNA, reflecting stellate ganglion activity; [Doychinova et al. Heart Rhythm. 2017]). Multiunit nerve activity was appraised using established and exploratory analytic approaches.

Results: Changes in participant's conscious state were reflected in the activity of peripheral sympathetic nerves. This was particularly observed during indication of the rubber hand illusion. Changes in sympathetic activity broadly reflected the degree to which participants adopted the illusion of body-ownership of an artificial limb. Individual differences in interoceptive ability accounted for within-group variation

Conclusions: Our findings support the hypothesis that self-representation is built in part on principles of interoceptive active inference, through the action of autonomic nerves and the precision of predicted visceral responses signalled via viscerosensory afferents.

Keywords: Active inference, Autonomic, Illusion, Interoception, Selfhood

E-mail contact: h.critchley@bsms.ac.uk

143/14 - "From audio-visual perception to action: The processing of spatio-temporal components"
Investigadores/*Researchers*: Sandra Mouta, Joana Vieira, Mariana Silva
Instituição/*Institution*: Association/ZGDV-Centro de Computação Gráfica, Guimarães (Portugal)
Duração estimada/*Estimated duration*: 2015/10 – 2018/04

Background: Vision is usually referred as a dominant modality in the scientific community, specifically in the context of spatial performance. On the other hand, recent investigation has shown that the auditory modality is a reliable source of information, mainly in temporal tasks. There is a gap in scientific reports that does not allow to understand the degree of expertise and adaptability of the perceptual system to dynamic events.

Aims: The aim of this project was to investigate how auditory and visual information could account for the perception of static and dynamic events. We proposed to study human perception in a continuum of judgement of unimodal events until the execution of motor actions in accordance with the displayed perceptual scenario.

Method: In a localization task, we tested how participants' could discriminate stimuli presented at various spatial positions, the effect of training and the effect of the type of audio device. In a temporal task, we measured the accuracy and precision of participants' estimation of an approaching object in a pass-by trajectory. In this experiment we manipulated the amount of information presented, the type of stimulus and the intensity level in which it was presented. The results from these experiments are compared with reference results from the visual modality. Additionally, a "when and where" cross-modal integration was tested with synchronization of biological motion, through the manipulation of auditory and/or visual cue availability.

Results: Auditory localization tasks have shown that training has a significant effect in the overall localization error, as has the equipment. Temporal tasks have demonstrated that participants can predict the approaching event regardless of the amount of information presented. Accuracy along the task was maintained through the use of different perceptual strategies. Synchronization tasks revealed no improved performance for audiovisual condition, in comparison with audio condition alone.

Conclusions: Within the scope of this project a mapping of the temporal and spatial resolution of the perceptual system was obtained. We studied several dimensions of the human action-perception system: time, space and motor action.However, some results need to be further explored in order to have a continuum between complexity of information processing and action.

Keywords: psychophysics, human perception, looming events, biological motion

Publications:
Noy, D., Mouta, S., Lamas, J., Sousa, E., Santos, J. A. (submitted). *Side-by-Side Walkers Synchronize Global Body Motion*. PLos ONE

Silva, R.M., Lamas, J., Silva, C.C., Coello, Y., Mouta, S. & Santos, J.A. (2017). *Judging Time-to-Passage of looming sounds: evidence for the use of distance-based information*. PLoS ONE, 12, 1-17.

Silva, C., Mouta, S., Santos J. (2016) *Choosing audio devices on the basis of Listeners Spatial Perception: A case study of Headphones vs In-earphones.* IEEE-ICCE Berlin Proceedings of the International Conference on Consumer Electronics.

E-mail contact: mariana.macedo.silva@gmail.com

150/14 - "Measuring the self: Behavioural and neural correlates of bodily awareness" - only abstract available

Investigadores/*Researchers*: Emmanuele Tidoni, Gaetano Tieri, Matteo Candidi, Salvatore Maria Aglioti
Instituição/*Institution*: Social Cognitive Neuroscience Laboratory, Department of Psychology, University of Rome "La Sapienza" (Italy)
Duração/*Duration*: 2015/02 – 2017/03

Background: The correct integration of different sensory (e.g. vision, proprioception, somatosensory, interoception) and motor information is fundamental to build and maintain the normal subjective experience of owing and controlling our body. Investigating the physiological responses associated to our sense of body ownership and agency is key to understand how body awareness arises. Contrary to the idea that experiencing a body is a stable percept, it is known that simple sensory illusions may alter the way we perceive our body.

Aims: The proposal aimed to investigate the contribution of brain visuo-motor areas and sensorimotor plasticity following the manipulation of subjective experience of body ownership by means of visual manipulation of body continuity.

Method: We collected subjective and physiological (skin conductance responses, motor evoked potentials) answerers in healthy participants immersed in a virtual reality environment and explored whether visual discontinuity between the hand and limb of an avatar could reduce a person's sense of ownership of the virtual body.

Results: We observed that placing different amounts of visual discontinuity between a virtual hand and limb differently modulate the perceived sense of ownership and control over observed virtual bodies and actions. Crucially autonomic reactivity but not motor evoked potentials were modulated by the felt ownership over the virtual body. Indeed, only high amplitudes of SCRs were found during the observation of both a normal hand-limb connection and a non-natural connection by means of a rigid wire. On the other hand, the analysis of subjective ratings revealed that only the observation of natural full connected virtual limb elicited high levels of ownership in all studies.

Conclusions: Our data show that mere observation of limb discontinuity can change a person's ownership and agency over a virtual body observed from a first-person perspective, even in the absence of any multisensory stimulation of the real body.
Importantly different measures of physiological activity were differently modulated by subjective body ownership sensations suggesting that different methods to elicit body ownership illusions may differently affect indirect indexes of body representation.

Keywords: Body ownership, TMS, Virtual reality, Skin conductance, Motor evoked potentials

Publications:

Tieri, G., Tidoni, E., Pavone, E. F., & Aglioti, S. M. (2015). Mere observation of body discontinuity affects perceived ownership and vicarious agency over a virtual hand. *Experimental Brain Research*. doi:10.1007/s00221-015-4202-3

Tieri, G., Tidoni, E., Pavone, E. F., & Aglioti, S. M. (2015). Body visual discontinuity affects feeling of ownership and skin conductance responses. *Scientific Reports*, *5*, 17139. doi:10.1038/srep17139

Tidoni, E., Tieri, G., & Aglioti, S. M. (2015). Re-establishing the disrupted sensorimotor loop in deafferented and deefferented people: The case of spinal cord injuries. *Neuropsychologia*, *79*(Pt B), 301–9.
https://doi.org/10.1016/j.neuropsychologia.2015.06.029

Tidoni, E., Scandola, M., Orvalho, V., & Candidi, M. (2016). Apparent Biological Motion in First and Third Person Perspective. *I-Perception*, *7*(5), 2041669516669156. https://doi.org/10.1177/2041669516669156

Fusco, G., Tidoni, E., Barone, N., Pilati, C., & Aglioti, S. M. (2016). Illusion of arm movement evoked by tendon vibration in patients with spinal cord injury. *Restorative Neurology and Neuroscience*, *34*(5), 815–826. https://doi.org/10.3233/RNN-160660

E-mail contact: etidoni@gmail.com

163/14 - "Sacred values underlying conflict proneness: A neuroimaging study of religious and nationalist radicals"

Investigadores/*Researchers*: Adolf Tobena, Clara Pretus, Joseph Hilferty, Oscar Vilarroya, Scott Atran
Instituição/*Institution*: Department of Psychiatry and Forensic Medicine UAB, Bellaterra Campus (Spain)
Duração estimada/*Estimated duration*: 2015/02 – 2018/04

Background: Intractable and violent intergroup conflicts are often motivated by commitments to abstract ideals such as god or nation, so-called "sacred" values that are relatively insensitive to material incentives or disincentives. There is scant knowledge of how the brain processes willingness to fight and die (WFD) for such cherished causes.

Aims: Our goal was to assess WFD for sacred compared to non-sacred values using fMRI in a within-subject study including supporters of a radical Islamist group.

Method: We selected 30 radicalized individuals out of 146 interviewed candidates from different neighborhoods in and around Barcelona, Spain. We measured their brain activity as they indicated their WFD for sacred and non-sacred values and observed peers' ratings for the same values.

Results: We observed diminished activity in dorsolateral prefrontal cortex (dlPFC), inferior frontal gyrus and parietal cortex while participants conveyed WFD for sacred relative to non-sacred values, regions that have previously been implicated in calculating costs and consequences. These differences could not be attributed to differences between sacred and non-sacred values in emotional intensity, familiarity or salience. An overlapping region of dlPFC was active when viewing conflicting ratings of sacred values from peers, to the extent participants were sensitive to peer influence, indicating that it is possible to induce flexibility in the way people defend sacred values.

Conclusions: Our results are consistent with a view that "devoted actors" motivated by a commitment to sacred values and abstract group identities rely on distinct decision mechanisms that render them insensitive to material tradeoffs. Such information may help to better policy for the common defense.

Keywords: Sacred values, Devoted actor, fMRI, Radicalization, Will to fight

Publications:

Clara Pretus, Nafees Hamid, Oscar Vilarroya, Jeremy Ginges, Hammad Sheikh, Molly J. Crockett, Adolf Tobeña, Susanna Carmona, Angel Gómez, Richard Davis and Scott Atran. Will to fight: Neuroimaging supporters of an Al Qaeda affiliate (*under review at PNAS*)

E-mail contact: clara.pretus@uab.cat

180/14 - "Neural mechanisms of word learning: Contributions from amnesic patients and fMRI on healthy ageing" - only abstract available

Investigadores/*Researchers*: Tânia Patrícia Gregório Fernandes, Ana Luísa Nunes Raposo, Maria Isabel Segurado Pavão Martins Catarino Petiz, Rita Isabel Saraiva Jerónimo
Instituição/*Institution*: Faculdade de Psicologia da Universidade de Lisboa - FP-ULisboa (Portugal)
Duração estimada/*Estimated duration*: 2016/02 - 2018/02

Background: Learning new words (e.g., cathedruke) is a lifelong skill with two facets which differ in time course and neurocognitive underpinnings. The memory facet is rapidly available and depends on hippocampal functioning; it is usually assessed directly with recall and recognition tests. The lexical facet involves the integration of the new word into lexical dynamics, competing for recognition with cohort members (e.g., cathedral), which slows down the recognition of these pre-existing words. This lexicalization process takes time to emerge and is supported by neocortical regions. Ageing is accompanied by hippocampus shrinkage and decline on declarative memory but expansion of vocabulary. Surprisingly, no study has hitherto examined its impact on lexicalization.

Aims: Here we tested the impact if healthy ageing on lexicalization of new words**.**

Method: Healthy young (18-28 years old) and older (61-80 years old) adults were exposed to spoken new words with a visual context during phoneme monitoring: orthographic (new-word's orthographic form) or semantic (with an item; e.g., axalotl). The two facets of new words were assessed in three sessions: Day 1 (immediately after encoding); Day 2 (24h after and before the 2nd encoding phase); Day 8 (1 week after without further exposition). The lexical facet was indirectly studied in a semantic categorization task on the base-words (from which the new words were created): if the new item (e.g., leoparna) were lexicalized, participants would be slower to recognize the base-words (e.g., leopardo) than control words (without any association with new words but with the same psycholinguistic properties as the base-words). Recall and recognition tests were used to assess the memory facet of new words in the three sessions.

Results: Older adults recalled and recognized less new words than young adults in all sessions. New words' memory facet was rapidly available and was less influenced by the visual context of learning in older than young adults. In contrast, the engagement of new words into lexical dynamics was affected by the visual context only on older adults. Both groups showed robust lexicalization effects on Day 8 but, for older adults, this only held true for words learnt in a semantic context.

Conclusions: For young adults, semantic information did not assist lexicalization (Dumay et al., 2004; Ferreira et al., 2016; Takashima et al., 2014). Yet, as happens during word recognition (Shapto et al., 2012), in older adults, the lexicalization process was preserved thanks to semantic information, which acted as a compensatory mechanism for lexical integration of new items.

Keywords: Word learning, Healthy ageing, Lexical competition, Memory consolidation

Publications:

Ferreira, J (2017). *A contribuição dos esquemas semânticos para as facetas lexical e episódica de novas palavras em jovens adultos*. Tese de Mestrado em Ciência Cognitiva. Universidade de Lisboa (orientação: Prof Doutora Tânia Fernandes, Faculdade de Psicologia, ULisboa).

Ferreira, J., Raposo, A. & Fernandes, T. *Are memory and language brothers in arms when learning new words?* Poster presented to the 2017 International Convention of Psychological Science, Vienna, Austria.

E-mail contact: taniapgfernandes@gmail.com; tpfernandes@psicologia.ulisboa.pt

206/14 - "Examination of brain coordination dynamics underlying hypnosis and volitional acts using intracranial electroencephalography" - only abstract available
Investigadores/*Researchers*: Jose Luis Perez Velazquez, Navinder Persaud, Taufik A. Valiante
Instituição/*Institution*: Hospital for Sick Children, Neurology, University of Toronto (Canada); Toronto Western Hospital (Canada)
Duração/*Duration*: 2015/05 – 2017/11

Background: The view of the brain as a reflexive organ whose neural activity is completely determined by incoming stimuli is being challenged by the "intrinsic" or spontaneous view of the brain. Nevertheless, the exact implications of resting state for brain function are far from clear (Schneider,2008), (Northoff, 2010). (Maandag, 2007) argue for the reconceptualization of resting state as an independent variable (brain's input) to a multidimensional activity modulator. The more we know about the electrophysiological underpinnings of resting state, both with eyes closed and eyes open, the better equipped we will be to understand brain dynamics, including both intrinsic activity and the processing of stimuli.

Aims: This paper addresses a fundamental question, are eyes closed and eyes open resting states equivalent baseline conditions, or do they have consistently different electrophysiological signatures? Previous studies have identified a reduction in the number of connections when the eyes closed condition is compared to the eyes open condition, in the alpha band (Tan, 2013). This is known as the "alpha desynchronization". We examine whether the eyes closed and eyes open resting states are equivalent baseline conditions by analyzing the differences between the two.

Method: First, we perform power and phase based connectivity analysis to asses whether the connectivity patterns calculated from intracranial recordings are able to differentiate between the two conditions. Additionally, we exploit the excellent temporal and spatial precision of ECoG to calculate the wiring cost for the connectivity maps.
Second, we investigate whether network topological properties have enough statistical power to be used as a feature/covariate to distinguish between the eyes closed and eyes open conditions.
Additionally, we provide a calculation of the wiring cost, defined in terms of the connectivity between electrodes weighted by the distance.

Results: The change in functional connectivity from eyes closed to eyes open, is here, for the first time, studied with intracranial recordings. We find that the wiring cost variation from eyes closed to eyes open is sensitive to eyes closed and eyes open conditions. The location of the electrodes is the most important factor to be considered when studying the alpha desynchronization in ECoG.

Conclusions: We do not find compelling evidence for the alpha desynchronization in phase-based connectivity analysis (except for interhemispheral and frontal electrodes). Power-based connectivity, on the other hand, is a more consistent predictor of alpha desynchronization, in particular within temporal electrodes. We find that the wiring cost does a better job in differentiating between eyes closed and eyes open than network metrics such as characteristic path length, clustering or the edge density.

Keywords: Intracranial electroencephalography, Resting state, Brain connectivity, Phase-lag index, Computational topology

Publications:
Gómez-Ramírez, J., Freedman, S., Mateos, D., Perez Velazquez, J. L., & Valiante, T. (2017). Exploring the alpha desynchronization hypothesis in resting state networks with intracranial electroencephalography and wiring cost estimates. *Scientific Reports, 7*(1):15670. doi: 10.1038/s41598-017-15659-0

E-mail contact: jd.gomezramirez@gmail.com

228/14 - "Pushing consciousness and selfhood towards their boundaries - An EEG neurophenomenological study"

Investigadores/*Researchers*: Joseph Glicksohn, Aviva Berkovich-Ohana, Tal Dotan Ben-Soussan
Instituição/*Institution*: Bar-Ilan University, Ramat Gan (Israel); Fondazione Patrizio Paoletti, Assisi (Italy)
Duração estimada/*Estimated duration*: 2015/02 - 2018/04

Background: The *Ganzfeld* is a method of perceptual deprivation, involving reduced patterning of stimulation, in which participants may experience altered states of consciousness (SOC). We look at both phenomenology and electrophysiology (EEG) of participants immersed in Whole-Body Perceptual Deprivation (WBPD).

Aims: To investigate a WBPD-induced shift in SOC and sense of self as well as synesthesia.

Method: The WBPD chamber was first flooded with white light, followed by red light and indigo light, enabling an immersive WBPD. The complete sample of the study comprised 32 experienced practitioners of breathing meditation (182 - 7280 hours). EEG and Time Production (TP) were examined. At the end of the session, an extensive interview was conducted.

Results: Our participants reported experiences of an unusual character, including changes in the experience of time. In addition, they reported changes in bodily sensations, coupled with a feeling of immersion. We found wide individual differences in EEG alpha profile, and in TP. For those participants reporting a marked change in time experience, such as "the sensation of time disappeared", their TP data could not be linearized using a log-log plot, hence indicating that for these individuals there might be a 'break' in the psychophysical function.

Conclusions: In spite of the existence of these individual differences, we can make the following tentative claims. First, when "time disappeared", TP becomes haphazard. Second, when "time was slower" or "time was expanded", TP is lengthened. In addition, our EEG data indicate that male and female participants should not be pooled, because their alpha asymmetry profiles are diametrically opposed.

Keywords: Alpha, EEG, *Ganzfeld*, Time perception, Self

Publications:

Glicksohn, J., Berkovich-Ohana, A., Mauro, F., & Ben-Soussan, T. D. (2017). Time perception and the experience of time when immersed in an altered sensory environment. *Frontiers in Human Neuroscience*, *11*, article 487.

E-mail contact: jglick@post.bgu.ac.il

233/14 - "Training anomalous cognition in a motor task with subliminal auditory feedback"
Investigador/*Researcher*: John Albert Palmer
Instituição/*Institution*: Rhine Research Center, Durham, NC (USA)
Duração/*Duration*: 2015/04 – 2018/02

Background and aims: The purpose of the study was to train anomalous cognition (AC) in a motor-automatism task with subliminal auditory feedback in 5 participants (Ps) selected on evidence of high state dissociation (reports of hand being moved by an outside force during the AC task) and trait dissociation (high scores on the Detachment subscale of the Dissociative Processes Scale) in a previous motor automatism experiment. The formal hypothesis was significantly higher AC scoring after training than before training by the 5 Ps both individually and collectively.

Method: The motor task is administered on a computer writing tablet on top of which is affixed a 4 inch grid conceptually divided into 16 1-in. squares which are conceptually divided into 4 quadrants of 4 squares each. One of the squares is randomly assigned as the target for each of the 60 trials in a run. Participants (Ps) are instructed to explore the grid by moving the computer pen over its surface until their intuition tells them to stop. After they stop for 1 second their response is registered as the corresponding square. If they stop on the target square they get a "square hit" ($P = 1/16$). If they stop on any square in the correct quadrant they get a "quadrant hit" ($P = 1/4$). The two hit totals are converted to *z*-scores, the average of which represents "location *z*s", the dependent variable. Ps attended 2 1-run "baseline" sessions at the beginning of their participation and 2 1-run "test" sessions at the end. In between, they were to complete 15-20 1-run training sessions. The procedure for these runs differs only in that after each trial P hears 1.5 seconds of brownian (similar to pink) noise. If the trial is a quadrant hit, the noise has superimposed on it the spoken word "good". If the trial is a square hit, the words "good good" are superimposed. A threshold test prior to training assured that the words were subliminal.

Results: 1 of the 5 Ps (P5) confirmed the hypothesis. There was significant or suggestive evidence of AC in the baseline and/or test results of 4 of the 5 Ps and the five difference scores showed significant between-subjects variability.

Conclusions: There was no evidence of learning in the training sessions, and the success of P5 cannot be attributed to learning. According to the underlying theory, the conditions for learning were not met because Ps were overly attentive to the feedback, often interpreting shown-to-be imagined variations in the sound as indications of hitting.

Keywords: Anomalous cognition, Motor automatism, Dissociation, Auditory feedback, Subliminal

Publications:
Palmer, J. (2017). Training anomalous cognition in a motor task with subliminal auditory feedback. *Abstracts of presented papers. 60th Annual Convention of the Parapsychological Association,* pp. 24-25.

E-mail contact: john@rhine.org

244/14 - "Induced brain plasticity after perinatal stroke: Structural and functional connectivity"
Investigadores/*Researchers*: Antoni Rodriguez-Fornells, Alfredo García-Alix, Carme Fons, Clément François, Jordi Muchart, Laura Bosch, Mónica Rebollo, Pablo Ripollés
Instituição/*Institution*: Department of Basic Psychology, University of Barcelona (Spain); Hospital Sant Joan de Deu, Esplugues de Llobregat (Spain)
Duração/*Duration*: 2015/02 – 2017/09

Background: Despite a rather large body of literature on typically developing children, little is known on the effect of early brain lesion on the stepwise acquisition of linguistic functions in young children. Patients who have suffered from early left hemisphere injury during the perinatal period are of great interest, as they present individual differences in their degree of language recovery. Only few fMRI data collected in children with perinatal left-hemisphere brain lesions have brought evidence that the undamaged right-hemisphere is able to take over language functions as revealed by near to normal linguistic processing, thus supporting a model of recovery based on inter-hemispheric transfer of function. More recent studies have detected subtle language processing deficits on these children. As a consequence, it is still an open question to which extent the nature and extent of language reorganization and plasticity after an early brain insult is enough for normal language development.

Aims: The aims of the project were (i) to better understand how functional and structural white-matter connectivity during brain maturation is reorganized after perinatal ischemic stroke and (ii) to evaluate to which extent language functions in these children are associated with functional and structural brain changes occuring due to the large plasticity of the underlying neural networks.

Method: Nine patients with pre- or perinatal stroke (3 with lesion over the right hemisphere and 6 with lesions over the left hemisphere) took part in the present study. Neurocognitive development was assessed at 42 months of age. Language outcomes were extensively evaluated with measures on receptive vocabulary, phonological whole-word production and linguistic complexity in spontaneous speech. Word learning abilities were also assessed using a fast-mapping task designed to assess immediate and delayed recall of the mapped words.
We also acquired functional and structural imaging data as well as a measure of intrinsic connectivity.

Results:
1) We found converging functional and structural evidence for a right reorganization of the language network in the sub-group of children with a left perinatal stroke. Specifically, BOLD activations during the passive listening task were found to be clearly right lateralized with significant clusters over the right Inferior frontal and right middle temporal gyri.
2) We found converging evidence from both DTI tractography and rs-fMRI data that a greater structural-functional reorganization to the right hemisphere was related to better outcomes in several productive language related tasks.

Conclusions: To our knowledge, no previous studies have provided a 3D reconstruction of the dorsal and ventral language white-matter pathways in a homogeneous group of young 4-year old children with perinatal ischemic stroke.
Our results suggest that the amount of right lateralized reorganization induced by early left lesion is may predict productive and receptive aspects of language at this age.

Keywords: Perinatal stroke, Brain plasticity, Language development, NeuroImaging data, functional and structural connectivity

Publications:
François, C., Ripolles, P., Bosch, L., Garcia-Alix, A., Muchart, J., Sierpowska, J., Fons, C., Solé, J., Rebollo, M., Gaitán, H., Rodriguez-Fornells, A. (2016). Language learning and brain reorganization in a 3.5-year-old child with left perinatal stroke revealed using structural and functional connectivity. *Cortex, 77*: 95-118.
François, C., Ripolles, P., Ferreri, L., Bosch, L., Garcia-Alix, A., Muchart, J., Sierpowska, J., Fons, C., Solé, J., Rebollo, M., Rodriguez-Fornells, A. (in preparation). Structural and functional reorganization of language functions in young children with perinatal ischemic stroke.

E-mail contact: arfornells@gmail.com

246/14 - "Anomalous/paranormal experiences reported by nurses themselves and in relation with theirs patients in hospitals: Examining psychological, personality and phenomenological variables"
Investigador/*Researcher*: Alejandro Enrique Parra
Instituição/*Institution*: Instituto de Psicologia Paranormal, Buenos Aires (Argentina)
Duração/*Duration*: 2015/03 – 2017/03

Background: There is a number of anomalous/paranormal experiences (APE) reported by nurses and carers consisting of apparitions, "coincidences," death-bed visions, and other anomalous phenomena, sometimes in relation to patients, and other by nurses, carers and doctors themselves in hospital settings

Aims: To determine the degree of occurrence of certain unusual perceptual experiences in hospital settings. We hypothesized that: (H1) nurses who report APEs will tend to score higher on work stress; (H2) higher on schizotypy proneness, (H3) higher on absorption, and (H4) higher on empathy than those who do not report such experiences.

Method: Three hundred forty-four nurses were recruited from 36 hospitals and health centers in Buenos Aires, Argentina, who were grouped 235 experiencers and 109 nonexperiencers. A self-report which has 13 yes/no items was designed. Four additional scales to measure absorption, empathy, and schizotypy proneness.

Results: The most common experiences are sense of presence and/or apparitions, hearing noises, voices or dialogues, crying or complaining, intuitions and ESP experiences and as listeners of experiences of their patients, such as near-death experiences, religious interventions, and many anomalous experiences in relation with children. Nurses reporting APEs tended higher on absorption, proneness to schizotypy, and cognitive empathy and Emotional comprehension, which also tended to score higher than non experiencers.

Conclusions: Capacity for absorption appears to be only one of a constellation of related factors. It may be that cognitive style is more important than capacity or skill, as in the case of absorption, which refers to the extent to which a person can be so engrossed in a mental experience at a given moment that reality monitoring is temporarily inhibited. However, neither of these variables (absorption or hallucination proneness) was found to be related to work stress, although it could be argued that the psychological pressure of the working conditions of nurses triggers such anomalous perceptual experiences. Nor were there indicators of psychosis proneness found, even in the experiencers with hallucinatory experiences.

Keywords: Nursing, Absorption, Anomalous experiences, Cognitive style, Schizotypy

Publications:
Parra, A. (2015). Visiones en el lecho de muerte: Enfermeras, testigos de excepción. *Más Allá, 26*(318), 22-31.
Parra, A. & Giménez Amarilla, P, (2017). Anomalous/paranormal experiences reported by nurses in relation to their patients in hospitals. *Journal of Scientific Exploration, 31*(1), 11–29.
Parra, A. (2017). Factores de personalidad, perceptuales y cognitivas asociadas con las experiencias anómalo/paranormales en personal de enfermería. *Cuidarte*, *8*(3), 78-87
Parra, A. & Giménez Amarilla, P. (2016). Relación entre estrés laboral, alucinación y experiencias anómalas entre profesionales de enfermería. *Ciencia & Cuidado, 13*(2), 22-40.

E-mail contact: rapp@alipsi.com.ar

253/14 - "The impact of lipid signaling modulation in cognition"

Investigadores/*Researchers*: Tiago Gil Rodrigues Oliveira, Isabel Maria Sousa Castanho, Neide Marina Vieira Pereira, Rita Catarina Ribeiro da Silva, Vítor Manuel da Silva Pinto
Instituição/*Institution*: Life and Health Sciences Institute - ICVS, School of Health Sciences, University of Minho, Braga (Portugal)
Duração estimada/*Estimated duration*: 2015/05 – 2018/04

Background: Over the past years increasing amount of attention has been given to signaling lipids as well as to its modulating enzymes, such as phospholipases. Specifically, phospholipase D (PLD), that converts phosphatidylcholine to phosphatidic acid, has been shown to exhibit a role in neurological development and physiology. Several studies have been associating PLD1 and PLD2, the two main mammalian PLD isozymes, to neurological processes, including neurotransmitter release, dendritic branching, cognition, and brain development. Also, the hippocampus has been suggested as one of the brain regions showing the highest PLD activity and neurodegenerative conditions such as Alzheimer's disease associated pathways have been shown to be modulated by PLD signaling.

Aims: Thus, the aim of this project is to better understand the potential role of PLD in hippocampal function in adult mice upon *Pld1* or *Pld2* genetic ablation.

Method: We performed (1) a biochemical validation of PLD1 and PLD2 mutant mice by western blot and mass spectrometry; (2) a hippocampal related behavioral characterization of these animals by Open Field, Elevated Plus Maze, Morris Water Maze and Novel Object Recognition; (3) a structural analysis regarding dendritic morphology using dorsal and ventral hippocampal slices with Golgi staining; (4) electrophysiologic synaptic plasticity paradigms of dorsal and ventral hippocampal slices, namely long-term potentiation (LTP) and depression (LTD) protocols; and (5) a full lipidomic mass spectrometry analysis of dorsal and ventral hippocampal samples.

Results: Our results show that PLD1 is the major contributor for total PLD activity. The behavior analysis showed that while PLD1 KO mice have minor deficits in novel object recognition, PLD1 and PLD2 KO mice have no other major deficits in behaviors relying in the hippocampus. Interestingly, in the dendritic structure analysis PLD1 KO presented increased spine density in the ventral hippocampal CA1 region and PLD2 KO presented increased dendritic length in the dorsal hippocampal CA1 region. Remarkably, while PLD1 KO animals had decreased LTP both in the dorsal and ventral hippocampus, PLD2 KO had only decreased LTP only in the ventral part. Finally, the lipidomic analysis showed that PLD1 KO presented a major decrease in multiple PA species both in the dorsal and ventral hippocampus and PLD2 KO animals presented only minor alterations in PA species in the ventral hippocampus.

Conclusions: Overall, our results show that even though PLD1 and PLD2 perform the same enzymatic reaction, they contribute in a differential manner to the function of the hippocampus. Since the PLD pathway has been implicated in disease processes that affect the hippocampus, these findings highlight not only its fundamental of role in learning and memory but also as potential therapeutical targets.

Keywords: Lipids, Cognition, Phospholipase D, Hippocampus, Memory

E-mail contact: tiago@med.uminho.pt

257/14 - "Genetics of psychic ability" - only abstract available
Investigadores/*Researchers*: Dean Radin, Garret Yount, Garry Nolan
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA); Stanford University (USA)
Duração estimada/*Estimated duration*: 2015/07 - 2018/04

Background: It is commonly believed that psychic ability, like many mental and physical traits, runs in families. This suggests the presence of a hereditary component. Using a genomic analysis technique known as Genome Wide Association Studies (GWAS), which analyses constellations of genetic networks to find correlations with human health, personality traits, talents, etc., this project is exploring if psychic ability has a discernible genetic component.

Aims: The objective of this study is to see if psychic ability correlates with specific sets of genes or genetic networks.

Methods: We screened 3,162 psychic candidates using two online surveys to locate people with claimed psi ability in themselves and their family members, to rule out exclusions (e.g., psychotic or delusional tendencies), and to collect measures of relevance to psychic ability (e.g. absorption, sensitivity, empathy). We then selected a subsample of these volunteers to be interviewed and to take additional online screening tests of psi ability. Then, using a case-control study design, 13 individuals were finally selected as "psychic cases," and 10 age and gender-matched individuals with no claims of psychic ability were selected as controls. DNA was collected from these 23 participants, and their DNA is being whole-genome sequenced and mapped using advanced BINA alignment algorithms. Genetic network analyses between the two groups will reveal if there are genes or networks of genes that can discriminate between the psychic and control cases.

Results: Genome sequencing is presently underway. GWAS and possibly other forms of genetic analyses will be conducted after the sequencing is complete.

Conclusions: This project is taking longer than we originally expected to complete, primarily due to the time it took us to sift through the psychic candidates and vet the final selections and matched controls, and also to the complexities involved in genomic sequencing and analysis. GWAS is a state-of-the-art technique that requires time and expertise to complete, so we are dependent on our geneticist collaborators to finish that portion of this study.

Keywords: Genetics of psi, Familial traits

Publications:
We will publish one or more articles on the results when the analyses are complete.

Email contact: dean@noetic.org

260/14 - "Psi-Q: A smartphone testing suite for psi ability" - only abstract available
Investigadores/*Researcher*s: Dean Radin, Arnaud Delorme
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA)
Duração/*Duration*: 2015/07 - 2017/07

Background: Small effect sizes observed in laboratory studies of psi phenomena can be amplified by gathering large amounts of data online. To help collect such data, we created a mobile app dubbed "PsiQ." It was released on June 12, 2017 and is available for free for the iPhone, iPad, and iPod Touch. To date it has been downloaded more than 2,000 times.

Aims: The goal was to create a smartphone app that uses games to collect more psi data than is typical for lab-based tests, to test different ways that psi can express itself, and to study possible hormonal influences on psi in women. Demographic and personality information are also being collected.

Method: The app tests for psychokinetic (PK) ability, precognition, and clairvoyance, especially in their nonconscious or implicit forms. There are three games: "Heart Quest" tests for PK. "Hidden Gurus" tests for conscious precognition, implicit auditory precognition, and implicit PK. "Future Feelings" tests for implicit precognition using Daryl Bem's retrocausal priming design. A truly random number generator (RNG) was created by using a Javascript RNG called KISS07, which passes the Die Harder tests for randomness, and XORing those values with the fastest-moving bit of the device's accelerometer. A professional games illustrator created graphics for the games to make them simple yet emotionally engaging.

Results: Based on data from the first 250 users, the results are not significant in any of the games, but there are interesting secondary effects suggesting differences between men and women, especially based on the presumed reproductive hormonal status of the women.

Conclusions: So far the preliminary results are interesting, especially for the secondary hypotheses of interest, and we look forward to collecting and analyzing more data.

Keywords: Smartphone application, Psi games, Precognition, Online experiments

Publications:
We have discussed the app and the preliminary results at various conferences, but we are waiting until the app has received data from 10,000 users before we submit an article for publication.

Email contact: dean@noetic.org

279/14 - "Facial and bodily temperature maps of emotions"

Investigadores/*Researchers*: Maria Lucia Martins das Neves Garrido, Lisa Katharina Kuhn, Nicholas Pound
Instituição/*Institution*: Division of Psychology, Department of Life Sciences, Brunel University, Uxbridge (UK)
Duração estimada/*Estimated duration*: 2015/01 - 2018/04

Background: William James (1884) argued that emotions are the subjective experience of bodily change, and thus different emotions are associated with distinct physiological responses. For the past 100 years, however, the question of whether these physiological responses are specific for each emotion or are instead generalized arousal responses has remained unsettled. A potential criticism is that most studies focused on global physiological responses (such as heart rate or respiration rate), or responses in single points in the body (such as temperature changes in a finger) and we may need richer datasets, consisting of spatial patterns of responses. Nummenmaa et al. (2014) addressed this issue by measuring subjective sensations across the whole body, permitting analysis of rich spatial patterns of responses. But these results were based on subjective reports, so an outstanding question is whether it is possible to *objectively* measure the patterns of physiological responses.

Aims: We used skin temperature maps of the whole face associated with each of six basic emotions to investigate whether those maps are distinct for different emotions.

Method: We conducted three experiments using thermal imaging (FLIR A655sc). We measured temperature in the face while participants were presented with images of facial expressions of emotion (Exp 1), images eliciting emotions (Exp 2), and videos eliciting emotions (Exp 3). In each experiment, we obtained facial temperature maps for each participant and each emotion. We used delineated landmarks to divide each facial map into 68 polygons, and tested: (1) whether there were changes in temperature in each polygon in response to each emotion compared to baseline, and (2) whether we could classify the temperature maps according to emotion.

Results: Our results showed that for each experiment, there were face regions (polygons) that consistently changed in temperature in response to perceiving or experiencing emotions. However, our results were not consistent across experiments. Moreover, our classification analyses so far have not shown clear evidence of distinct spatial temperature maps for each emotion.

Conclusions: We think that our work brings a highly innovative approach to the study of physiological changes associated with emotional states. However, more work is needed to assess the reliability of our findings and further test whether we can accurately classify specific emotions from facial temperature maps.

Keywords: Emotions, Facial temperature maps

E-mail contact: lucia.garrido@brunel.ac.uk

282/14 - "The mindful eye: Smooth pursuit and saccadic eye movements in meditators and non-meditators"

Investigadores/*Researchers*: Veena Kumari, Elena Antonova
Instituição/*Institution*: Institute of Psychiatry, King's College London (UK)
Duração/*Duration*: 2015/04 - 2017/01

Background: There is growing evidence for a positive effect of cultivated mindfulness (i.e. developed through training) on a range of cognitive functions. There are only few data at present examining the association between dispositional (trait) mindfulness, as measured in the general non-meditating population using self-report questionnaires, and cognitive function.

Aims: The aim of this study was to examine the effects of cultivated and dispositional (trait) mindfulness on smooth pursuit (SPEM) and antisaccade (AS) tasks known to engage the fronto-parietal network implicated in attentional and motion detection processes, and the fronto-striatal network implicated in cognitive control, respectively**.**

Method: Sixty healthy men (19-59 years), of whom 30 were experienced mindfulness practitioners and 30 meditation-naïve, underwent infrared oculographic assessment of SPEM and AS performance. Trait mindfulness was assessed using the self-report Five Facet Mindfulness Questionnaire (FFMQ).

Results: Meditators, relative to meditation-naïve individuals, made significantly fewer catch-up and anticipatory saccades during the SPEM task, and had significantly lower intra-individual variability in gain and spatial error during the AS task. No SPEM or AS measure correlated significantly with FFMQ scores in meditation-naïve individuals.

Conclusions: Cultivated, but not dispositional, mindfulness is associated with improved attention and sensorimotor control as indexed by SPEM and AS tasks. Eye movement tasks which have high test-retest reliability and known brain correlates and are easy to administer hold promise as objective measures of mindfulness training.

Publications:

Kumari V, Antonova E, Wright B, Hamid A, Hernandez EM, Schmechtig A, Ettinger U. The mindful eye: Smooth pursuit and saccadic eye movements in meditators and non-meditators. *Conscious Cogn*. 2017 Feb; 48:66-75. PMID: 27842243

Keywords: Mindfulness, Antisaccade, Cgnitive control, Attention, Intra-individual variability

Email contact: veena.kumari@kcl.ac.uk; vkumari10@hotmail.com

287/14 - "Cryptochrome (CRY) and Intention"

Investigadores/*Researchers*: Yung-Jong Shiah, Hsu-Liang Hsieh, Dean Radin
Instituição/*Institution*: Graduate Institute of Counseling Psychology and Rehabilitation Counseling of the National Kaohsiung Normal University, Kaohsiung (Taiwan); Photobiology Lab, Taipei (Taiwan)
Duração/*Duration*: 2015/09 – 2017/06

Background: Cryptochromes (abbreviated CRY) are blue photoreceptors, which respond to 400 to 500 nm signals. They exist in plants, bacteria, animals, and humans, and they are involved in the organism's growth and circadian rhythms. Any protein that has a DNA sequence 25–50% similar to that of photolysis, but that lacks photolysis' ability to use blue light to repair UV-induced DNA damage, is called a CRY. CRY was originally suggested as a mind–matter interaction (MMI) target by the first author, and if further work confirms that CRY is as robust a target as our observations suggest, it could provide such a mechanism. The speculation is that CRY, a flavoprotein present in all living systems, may be a "transducer" of intention because of its quantum biological characteristics. Among other things, these quantum effects are thought to account for the exquisite sensitivity to magnetic fields and light in living organisms. Arabidopsis thaliana, a small flowering weed in the mustard family with the popular name "mouse ear cress." This is one of the most-studied plants. Arabidopsis grows quickly in the laboratory and it contains a photosensitive flavoprotein called CRY. Three variations of CRY act either as photoreceptors or as transcription regulators; they are known as CRY 1, 2 and 3. These proteins play key roles in photomorphogenesis, circadian clocks, flowering time, seed germination, etc. The potential quantum biological properties of Arabidopsis made it an interesting system for exploring intentional effects.

Aims: To investigate the CRY Theory objectively, we studied whether Arabidopsis thaliana seeds hydrated under blinded conditions with intentionally treated vs. untreated water would show differences in hypocotyl length, anthocyanin, and chlorophyll.

Method: Three Buddhist monks focused their intention on commercially bottled water with the goal of improving the growth of seeds; bottled water from the same source served as an untreated control. Seeds with three variations of CRY were used: the wild type *Arabidopsis* (Columbia-4), a gain-of-function mutation (*His-cry2*), and a loss-of function mutation (*cry1/2*), where "gain" and "loss" refer to enhanced and reduced sensitivity to blue light, respectively. Seeds were hydrated with treated or untreated water under blinded conditions, then placed in random positions in an incubator. The germination process was repeated three times in each experiment, each time using new seeds, and then the entire experiment was repeated four times.

Results: Data combined across the four experiments showed a significant decrease in hypocotyl length in the *His-cry2* seedlings (treated mean 1.31 ± 0.01 mm, untreated mean 1.43 ± 0.01 mm, $p < 10^{-13}$), a significant increase in anthocyanin with all three forms of *cry*, particularly *His-cry2* (treated mean 17.0 ± 0.31 mg, untreated mean 14.5 ± 0.31 mg, $p < 10^{-4}$), and a modest increase in chlorophyll in *His-cry2* (treated mean 247.6 ± 5.63 mg, untreated mean 230.6 ± 5.63 mg, $p = 0.05$). These outcomes conformed to the monks' intentions because a decrease in hypocotyl length and increase in anthocyanin and chlorophyll are associated with enhanced photomorphogenic growth. These experiments suggest that the *His-cry2* mutation of *Arabidopsis* may be an especially robust "detector" of intention.

Conclusions: The present study suggests that elementary living systems with quantum-biological properties may be especially responsive targets. If future studies continue to replicate the results of the present experiments, then quantum-inspired models may be useful guides in developing hypotheses for understanding and testing the role of intention in the physical world.

Keywords: Cryptochrome, Intention, Mind–matter interaction

Publications:

Shiah, Y.-J., Hsieh, H.-L., Chen, H.-J., & Radin, I. D. (2017). Effects of intentionally treated water on growth of Arabidopsis Thaliana seeds with cryptochrome mutation. *EXPLORE: The Journal of Science & Healing, 13*(6), 371-378.

E-mail contact: shiah@nknu.edu.tw

308/14 - "A study of heterogeneity in parapsychological databases" - only abstract available
Investigador/*Researcher*: Peter Amalric Bancel
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA); Institut Métapsychique International, Paris (France)
Duração estimada/*Estimated duration*: 2015/06 – 2018/04

Background: Evidentiary support for psi phenomena (e.g. pre-cognition, psychokinesis (PK)) relies to a large degree on meta-analyses (MAs). In the last decades, MAs of psi protocols have been reported in mainstream journals. MAs of the Ganzfeld, pre-cognition, clairvoyance, micro-PK and presentiment effects all find evidence for significant deviations from the Null hypothesis. The results are controversial and may be due to publication bias, or other questionable research practices (Qrps). Recently Bierman et al. modeled Qrps via Monte Carlo (MC) simulations to assess the Ganzfeld. With reasonable Qrp frequencies, they account for no more than half of the effect. They conclude that a real effect remains even when controlling for the presence of multiple Qrps. Simulation is promising because it can strengthen the statistical evidence for an effect and provide better effect size estimates for replications. But a cost is high computational overhead, which puts some practical limits on the range of modeled Qrps.

Aims: Analysis is done on three MAs: the dataset of Bierman; the micro-PK MA; and the Global Consciousness Project (GCP). Technical developments enhance the scope, power and speed of the Qrp analyses.

Method: 8 distinct Qrps are modeled in >105 combinations and levels. A fitness function for each model tests the MA data against model Pcurves (distributions of P-values), effect size, heterogeneity and small-study effects. Each model is a weighted linear combination of 8 'basis' models. Thus only 8 MC's are needed which gives a speed-up of ~ 1000x.

Results: The Ganzfeld results follow Bierman et al.'s. Proper effect size definitions are unclear for m-PK and GCP. However, maximal Qrps so underestimate the m-PK heterogeneity that this independently supports rejecting the Null, despite the lack of effect size definition. Seeking a definition for the GCP led to determine that the GCP is a goal-oriented experimenter effect (see reference).

Conclusions: Qrp simulation can help settle interpretational questions of MAs.

Keywords: Parapsychology, Meta-analysis, Ganzfeld, Publication bias, Heterogeneity

Publications:
Bancel, P. A. (2017). Searching for Global Consciousness: A 17-Year Exploration. *Explore: Journal of Science and Healing, 13*(2), 94-101.

E-mail contact: pabancel@free.fr

318/14 - "Neural correlates of tracking changing positions of objects" - only abstract available
Investigadores/*Researchers*: Christina Jayne Howard, Matthew K Belmonte
Instituição/*Institution*: Division of Psychology, Nottingham Trent University (UK)
Duração/*Duration*: 2015/02 – 2017/07

Background: Perceiving the dynamic world around us involves maintaining up-to-date visual representations. In the multiple object tracking (MOT) task, in which observers attempt to keep track of moving target objects amongst distractors, it is becoming clear that individual differences affect performance e.g. age, expertise, cognitive development and computer gaming, to name some identified factors. Some studies have used event-related potentials (ERPs) or steady state visual evoked potentials (SSVEPs) to examine individual differences in MOT performance. However, most of these studies have either measured neural responses to task irrelevant changes, or have used relatively coarse measures of target-distractor identification as their performance metric.

Aims: We asked observers to monitor the positions of moving targets and used the precision of their position reports as a more direct measure of performance. In addition, we examined the neurophysiological basis of keeping up-to-date representations of moving objects using both pre-task resting EEG and ongoing EEG during the task.

Method: In two experiments similar to the multiple object tracking (MOT) task, we asked observers to monitor one or several targets as they moved unpredictably for a short, semi-random period. After targets and distractors disappeared, observers were immediately prompted to use a mouse click to report the perceived final position of one queried target with as much precision as possible.

Results: The precision of observers' position reports declined with attentional load. In addition, reports tended to most closely resemble positions occupied by the queried target between 0 and 30 ms in the past. ERPs showed a contralateral delay activity over occipital scalp, maximal in the right hemisphere. The peak power-spectral frequency of observers' eyes-closed resting occipital alpha oscillations reliably predicted performance, such that lower-frequency alpha was associated with superior spatial localisation. Unlike some previous similar work, we found no relationship between performance and either power or phase of ongoing occipital alpha oscillations.

Conclusions: Slower resting occipital alpha is associated with greater precision in a position monitoring task. Slower resting alpha might be associated with a cognitive style that depends less on memory-related processing and instead emphasises attention to changing stimuli.

Keywords: Attention, Spatial vision, Multiple object tracking, Alpha oscillations, Position monitoring

Publications:
Howard, C.J., Arnold, C.P.A. & Belmonte, M.K., 2017. Slower resting alpha frequency is associated with superior localisation of moving targets. *Brain and Cognition*, 117, Pp. 97-107.

E-mail contact: Christina.Howard@ntu.ac.uk

340/14 - "A question of belief: An analysis of item content in paranormal belief questionnaires"
Investigadores/*Researchers*: Lance Storm, Ken Drinkwater, Tony Jinks
Instituição/*Institution*: Brain and Cognition Centre, School of Psychology, University of Adelaide (Australia); Department of Psychology, Faculty of Health, Psychology and Social Care, Manchester (UK)
Duração/*Duration*: 2015/04 – 2017/07

Background: This study examined the degree to which paranormal believers, who profess 'strong' belief in the popular expression of a topic known as the primary item (e.g., There is such a thing as extrasensory perception), disagree with related items and/or the putative 'cause' of the topic, known as secondary items (e.g., Some people have an unexplained ability to predict the future). Related to this issue is that current thought in parapsychology has it that paranormal belief predicts depression and reality testing deficits. These findings may be based on a limited approach to paranormal belief.

Aims: It was theorised that scoring differences between primary and secondary items might identify certain kinds of paranormal believer, which might then allow us to conduct deeper analyses of paranormal belief (PB) and its putative relationships with depression and reality testing deficits.

Method: The Paranormal Belief Informedness Scale (PBIS) was constructed from extant PB scales—it consists of 10 primary items and 10 secondary items. PBIS subscale scores were used to identify three major PB types in the sample (N = 343): 'primary believers' (who believe in all 10 primary items), 'primary non-believers' (who believe in none of the 10 primary items), and 'mixed believers' (who believe in only some primary items).

Results: Significant response-rate differences were found between primary and secondary items across believer types, and across psi categories (i.e., ESP, PK, and life after death). For the full sample, it was shown that there is a significant relationship between PB and reality testing deficits (IPO-RT; Lenzenweger et al., 2001), but this relationship tended not to be significant across believer types. There was no evidence in the full sample, or in any believer type, that PB was correlated with depression as measured on the BDI-II (Beck et al., 1996).

Conclusions: We suggest that paranormal believers have differences that may be reflected in their responses to predictor variables, and/or how informed their paranormal belief is; Linear trends may be misleading when dealing with paranormal belief as a predictor of deficits and dysfunctions.

Keywords: Paranormal belief, Depression, Informed belief, Quasi-belief, Reality testing

Publications:
Storm, L., Drinkwater, K., & Jinks, A. L. (2017). A question of belief: An analysis of item content in paranormal belief questionnaires. *Journal of Scientific Exploration*, *31*(2), 187-230.

E-mail contact: lance.storm@adelaide.edu.au

344/14 - "An integrative approach to the neural basis of hypnotic suggestibility"
Investigador/*Researcher*: Devin Blair Terhune
Instituição/*Institution*: Goldsmiths, University of London (UK)
Duração/*Duration*: 2015/04 – 2016/07

Background: Despite recent advances in understanding the neurophysiology of hypnosis, current knowledge of the neuroanatomical and neurochemical correlates of hypnotic suggestibility remain poorly understood.

Aims: This study sought to determine whether individual differences in hypnotic suggestibility and distortions in the sense of agency during hypnotic responding could be predicted from neurochemical concentrations and gray matter volumes in brain regions previously implicated in hypnosis and germane constructs.

Method: In two studies, participants were screened for hypnotic suggestibility using the Stanford Hypnotic Susceptibility Scale: Form C in individual sessions. In study 1 (N=28), participants' GABA and glutamate concentrations were recorded from primary motor and visual cortices. In study 2 (N=20), participants' GABA and glutamate concentrations were recorded from pre-supplementary motor area, anterior putamen, and posterior cerebellum in right hemisphere. Participants in both samples also underwent a whole-brain structural (T1) scan, for which data from 57 participants were available.

Results: In Study 1, after correction for multiple comparisons, motor cortex GABA concentrations negatively correlated with hypnotic suggestibility whereas in Study 2, no correlations between metabolite concentrations and hypnotic suggestibility achieved statistical significance. Hypnotic suggestibility did not correlate with gray matter volumes whereas involuntariness during hypnotic responding was positively associated with gray matter volumes in a broad network comprising right superior cerebellum, bilateral thalamus, and brainstem.

Conclusions: Hypnotic suggestibility can be predicted from motor cortex GABA concentrations, thereby implicating mototor inhibition in hypnotic responding. Distorted agency during hypnotic responding is associated with increaed gray matter volume in a thalamic-cerebellar network, potentially reflecting the roles of cerebellum in the experience of authorship and subcortical structures in the regulation of the information that breaches conscious awareness.

Keywords: Agency, GABA, Glutamate, Hypnosis, Hypnotic suggestibility, Neuroanatomy

Publications:
Terhune, D. B. & Cardeña, E. (2018). Nuances and uncertainties regarding hypnotic inductions: Towards a theoretically informed praxis. In V. K. Kumar & S. R. Lankton (Eds.), *Hypnotic induction: Perspectives, strategies and concerns*. New York, NY: Taylor & Francis/Routledge.

Terhune, D. B., Cleeremans, A., Raz, A., & Lynn, S. J. (in press). Hypnosis and top-down regulation of consciousness. *Neuroscience and Biobehavioral Reviews*

Jensen, M. P., Jamieson, G., Bányai, É., Demertzi, A., De Pascalis, V., Mazzoni, G., Lutz, A., McGeown, W. J., Rominger, C., Santarcangelo, E. L., Vuilleumier, P., & Faymonville, M.-E., & Terhune, D. B. (2017). New directions in hypnosis research: Strategies for advancing the cognitive and clinical neuroscience of hypnosis. *Neuroscience of Consciousness,* 1-14.

Terhune, D. B. & Cardeña, E. (2016). Nuances and uncertainties regarding hypnotic inductions: Towards a theoretically informed praxis. *American Journal of Clinical Hypnosis*, *59*, 155-174.

Terhune, D. B., Polito, V., Barnier, A. J., Woody, E. Z. (2016). Variation in the sense of agency during response to hypnotic suggestions: Insights from latent profile analysis. *Psychology of Consciousness: Theory, Research, and Practice, 3,* 293-302.

Yin, B., Smythies, J., Terhune, D. B., & Meck, W. H. (2016). Claustrum, consciousness, and time perception. *Current Opinion in Behavioural Sciences, 8*, 258-267.

Terhune, D. B. & Cardeña, E. (2015). Dissociative subtypes in posttraumatic stress disorders and hypnosis: Neurocognitive parallels and clinical implications. *Current Directions in Psychological Science, 24,* 452-457.

E-mail contact: d.terhune@gold.ac.uk

355/14 - "Cognitive and personality differences in supernatural belief"
Investigadores/*Researchers*: Ian Scott Baker, David Sheffield, Malcolm Schofield, Paul Staples
Instituição/*Institution*: College of Life and Natural Sciences, University of Derby (UK)
Duração/*Duration*: 2015/06 – 2017/09

Background: This project examined if we believe in certain things because we think in a certain way or have certain personalities. This required the development of the scale to enable the study of cognition and personality with relation to belief, leading to the development of a model of supernatural belief, personality and cognition.

Aims: Examine cognition and personality of people who hold different types of supernatural belief.

Method: Four studies were conducted at the University of Derby and via social media, testing over 1000 participants in total. Studies one and two created and validated a new scale. Studies three and four used various measures of cognition and personality to create a new model.

Results: Studies one and two created and validated the Belief in the Supernatural Scale, a 44-item scale with five factors: 'mental and psychic phenomena', 'religious belief', 'psychokinesis', 'supernatural entities', and 'common paranormal perceptions'. The final two studies revealed subtly different profiles of cognition (study three) and personality (study four) in relation to the different beliefs. Structural Equation Modelling was then used to test different models finding that personality predicted belief, and belief predicted cognition.

Conclusions: This project indicated a clear separation of religious and paranormal belief within the new scale, that spiritual belief overlaps between these two beliefs, and 'sceptics' and 'religious believers' have remarkably similar profiles. The 'paranormal believers' did not think critically or analytically. Schizotypy was the main predictor of belief, and belief was the main predictor of cognition.

Keywords: Supernatural, Belief, Cognition, Personality, Paranormal, Religious

Publications:
Schofield, M. B., Baker, I. S., Staples, P., & Sheffield. (accepted). The creation and validation of the Belief in the Supernatural Scale. *Journal of Parapsychology.*

E-mail contact: i.s.baker@derby.ac.uk

366/14 - "Changes in subjective time as indication of increased mindfulness after meditation"
Investigador/*Researcher*: Marc Christoph Wittmann
Instituição/*Institution*: Institute for Frontier Areas of Psychology and Mental Health, Freiburg (Germany); Department of Psychosomatic Medicine, University Medical Center Freiburg (Germany)
Duração estimada/*Estimated duration*: 2015/04 – 2018/04

Background: We based our study on conceptualizations pertaining to the relationship between meditation, subjective time, and psychophysiology.

Aims: We conducted a series of experiments probing for changes in temporal-integration processes after meditation. The aim was to assess whether physiological parameter changes of heart rate and breathing rate during meditation would influence the timing of perceived events.

Methods: We employed three psychophysical tasks related to perception of sequence in the milliseconds range, the integration of metronome beats, and the perception of alternations in the ambiguous Necker cube. The tasks were administered before and after the intervention. 91 participants were experienced mindfulness meditators who in three separate 10 minute sessions either meditated by following a meditation session (n=44) or listened to an audio play (*n*=47), the three counterbalanced sessions being conducted on three separate days. During the intervention heart-rate and breathing rate were recorded and compared to a resting-state condition.

Result: Applying statistical path analyses, we found several mediating and moderating effects. Regarding subjective scales, those meditators who were less aware of the passage of time felt less emotional arousal. Regarding psychophysiology and the switching of the aspects of the Necker cube, breathing rate significantly mediated the effect of meditation across all participants. The slower the breathing during meditation, the slower the switches of the two aspects of the Necker cube. Additionally, a moderator effect showed that higher trait-mindfulness leads to slower switching times in meditators. Regarding the metronome task, and over all frequencies meditation in more experienced meditators (n > 100 hours) lead to a decrease of the duration of integration intervals. However, for the fastest (ISI = 0.3 s) and slowest (ISI = 3 s) metronome frequencies, an opposite effect occurred: the larger RMSSD, a measure of heart rate variability, during meditation. the larger the integration interval.

Conclusions: Overall, these findings add evidence to meditation-induced changes in subjective time and the general notion of the embodiment of mental functioning. Specific effects of breathing rate and heart-rate variability are indicative of physiological arousal effects on temporal processing functions after meditation.

Keywords: Mindfulness meditation, Temporal integration, Necker cube, Metronome, Sequencing

Publications:
Linares Gutierrez D, Kübel S, Giersch A, Schmidt S, Meissner K, Wittmann M (2017). *Meditation-induced changes in subjective time are mediated by heart-rate variability and breathing rate*. Poster presentation at the 1st Conference of the Timing Research Forum, Strasbourg.

E-mail contact: wittmann@igpp.de

372/14 - "Development and implementation of a comprehensive survey of secular American mediums" - only abstract available
Investigadores/*Researchers*: Julie Beischel, Chad Mosher, Mark Boccuzzi
Instituição/*Institution*: The Windbridge Institute for Applied Research in Human Potential, Tucson (USA)
Duração estimada/*Estimated duration*: 2015/07 – 2018/04

Background: Previous research with mediums can only be generalized to specific belief system- and geographically-associated populations. The subset of American mediums not associated with any formal organization and who hold no organized belief system are the majority in the US but their general demographics and other characteristics have not been specifically assessed.

Aims: This study aimed to gather novel data regarding demographic, cognitive, psychological, physiological, and phenomenological characteristics of self-identifying mediums in the US.

Methods: This study used established survey development and piloting methods to create novel web-based instruments and included quantitative and qualitative data collection and analysis methods and computerized text analysis techniques. The survey used standard questionnaires and newly developed items. Data was collected from 1,068 non-mediums and 316 mediums.

Results: The medium and non-medium participants showed no significant differences in age, race, gender, education, or income. Mediums demonstrated statistically significantly higher psychological well-being, Agreeableness, Conscientiousness, fantasy proneness, disease burden, childhood trauma, and environmental sensitivities. Roughly 97% of medium respondents reported being able to tell the difference between communication from the deceased and psychic information about the living. Quantitative differences in the two experiences included social and perceptual processes and insight. Qualitative analyses demonstrated that psychic information about the living comes from various sources including the deceased.

Conclusions: Secular American mediums have unique psychological, personality, cognitive, and experiential characteristics; descriptions of mediumistic and psychic experiences are quantitatively different; the current language used to discuss mediumship does not accurately reflect the actual phenomenon; and pluralist methods can be used to study mediumship.

Keywords: Medium, Survey, Quantitative, Qualitative, Computerized text analysis

Publications:
Beischel, J., Mosher, C., & Boccuzzi, M. (2017). Quantitative and qualitative analyses of mediumistic and psychic experiences. *Threshold: Journal of Interdisciplinary Consciousness Studies, 1*(2), 51-91.

E-mail contact: info@windbridgeinstitute.com

373/14 - "Multimodal mapping of visual motion perceptual decision: Dissecting the role of different motion integration areas in visual surface reconstruction"

Investigadores/*Researchers*: Miguel de Sá e Sousa de Castelo Branco, Gabriel Nascimento Ferreira da Costa, Gilberto Silva, João Valente Duarte, Ricardo Martins
Instituição/*Institution*: ICNAS - Institute for Nuclear Sciences Applied to Health, Coimbra (Portugal); IBILI - Institute for Biomedical Imaging and Life Sciences, Coimbra (Portugal)
Duração/*Duration*: 2016/02 - 2017/10

Background: Neural models of perceptual decision are often studied using bistable perceptual decision paradigms. Causal bottom vs top-down mechanisms remain to be elucidated.

Aims: We asked whether hMT+ is pivotal for perceptual integration of motion signals in terms of bottom-up vs top-down interactions. Moreover, if hMT+ is indeed a causal hub in the decision-making network, then it should also provide long range integration at the inter hemispheric level, which is a testable prediction. We tested whether one can find fingerprints of perception related neural coherence. Finally, we aimed to elucidate the general relation between sensory and decision modules within saliency and frontoparietal networks.

Methods: We combined EEG and fMRI methods, to understand perceptual decision mechanisms, their neural correlates and functional connectivity (with a focus on interhemispheric interactions).

Results: We found out that human hMT+ is a causal hub which contributes to maintain perceptual representations when other competing percepts are available for cognition. We further confirmed the prediction that it should also subserve long range perceptual integration, through increased interhemispheric connectivity between left/right hMT+. EEG data revealed that bound perceptual interpretations relate with parietal beta power under ambiguous conditions. Together with our findings using other decision paradigms inside and outside the visual domain, we show a modular architecture of perceptual decision-making network.

Conclusions: Our work provides a clearcut functional segregation at different time scales, between sensory representations, and the role of the general decision modules within saliency and frontoparietal networks.

Keywords: Perception, Decision-making, EEG, fMRI, Granger causality analysis, Visual motion, Bistability.

Publications:

Costa GN, Duarte JV, Martins R, Wibral M, Castelo-Branco M. Interhemispheric Binding of Ambiguous Visual Motion Is Associated with Changes in Beta OscillatoryActivity but Not with Gamma Range Synchrony. *J Cogn Neurosci*. 2017 Jun 27:1-16. doi: 10.1162/jocn_a_01158. [Epub ahead of print] PubMed PMID: 28654360.

Duarte JV, Costa GN, Martins R, Castelo-Branco M. Pivotal role of hMT+ in long-range disambiguation of interhemispheric bistable surface motion. *Hum Brain Mapp*. 2017 Jun 28. doi: 10.1002/hbm.23701. [Epub ahead of print] PubMed PMID:28660667.

E-mail contact: mcbranco@fmed.uc.pt

380/14 - "Using neural stimulation to modulate paranormal beliefs"

Investigadores/*Researchers*: Miguel Farias, Ute Kreplin
Instituição/*Institution*: Centre for Research in Psychology, Behaviour and Achievement, Coventry University (UK)
Duração/*Duration*: 2015/12 – 2017/10

Background: What drives our beliefs in gods and the paranormal? The cognitive psychological literature advocates a direct link between intuitive thinking and belief in gods, by explaining that such beliefs are innate, pre-conscious, or an intuitive form of information processing. They thus suggest that paranormal and supernatural beliefs are underpinned by a weak analytical thinking style and by a strong intuitive thinking style.

Aims: To develop new experimental manipulations to causally test the role of cognitive inhibition and intuitive/analytical thinking in the modulation of paranormal and supernatural beliefs.

Method: We used a brain stimulation technique and developed a training programme to manipulate cognitive inhibition and intuitive/analytical thinking. Study 1 tested the role of cognitive inhibition in modulating paranormal beliefs. We used transcranial direct current stimulation over the right Inferior Frontal Gyrus with anodal and sham stimulation in two separate sessions. In study 2 we developed a two-week long training programme with the aim of increasing either intuitive or analytical thinking in two separate groups.

Results: For study 1, we were able to successfully increase cognitive inhibition but found no relationship between intuitive/analytical thinking and paranormal beliefs. In study 2, we found that although the training had an effect on cognitive styles, neither group experienced changes in their paranormal beliefs.

Conclusions: After experimentally manipulating cognitive inhibition, via brain stimulation, and intuitive/analytical thinking using a two-week training programme, we found no relationship between these cognitive processes and paranormal or supernatural beliefs. Supernatural and paranormal beliefs may be rooted in society and culture, rather than in some primitive gut intuition.

Keywords: Paranormal beliefs, Brain stimulation, Intuitive/analytical thinking, Cognitive inhibition

Publications:

Farias, M., van Mulukom, V., et al (under review). Cognition and Religion: Evidence Against the Supernatural Intuitive Belief Hypothesis. *Nature Scientific Reports*.

van Mulukom, V., Maraldi, E. Jong, J., & Farias, M. (under review). Does cognitive style training impact supernatural beliefs? A causal test of the Intuitive Belief hypothesis. *Psychology of Religion and Spirituality*.

E-mail contact: miguel.farias@coventry.ac.uk

385/14 - "Affective and cognitive modulation of pain by using real-time fMRI neurofeedback"

Investigadores/*Researchers*: Pedro Jose Montoya Jimenez, Beatriz Rey Solaz, Inmaculada Riquelme, Miguel Angel Munoz Garcia, Niels Birbaumer
Instituição/*Institution*: Research Institute on Health Sciences, University of Balearic Islands, Palma (Spain)
Duração estimada/*Estimated duration*: 2015/03 – 2018/04

Background: Humans can be trained to gain voluntary control of brain activity with high specificity by operant training using neurofeedback. It has been also demonstrated that individuals are able to induce significant and relevant behavioral changes in perception, movement, emotion, and cognition.

Aims: We focus on individuals' ability to control brain responses in order to alleviate pain. In particular, we hypothesize that chronic pain patients will be able to learn the self-regulation of brain activity (functional connectivity and power of the sensoriomotor EEG rhythm) with a neurofeedback training and, consequently, to reduce pain perception.

Method: We carried two different studies for testing our hypothesis. In the **first study**, we have trained 15 patients with chronic pain to regulate the somatosensoy EEG rhythm. In addition, activation and fucntional connectivty data obtained from fMRI were analyzed before and after five EEG training sessions (power modulation within 10-23 Hz over the centro-parietal electrode locations). Subjects were instructed to self-regulate brain activity in order to move a ball to the left or the right of a computer screen. In the **second study**, 4 chronic pain patients were trained to regulate the functional connectivity between ACC and insula. Two neurofeedback training sessions were performed to self-regulate functional connectivity. Subjects were instructed to imagine their pain experience during the presentation of a discriminative stimulus, followed by the imagery of a pleasant experience during the presentation of a second discriminative stimulus. Subjects were also asked to rate pain experience after each trial. During the neurofeedback learning task, successful trials were followed by a monetary reward.

Results: Data from the first study revealed that subjects were able to synchronize and desynchronize somatosensory EEG rhythm. These changes were followed by significant increases of functional connectivity within the somatosensory and default-mode resting-state networks. Data from the second study revealed relevant changes of brain connectivity of the pain-related network from pre- to post-training sessions. None of these neurofeedback training procedures were able to reduce pain in patients.

Conclusions: Our findings revealed that chronic pain patients are able to self-regulate several parameters of brain functioning over relevant brain regions involved in pain perception.

Keywords: Neurofeedback, Chronic pain, Functional connectivity, EEG self-regulation

E-mail contact: pedro.montoya@uib.es

386/14 - "Remote meditation support - A multimodal distant intention experiment"
Investigadores/*Researchers*: Stefan Schmidt, Han-gue Jo, Marc Wittmann, Thilo Hinterberger, Wolfgang Ambach
Instituição/*Institution*: Department of Psychosomatic Medicine, University Medical Center Freiburg (Germany); Institut für Grenzgebiete der Psychologie und Psychohygiene, Freiburg (Germany)
Duração estimada/*Estimated duration*: 2015/05 - 2018/04

Background: We assessed in our study whether one meditator can help another meditator from a distance to focus his/her attention by using the classical experimental DMILS setup from parapsychology.

Aims: We performed a distant intention experiment with a behavioral and a physiological variable. Our aim was to find a more pronounced distant intention effect by a specific selection procedure for participants. Thus, participants were selected and paired according to their performance in a simple psi experiment (ball test). All participants had at least two years of meditation experience.

Methods: We invited participants with meditation expertise for a simple psi test (ball drawing experiment). Next participants were grouped in pairs according to their hit rate and were invited for a distant intention experiment. One participant functioned as helpee and the other as helper. The helpee had the task to focus his/her attention to a candle and to indicate lapses of attention by a button press, simultaneously EDA was measured. The helper was in a different room. During helping epochs the helper also focused on a candle and tried to connect with the helpee. During control epochs the helper read a text not related to the experiment. There were 4 helping and 4 control epochs lasting 3 min each that were in a randomized order. Dependent variables were number of button presses and EDA activity.

Result: $N = 38$ participants performed 30 sessions, with 22 participants contributing to two sessions and 16 to only one. In one session EDA measurement failed. We found no significant differences for skin conductance level (confirmatory hypothesis, $N = 29$, $T = 1.295$, $df = 28$, $p = .21$) or number of non-specific skin conductance responses (exploratory, $N = 29$, $T = 0.52$, $df = 28$, $p = .61$). The number of button presses was not normally distributed and a non-parametric Wilcoxon test was used. No significant remote helping effect could be found ($N = 30$, $z = 0.41$, $p = .97$).

Conclusions: We found no distant intention effect in our study. Selecting and pairing participants as well as meditation experience did not result in finding a psi effect.

Keywords: Distant intention, Meditation, EDA, Remote helping

E-mail contact: stefan.schmidt@uniklinik-freiburg.de

388/14 - "Are free will and moral responsibility real or illusory? On the causal role of consciousness in decision-making, a combined EEG and intracranial study" - only abstract available
Investigador/*Researcher*: Uri M. Maoz
Instituição/*Institution*: California Institute of Technology – Caltech, Pasadena (USA)
Duração estimada/*Estimated duration*: 2016/02 - 2018/04

Background: The onset of the readiness potential (RP) - a key neural correlate of upcoming action - was repeatedly found to precede subjects' reports of having made an internal decision. This has been taken by some as evidence against a causal role for consciousness in human decision-making and thus as a denial of free-will. Yet those studies focused on purposeless, unreasoned, arbitrary decisions, bereft of consequences. It remains unknown to what degree these specific neural precursors of action generalize to deliberate decisions, which are more ecological and relevant to real life, and certainly pertain more to the realm of moral responsibility.

Aims: We aimed to test whether arbitrary and deliberate decision-making share the same neural mechanisms. In particular, we wanted to test whether the RP is similar between arbitrary and deliberate decisions.

Method: We directly compared the neural correlates of deliberate and arbitrary decision-making during a $1000-donation task to non-profit organizations using EEG.

Results: While we found the expected RPs for arbitrary decisions, they were strikingly absent for deliberate ones.

Conclusions: Our results are congruent with the RP representing the accumulation of noisy, random fluctuations, which drive arbitrary - but not deliberate - decisions. The absence of RPs in deliberate decisions challenges the generalizability of studies that argue for no causal role for consciousness in decision making from arbitrary to deliberate, real-life decisions.

Keywords: Volition, Decision-making, EEG, Deliberate decisions, Arbitrary decisions

Publications:
The study is currently under review. It has been published in bioRxiv (a preprint server).

E-mail contact: maoz@chapman.edu; urim@caltech.edu

400/14 - "Is the matrix-experiment really a robust and artifact free experimental model to demonstrate generalized entanglement effects?"

Investigador/*Researcher*: Harald Walach
Instituição/*Institution*: Institute of Transcultural Health Studies, European University Viadrina, Frankfurt Oder (Germany)
Duração estimada/*Estimated duration*: 2016/01 - 2018/06

Background: Parapsychology is beset with a replication problem. The matrix-experiment, first developed by Walter von Lucadou and replicated by him successfully several times (1-9), has been replicated by our group successfully as well (10). In order to establish a replicable experimental system a consensus protocol by an international group of experts was to be developed.

Aims: To establish a replicable experimental protocol on a consensus basis and pilot this experiment.

Method: First, an expert symposium was convened and an extensive round of Delphi-consultations was started. The protocol was then used by two groups to conduct new experiments. In essence, the experiment follows the logic of a micro-PK experiment, where participants try to intentionally influence a display driven by a random number generator. But in contrast to classical PK experiments, the experimental target is not a deviation from randomness. Instead, a large matrix with 2025 cells is being constructed of correlations between 45 physical variables and 45 psychological variables derived from the experiment. The number of significant correlations is predicted to be larger than expected by chance and larger than found in a control matrix.

Results: The old protocol was refined and important innovations were carried out that were also retrospectively applied to the previous study:

a) A new analysis method for the data was developed and implemented by TH: A randomization test with 10.000 iterations was run against the experimental matrix and the true p-value was decided by such a test. The p-value for the result of the permutation test was $p < 0.03$ or lower.
b) The consortium arrived at a new protocol with a few ideas, the most important of which is to use a different type of REG and a different type of analysis.
c) Using this new protocol and these ideas, two new experiments are being conducted that will be reported.

Conclusions: The original data are robust against a much more conservative analytical method. A consensus protocol has been established and an international group of researchers has been assembled that are ready to do their own experiments. First pilot experiments have been conducted.

Keywords: Parapsychology, PK, Matrix experiment, Randomization test, Delphi method, Consensus protocol

References:

1. Lucadou, W. v. (1986). *Experimentelle Untersuchungen zur Beeinflußbarkeit von stochastischen quantenphysikalischen Systemen durch den Beobachter*. Frankfurt: Haag + Herchen.
2. Lucadou, W. v. (1987a). A multivariate PK experiment. Part I. An approach combining physical and psychological conditions of the PK process. *European Journal of Parapsychology, 6*(4), 305-345.
3. Lucadou, W. v. (1987b). A multivariate PK experiment. Part III. Is PK a real force? The results and their interpretation. *European Journal of Parapsychology, 6*(4), 369-428.
4. Lucadou, W. v. (1991). *Locating Psi-bursts - correlations between psychological characteristics of observers and observed quantum physical fluctuations*. Paper presented at the The Parapsychological Association 34th Annual Convention, Proceedings of Presented Papers.
5. Lucadou, W. v. (2000). *Backward causation and the Hausdorff-Dimension of singular events.* Paper presented at the Proceedings of Presented Papers, The Parapsychological Association 43rd Annual Convention August 17-20, Freiburg.
6. 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.
7. Lucadou, W. v. (2015, July 16-19, 2015a). *The correlation-matrix method (CMM) - a new light upon the repeatability problem of parapsychology.* Paper presented at the 58th Annual Convention of the Parapsychological Association, University of Greenwich.
8. Lucadou, W. v. (2015b). The Model of Pragmatic Information (MPI). In E. C. May & S. Marwaha (Eds.), *Extrasensory Perception: Support, Skepticism, and Science: Vol. 2: Theories and the Future of the Field* (pp. 221-242). Santa Barbara, Ca: Praeger

9. Lucadou, W. v., Lay, B., & Kunzmann, H. (1987). A multivariate PK experiment. Part II. Relationships between psychological variables. *European Journal of Parapsychology, 6*(4), 347-368.
10. Walach, H., Horan, M., Hinterberger, T., & von Ludacou, W. (submitted). Evidence for a generalised type of nonlocal correlations between human behaviour and random event generators. *PLos One*.

E-mail contact: hwalac@gmail.com

402/14 - "Skin Conductance Feedback Meditation (SCFM) – Exploring the role of skin conductance in meditative practice"

Investigador/*Researcher*: Thilo Hinterberger
Instituição/*Institution*: Department of Psychosomatic Medicine, Clinic of the University of Regensburg (Germany)
Duração estimada/*Estimated duration*: 2016/03 - 2018/04

Background: Mindfulness meditation with attention to the own breathing can be regarded as a mixture of open monitoring and focused attention. The focus should help meditators maintaining a state of mindful presence. A form of pure open monitoring however should not have such a focus of attention. In order to bring meditators back to the state of presence in open monitoring an externally triggered reminder would be helpful.

Aims: Measures of skin conductance (SC) are supposed to be related to mental distractions with emotional content. Thus, feedback of SC could serve as such a reminder to return to the state of presence. We tried to measure and feedback SC in real-time during meditation sessions and evaluated physiological and psychological measures of such a novel approach for training meditation.

Method: Thirty participants, 15 of them were meditators with ongoing practice and 15 non-meditators, attended six sessions of meditation in three days. Four sessions were conducted as SC feedback meditation (SCFM) sessions and two sessions as ordinary mindfulness meditations. Each was evaluated with a feedback questionnaire and measures of skin conductance, heart rate variability, respiration and EEG which were recorded during meditation. Feedback items were assessing subjective changes in body sensation, emotional condition, and mental state.

Results: The 14 feedback items could be merged into the dimensions expansiveness and contentedness. At average, 68.3% of the participants felt more expanded and over 80% were more contented after SCFM sessions while only 3.3% felt more limited and discontented after the sessions. This result was not significantly different from the changes after ordinary mindfulness meditation. SCFM sessions were tested to be non-inferior to mindfulness meditations. Twenty participants were using a button to indicate SC reactions correlating with distracting thoughts. 52% of the button presses followed preceding SC reactions. There were no significant differences in the number of SC reactions between meditators and non-meditators and also not between ordinary mindfulness and SCFM.

Conclusions: Despite finding only few significant differences in psychological and physiological measures between mindfulness meditation and SCFM, both methods seem to be comparably good in their effects on meditators with the advantage of SCFM that no focus of attention is suggested in the meditation.

Keywords: Meditation, Skin conductance, Biofeedback, Mindfulness

Publications:

Thilo Hinterberger, Felicitas Baierlein and Natalie Breitenbach (in preparation). Skin Conductance Feedback Meditation (SCFM): Evaluating a Method for Meditation in a State of Open Monitoring"

E-mail contact: Thilo.Hinterberger@ukr.de

413/14 - "The role of dopamine in behavioral exploration and action selection"
Investigador/*Researcher*: Aaron Christopher Koralek
Instituição/*Institution*: Champalimaud Neuroscience Programme, Lisboa (Portugal)
Duração estimada/*Estimated duration*: 2015/03 – 2018/04

Background: We are constantly faced with the trade-off between exploiting past actions with known outcomes and exploring novel actions whose outcomes may be better. When environmental rewards are stable, it is preferable to perform actions known to be rewarding. However, when environmental rewards are changeable, it is adaptive to explore alternative actions and revisit previous actions whose value may have changed. This exploration-exploitation balance is thought to be strongly influenced by dopaminergic neurons of the substantia nigra pars compacta (SNc) and noradrenergic neurons of the locus coeruleus (LC). However, little is known about the ways that environmental changes impact action selection, and even less is known about SNc and LC network dynamics during exploration.

Aims: We aimed to investigate variability in action selection in response to stable and unstable environments, as well as to characterize dopaminergic and noradrenergic signaling during these distinct behavioral states.

Method: We developed a novel behavioral paradigm in mice to investigate how changes in environmental stability affect behavioral variability. Mice were placed in environments with three equidistant nose poke ports and had to explore the environment to discover which sequence of three nose pokes was rewarded. When mice began to exploit the rewarded sequence and reached a performance criterion, the rewarded sequence was changed. We then performed calcium imaging in either the SNc or LC of freely behaving mice during performance of this task, which allowed us to simultaneously record activity in large populations of genetically-identified neurons when mice were in exploratory or exploitative states.

Results: Actions were variable as mice explored to find the rewarded sequence, but became stable as they learned to exploit the rewarded sequence. When the rewarded sequence was changed, mice returned to a relatively more variable state. Dopaminergic networks expressed higher levels of sustained activity when mice were exploiting relative to exploring, and these differences could not be accounted for by low-level differences in reward occurrence. Conversely, noradrenergic networks exhibited higher levels of sustained activity when mice were exploring relative to exploiting. In addition, dopaminergic networks exhibited different correlation structures during exploitation and exploration, while noradrenergic networks exhibited a more stable network structure.

Conclusions: These experiments support a role for dopaminergic and noradrenergic networks in behavioral exploration. In particular, our data suggest that exploitation is associated with higher sustained levels of dopaminergic activity and lower sustained levels or noradrenergic activity, with potentially important consequences for downstream circuits.

Keywords: Dopamine, Exploration, Action selection, Basal ganglia

E-mail contact: aaron.koralek@neuro.fchamplimaud.org

480/14 - "The role of experimenter and participant mindset in the replication of psi experiments: Phase II of a global initiative"

Investigador/*Researcher*: Marilyn Schlitz
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA)
Duração/*Duration*: 2015/07 - 2017/07

Background: This study addressed the replication problem in parapsychology through the examination of experimenter and participant belief in psi and their impact on the outcome of a psi task.

Aims: This experiment involves a modified version of the previous attempt where we are influencing expectancies of experimenters and subjects. In this experiment, after showing either randomized pro or anti-psi statements (for participants) and videos (for experimenters), we are assessing the experimenters' and/or participants' expectation using questionnaires.

Method: This study made use of a standardized psi protocol developed by Daryl Bem that has been the focus of several recent replication attempts and that allows for a systematic collection of data under well-controlled conditions. The study required no instrumentation beyond a desktop computer, thirty minutes per session, and requiring statistical analyses no more complex than a t-test across sessions or participants. Specifically, the replication protocol tested the retroactive priming aspect of experiment 4 of Bem, 2011) by examining reaction time for congruent or incongruent pairing of words and pictures.

Results & Conclusions: The results of the psi task are the dependent measure for both the psi replication attempts and for the experimenters' and subjects' expectancy effects. We have completed data collection and will present our results at the BIAL conference.

Keywords: Priming, Expectancy effect, Experimenter effect, Retrocausation

E-mail contact: mjmschlitz@gmail.com

489/14 - "An examination of the effects of mood and emotion on a real-world computer system and networking environment"
Investigador/*Researcher*: John G. Kruth
Instituição/*Institution*: Rhine Research Center, Durham (USA)
Duração estimada/*Estimated duration*: 2015/05 - 2018/04

Background: Radin (1990) found unusual effects on a RNG embedded in a computer system. A study by the author (2015) revealed unconscious PK effects on computers and electronics was reduced using relaxation techniques.

Aims: This study explores whether the mood and emotion of a computer operator can produce errors in a network simulating a real-world working environment.

Method: 130 participants completed normal computer tasks while a separate network system was continuously monitored for errors. Experimental and control groups completed the same tasks, but the experimental group was obstructed with inoperative software designed to induce anxiety. Rewards were used to motivate participants to complete the timed tasks quickly. Participants self-rated anxiety levels.
Custom network software logged errors and avoided automatic error correction. Participants were not aware of the network and did not interact with it, but those with higher anxiety were expected to unconsciously produce more errors in the network.
Sessions were also run when no user was present. There were three categories of data: sessions with high anxiety, lower anxiety, and no users. Errors were collected from the network for each group.

Results & Conclusion: Participants who reported higher anxiety during their session produced more errors than those who reported less anxiety ($p<.038$; Effect size: $d=0.45$; power: .61). Sessions run with participants did not produce more errors than random sessions without participants ($p=0.353$).
Real-world computer networking environments and other electronics may be affected by the mood of high anxiety workers. This should be considered when designing a work environment and providing technical support to computer users.

Keywords: Psychokinesis, Technology, Emotion, Computer, Network

E-mail contact: john.kruth@rhine.org

495/14 - "Episodic memory enhancement in aging: The role of cognitive training combined with (bilateral) tDCS in the medial-temporal cortex and cerebellum on episodic memory performance in the elderly"

Investigadores/*Researchers*: Mário Manuel Rodrigues Simões, Filipe Fernandes, Jorge Evandro de Araújo Alves, Marcel Simis, Ana Rita Simões Martins, Jorge Almeida
Instituição/*Institution*: CINEICC - Centro de Investigação do Núcleo de Estudos e Intervenção Cognitivo-Comportamental/Universidade de Coimbra (Portugal)
Duração estimada/*Estimated duration*: 2015/07 - 2018/04

Background: In recent years, numerous strategies have been developed in an attempt to maintain or enhance cognitive functions in the elderly. Cognitive training (CT) has been widely implemented and it is currently accepted as the most promising method to alleviate cognitive decline. Several techniques have been combined with CT to explore the synergetic effects and, recently, a beneficial effect has been shown after the combination with transcranial direct current stimulation (tDCS).

Aims: Here we combined multiple sessions CT with tDCS to assess verbal episodic memory improvement in healthy elderly subjects, compared with sham and a wait list group.

Method: We used an innovative design to further explore the synergetic effects of CT combined with tDCS. Specifically, we tested whether CT and excitatory tDCS over the left dorsolateral prefrontal cortex (lDLPFC) or right cerebellar cortex (rCC) facilitates verbal episodic memory, compared with sham stimulation and a wait list control group. CT was applied daily for 1 hour, after 20 minutes of tDCS, over 12 sessions. Performance on memory and other cognitive tasks was evaluated at baseline and post-intervention, using behavioral and neuroimaging tools. Participants were healthy elderly, ≥ 60 years, right handed, without history of neuropsychiatric disease.

Results: 53 healthy elderly completed the study (mean age=68.4, *SD*=4.8) (ongoing recruitment). Participants received either CT and sham (*n*=13) or excitatory tDCS over the lDLPFC (*n*=14) or rCC (*n*=14), or a wait list control group (*n*=12). Data suggest an improvement in verbal episodic memory tasks in the groups receiving CT + tDCS. Interestingly, there is a greater improvement and consistency in the group receiving CT + tDCS in the rCC. Neuroimaging data supports the results from the neuropsychological assessment. Specifically, tDCS over the right cerebellum + CT increased the functional connectivity in the left hippocampus.

Conclusions: These data suggest that CT and neuromodulation hold promise as a means to enhance cognitive functions in healthy elderly. Greater light is also shed on the role of the cerebellar cortex in cognitive processing.

Keywords: Aging, Cognitive enhancement, tDCS, fMRI, Cerebellum

Publications:

Amaral, L., Martins, A. R., Alves, J., Fernandes, F., Fregni, F., Simis, S., Almeida, J., Simões, M. R. (2017). Memory enhancement in aging - the role of cognitive training combined with tDCS: preliminary results (Conference Abstract). *Brain Stimulation*, *10*, 346-540, 2017.

E-mail contact: simoesmr@fpce.uc.pt

506/14 - "The Selfield: Optimizing precognition research"
Investigadores/*Researchers*: Mario Varvoglis, Peter Bancel
Instituição/*Institution*: Institut Metapsychique International, Paris (France); Institute of Noetic Sciences, Petaluma, California (USA)
Duração estimada/*Estimated duration*: 2015/09 - 2018/04

Background: The Selfield is part of an ongoing effort to design protocols that are both efficient in terms of data-collection and apt to produce positive psi-scoring with unselected participants. As in our previous Bial project (190/10) we combined optimization procedures (typical of free-response studies like the Ganzfeld) with a forced-choice protocol involving multiple trials per session; the focus in this experiment was precognition.

Aims:
1. Assess whether the use of attention-focusing procedures would enhance participants' scoring in a forced-choice precognition task.
2. Assess whether trial-by-trial feedback improves scoring over no-feedback conditions.

Method: A preset total of 3000 binary choice trials were collected over a 7-week period, from 82 participants, including 26 meditation practitioners recruited from a Tibetan Buddhism center. Each participant contributed 20 or 40 binary-choice trials, whereby they had to guess the presence or absence of a hidden picture. The psi task took place in a specially constructed immersive environment, and consisted of selecting graphical spheres that emerged out of a hypnotic animated starfield and that they felt would contain an image. Following their choice, the program would randomly determine whether or not that sphere indeed contained an image, and whether or not feedback would be shown. A hit resulted in the emergence of a face (selected from a pool of possibilities) that stared directly at the participant; for misses the sphere withdrew back into the starfield, and for no-feedback trials it simply faded out with no hit-miss information.

Results: Overall results were nonsignificant. Secondary analyses showed quite encouraging trends that, if replicated in further studies, may reveal something about psi-conducive cognitive factors.
1. When examined across all 150 20-trial series, results show a significant incline in scoring ($p=.04$, two-tailed) over the course of the series, suggesting that participants may have progressively found a mental strategy that produced better scoring.
2. While not attaining significance ($p=.12$, two-tailed), scoring in feedback trials was superior to no-feedback trials; this suggests that feedback can be useful for learning if it avoids inducing a stressful, performance-oriented mindset.
3. The 26 meditators' scores were suggestively high ($p=.09$, 1-tailed), while the 14 most experienced amongst them (generally those with 10 or more years meditation experience), showed a significant effect ($p=.012$, 1-tailed).

Conclusions: Our findings contribute to the literature suggesting that sustained meditation practice may favor experimental psi results. They also suggest that, people's psi scoring may improve under the right feedback conditions. We hope to share our software with other laboratories to further explore these promising directions.

Keywords: Precognition, Forced choice, Optimization, Meditators

Publications:
Book of Abstracts, 60th Annual P.A. Convention, July 20-23, 2017, Athens.

E-mail contact: contact@mario-varvoglis.com

534/14 - "Exploring unconscious knowledge: Individual differences in ideomotor response" - only abstract available
Investigadores/*Researchers*: Jeremy Olson, Amir Raz, Mathieu Landry
Instituição/I*nstitution*: Raz Cognitive Neuroscience Lab, McGill University, Montreal (Canada); Montreal Neurological Institute (Canada)
Duração/Duration: 2015/08 - 2017/06

Background: For centuries, people have asked questions to hand-held pendulums and interpreted their movements as responses from the divine. These movements occur due to the ideomotor effect, wherein priming or thinking of a motion causes muscle movements that end up swinging the pendulum.

Aims: We investigated whether such pendulums can aid decision-making and which personality traits correlate with this performance.

Study 1: Method - Participants (N=80) completed a visual detection task in which they searched for a target letter among rapidly presented characters. In the verbal condition, participants stated whether they saw the target in each trial. In the pendulum condition, participants instead mentally "asked" a hand-held pendulum whether the target was present; particular motions signified *yes* and *no*. We measured the accuracy of their responses and several personality measures. **Results -** Locus of control (feelings of control over one's life) predicted verbal performance and transliminality (sensitivity to subtle stimuli), predicted pendulum performance. Accuracy was low in both conditions, but signal detection theory's bias was higher in the verbal condition (d=1.10).

Study 2: Method - We next explored how these findings apply to memories. Participants (N=91) answered questions about 18 short videos of mundane scenes. We tested similar personality measures across verbal and pendulum tasks. **Results -** Transliminality again predicted performance only in the pendulum task. Unlike the previous study, however, there was a *negative* correlation between transliminality and sensitivity (r=-0.25, p=.026). Further, sense of agency over the pendulum movement weakly predicted performance (r=0.04, p=.005).

Conclusions: Our findings suggest that people have different decision strategies when using a pendulum compared to conscious guessing. These findings may help explain why some people can answer questions more accurately with pendulums and Ouija boards. Identifying the differences between ideomotor and verbal responses could lead to practical ways to improve decision-making.

Keywords: Ideomotor action, Agency, Implicit cognition

Publication:
Olson, J. A., Jeyanesan, E., & Raz, A. (2017). Ask the pendulum: Personality predictors of ideomotor performance. *Neuroscience of Consciousness*, *3*(1), 1–11.

E-mail contact: jay.olson@mail.mcgill.ca

"The Aging Social Brain - Neural and behavioral age-related changes in social cognition and decision-making"

Investigadores/*Researchers*: João Eduardo Marques Teixeira, Manuel Fernando Santos Barbosa, Fernando Ricardo Ferreira Santos, Pedro Manuel Rocha Almeida, Hugo Daniel Leão Sousa
Instituição/*Institution*: Faculdade de Psicologia e de Ciências da Educação, Universidade do Porto (Portugal)
Duração/*Duration*: 2014/11 – 2018/01

Background: Social cognition comprises four main components: emotional recognition; theory of mind (ToM); moral judgment; and economic decision-making. Age-related changes on these components and their neurophysiological correlates are scarcely studied.

Aims: This study aims to analyze age-related changes in behavioral and neurophysiological correlates of social cognition, and the role of cognitive functioning in these changes.

Method: A sample of 30 younger (YA; *M*age=26.6, *SD*=4.05), 30 middle-aged (MA; *M*age=48.4, *SD*=5.50) and 29 older adults (OA; *M*age=64.5, *SD*=4.10) performed a set of experimental tasks targeting each social cognition components, during an EEG recording.

Results/Conclusions: Regarding emotional recognition, OA had higher N170, despite similar behavioral performances in all groups. In the ToM task, participants decided if facial expressions were congruent or incongruent with previous scenarios portraying neutral and emotional scenes. YA and MA outperformed OA, but executive functions (EF) were the main predictor of better performance. YA and MA showed higher late positive potentials (LPP) in congruent than incongruent conditions, while OA had similar amplitudes in both. This may affect OA's ability to use others' facial expressions to understand their inner states. OA were also less accurate than YA in identifying intentionality in moral transgressions, which is consistent with the N2 attenuation during the perception of accidental/intentional harm, as this component is considered a correlate of empathy for physical harm. In social economic decision-making, assessed by the Ultimatum Game, OA had the best economic strategy, accepting more unfair offers than YA and MA. As the Medial Frontal Negativity amplitude did not differ between groups, behavioral responses may be explained by different economic/social preferences, rather than different unfairness sensitivity. When making decisions under risk, OA were less risk-averse than YA. YA had higher Feedback Related Negativity for favorable than for unfavorable outcomes, while MA and OA had similar amplitudes in both. Similarly, the P3 amplitude of OA did not differ between gains and non-gains, and was correlated with poorer memory and EF performance. Our results suggest that aging is accompanied by a decline in the ability to adjust economic decisions according to feedback, which may underlie OA's preference for risk-taking.

Keywords: Aging, Social cognition, Moral judgment, Decision-making, ERPs

Publications:

Journal Articles:

Fernandes, C. (2017). Age-Related Changes in Frontal, Striatal, and Medial Temporal Activity during Expected Value Evaluation. *Journal of Neuroscience, 37*, 3442-3444. doi:10.1523/JNEUROSCI.0033-17.2017.

Pasion, R., Gonçalves, A. R., Fernandes, C., Ferreira-Santos, F., Barbosa, F. & Marques-Teixeira, J. (2017). Meta-analytic evidence for a reversal learning effect on the Iowa Gambling Task in older adults. *Frontiers in Psychology*, 1-16. doi: 10.3389/fpsyg.2017.01785.

Manuscripts under review:

Fernandes, C., Gonçalves, A., Pasion, R., Ferreira-Santos, F., Melo e Castro, J., Paiva, T. O., Barbosa, F., Barbosa, F. & Marques-Teixeira, J. (2017). European Portuguese adaptation and validation of dilemmas used to assess moral decision-making (under review at *Trends in Psychiatry and Psychotherapy*).

Fernandes, C., Gonçalves, A., Pasion, R., Ferreira-Santos, F., Barbosa, F., Martins, I. P. & Marques-Teixeira, J. (2017). Age-related changes in social decision-making: An electrophysiological analysis of unfairness evaluation in the Ultimatum Game (under review at *Biological Psychology*).

Pasion, R., Fernandes, C., Gonçalves, A., Ferreira-Santos, F., Barbosa, F. & Marques-Teixeira, J. (2017). Aging effect on the intentionality misperception: an ERP study (under review at Social Neuroscience).

Fernandes, C., Pasion, R., Gonçalves, A. R., Ferreira-Santos, F., Barbosa, F., Martins, I. P. & Marques-Teixeira, J. (2017). Age differences in neural correlates of feedback processing after economic decisions under risk (under review at *Neurobiology of Aging*).

Conference activity:

Fernandes, C., Gonçalves, A. R., Ferreira-Santos, F., Barbosa, F. & Marques-Teixeira, J. (2015, July). *The aging brain and social cognition: a systematic review*. Poster presented at the 1st International Congress of Psychobiology, Oviedo, Spain.

Fernandes, C., Gonçalves, A. R., Ferreira-Santos, F., Sousa, H., Barbosa, F. & Marques-Teixeira, J. (2016, March). *Neural and behavioral age-related changes in social cognition: a systematic review*. Abstract presented at the 11th Symposium of The Bial Foundation Behind And Beyond The Brain, Porto, Portugal.

Fernandes, C., Gonçalves, A., Ferreira-Santos, F., Barbosa, F., Martins, I. P. & Marques-Teixeira, J. (2016, April). *The aging brain and social and economic decision-making: a systematic review*. Poster presented at the Social & Affective Neuroscience Society Annual Meeting 2016, New York, USA.

Fernandes, C., Gonçalves, A., Ferreira-Santos, F., Barbosa, F., Martins, I. P. & Marques-Teixeira, J. (2016, June). *The aging brain and social and economic decision-making: a systematic review*. Comunicação apresentada na 30ª Reunião do Grupo de Estudos de Envelhecimento Cerebral e Demência, Lisboa, Portugal.

Fernandes, C., Gonçalves, A., Ferreira-Santos, F., Melo e Castro, J., Paiva, T. O., Barbosa, F., Barbosa, F. & Marques-Teixeira, J. (2016, June). *Stimuli in moral judgment and theory of mind tasks: a validation study for the Portuguese population*. Poster presented at the 3rd International Conference of the European Society for Cognitive and Affective Neuroscience, Porto, Portugal.

Fernandes, C., Gonçalves, A., Pasion, R., Ferreira-Santos, F., Barbosa, F., Martins, I. P. & Marques-Teixeira, J. (2017). *Outcome processing in the context of gains versus losses: the influence of feedback valence in Feedback-P3* (poster to present at the congress of Society for Psychophysiological Research, Viena).

Fernandes, C., Pasion, R., Gonçalves, A., Ferreira-Santos, F., Barbosa, F., Martins, I. P. & Marques-Teixeira, J. (2017). *Neurocognitive characterization of healthy aging* (Oral comunication to presente at X Congreso Internacional Y XV Nacional de Psicologia Clínica, Espanha)

E-mail contact: carinafernandes@fpce.up.pt

"Aware Mind-Brain: Bridging insights on the mechanisms and neural substrates of human awareness and meditation"

Investigadores/*Researchers*: Antonino Raffone, Salvatore Maria Aglioti, Henk P. Barendregt, Fabio M. Giommi, Juliana Jordanova, Peter Malinowski, Stephen Whitmarsh
Instituição/*Institution*: ECONA - Interuniversity Center for Cognitive Processing in Natural and Artificial Systems, Università degli Studi di Roma "La Sapienza" (Italy)
Duração estimada/*Estimated duration*: 2015/11 - 2018/04

Background: Understanding consciousness and its neural substrates is one of the greatest scientific challenges of our time. Consciousness research crucially involves subjective (or first-person) reports. However, in most consciousness studies related to perception and emotion participants are not trained in attention and introspective awareness.

Aims: The *Aware Mind-Brain* project bridges research on the mechanisms of visual and emotional awareness with research on meditation, with a particular involvement of long-term ('virtuoso') mindfulness or insight meditators, i.e. Theravada Buddhist monks. The project has also included theoretical and modelling investigations about the mechanisms of consciousness and meditation as well as investigations of neurocognitive and neurocognitive effects of intensive insight meditation retreats and mindfulness programmes enhancing attention and emotion regulation.

Method: In this report we focus on five experiments with Theravada Buddhist monks and a control group in which we have used electroencephalographic (EEG), magnetoencephalographic (MEG) and functional Magnetic Resonance Imaging (fMRI) methods the neural correlates (bases) of different forms of meditation (Focused Attention Meditation; Open Monitoring Meditation; Loving Kindness Meditation), also contrasted with a non-meditative Rest condition. These forms of meditation involve different attentional, awareness and emotional processes. In three of the experiments (using EEG, MEG and fMRI) we have investigated the neural correlates of the forms of meditation and the effects of meditation expertise on brain activity patterns. In the last two (EEG) experiments we have investigated dimensions of phenomenological (subjective) experience associated to pain and visual emotional stimuli, and their modulation by different forms of meditation and meditation expertise.

Results: Taken together the findings in these experiments show that the investigated forms of meditation involve differential brain activity patterns in terms of oscillatory frequencies, coherence patterns and brain networks, with a deep modulation of these patterns in the Buddhist monks. Furthermore, dimensions of phenomenological experience associated to pain and emotional stimuli as well as their electrophysiological correlates are modulated by different forms of meditation as well as by meditation expertise.

Conclusions: The findings in our investigations have relevant implications for an enhanced understanding of the consciousness processes and the brain mechanisms implicated in meditation and mindfulness. They also lead to an increased understanding about how long-term mental training based on meditation leads to functional neuroplasticity associated to enhanced regulation of pain and emotion.

Keywords: Consciousness, Meditation, Pain, Emotion, Brain networks

Publications:

Raffone, A., & Srinivasan, N. (2017). Mindfulness and cognitive functions: Toward a unifying neurocognitive framework. *Mindfulness*, *8*, 1-9.

Simione, A., Akyurek, E.G., Vastola, V., Raffone, A., & Bowman, H. (2017). Illusions of integration are subjectively impenetrable: Phenomenological experience of Lag 1 percepts during dual-target RSVP. *Consciousness and Cognition*, *51*:181-192. Available at: http://doi.org/10.1016/j.concog.2017.03.004.

Giannandrea, A., Simione L., Pescatori, B., Olivetti Belardinelli, M., Hickman, S. & Raffone, A. (submitted).

Raffone A., et al. (in preparation). A magnetoencephalographic investigation of brain networks in different forms of meditation in long-term meditators.

Guidotti, R., et al. (in preparation). Prediction of meditation experience using fMRI functional connectivity and multivariate pattern analysis.

Mauro, F. et al. (in preparation). Bridging subjective experiences and event-related potentials in response to visual emotional stimuli in long-term meditators.

Nicolardi, V. et al. (in preparation). Pain experiences and their electrophysiological correlates in different forms of meditation.

Jordanova, J., Kolev, V., et al. (in preparation). Electroencephalographic oscillatory and coherence patterns during different forms of meditation in long-term meditators.

E-mail contact: antonino.raffone@uniroma1.it

2016

97/16 - "Reproductive hormonal status as a predictor of precognition"
Investigadores/Researchers: Julia Mossbridge, Daryl Bem
Instituição/Institution: Institute of Noetic Sciences, Petaluma, California (USA); Department of Psychology, Cornell University, Ithaca (USA)
Duração estimada/*Estimated duration*: 2017/02 – 2018/04

Background: Certain measures of precognition are dependent on both gender and age. Here we test the hypothesis that reproductive hormone levels could be related to precognitive ability.
Aims: In four experiments, we examined how markers of reproductive hormonal status in women are related to implicit precognition. Specifically, we originally aimed to test the hypothesis that women of reproductive age will show opposing effects to those of men and women showing menopausal or post-menopausal symptoms. However, our test of menopausal symptoms was not correlated with actual menopause, as had been previously claimed by the authors of the test. Thus, to allow us to gain insight into the currently unknown physiological mechanisms correlated with precognitive effects, we instead compared five populations, differing from each other in hormonal state, performed on an implicit precognition task.

Method: Eventually we aim to correlate measured hormonal levels with precognitive performance, but as a first step we correlated performance on an online precognition task with presumed hormonal status given self-reported information on gender, date of last menstrual period, pregnancy, and the presence or absence of a uterus. Our task was a quick-thinking version of the retroactive-facilitation-of-recall experiment. We performed the experiment four times, recruiting a total of 2479 participants, the third and fourth experiments were pre-registered with the Koestler Parapsychology Registry. In addition to the principle aim, we examined the Big-5 personality traits and their relationship to performance across all participants

Results: The general trend that emerged is that precognitive effects on this task are not apparent for cycling women, men, and menopausal women, while they are more regularly apparent for pregnant women and women without uteruses who do not take replacement hormones. Although this general trend was consistent across all four experiments, it was rarely statistically significant, likely due to the limited number of participants we were able to recruit in these two relatively unusual physiological states. We found weak correlations between extraversion, agreeableness and openness and measures of implicit precognition.

Conclusions: Because both pregnancy and not having a uterus are extreme hormonal states for women, the results suggest that taking into account reproductive hormone status, at least in women, can further reduce the signal-to-noise ratio of implicit precognition experiments. These results warrant follow-up with a larger participant pool in the two targeted populations (pregnant women and women who have had hysterectomies and are not taking replacement hormones)

Keywords: precognition, presentiment, PAA, prediction, hormones

Publications:
Mossbridge, J. A. and Radin, D. A. (March 2018 [in press]) Precognition as a Form of Prospection: A Review of the Evidence in *Psychology of Consciousness Theory, Research, and Practice*
Mossbridge, J. A. and Radin, D. A. (March 2018 [in press]) Plausibility, Statistical Interpretations, Physical Mechanisms and a New Outlook: Response to commentaries on a Precognition Review in *Psychology of Consciousness Theory, Research, and Practice*

E-mail contact: jmossbridge@gmail.com

124/16 - "The missing photon experiment: Does focused attention employ matter as an agent for interacting with light?" - only abstract available
Investigador/*Researcher*: Loren Carpenter
Instituição/*Institution*: Institute of Noetic Sciences, Petaluma, California (USA)
Duração estimada/*Estimated duration*: 2017/02 – 2018/04

Background: As part of a research program studying the role of consciousness in the physical world, the Institute of Noetic Sciences (IONS) conducted two mind-photon interaction experiments in early 2016. That study showed significant but unexpected results.
A 2015 experiment designed by the PI tested whether focused attention could collapse the quantum *spin* wavefunction. The hypothesis predicted that any change in photon spin would produce an increase in light passing through a pair of two perpendicularly crossed polarizers. Unpredictably, significantly *less* light emerged from the second polarizer.
Was the light scattered or absorbed or…? This experiment will look for scattering.
Primary hypothesis: The total of camera pixels will be lower only during focused attention periods.
Secondary hypothesis: The photodetector will record scattered photons only during the same periods.

Aims: Does focused attention result in attenuation of a laser beam in an integrating sphere?
Is the attenuation of light the result of photon scattering and/or photon absorption, or neither?
Do the results of IONS' previous mind-photon interaction experiments show evidence of light attenuation?

Method: The experimental setup consists of a 10 cm hollow light-integrating sphere, 632-nanometer laser beam that passes through the center of the sphere and into a camera on the far side, a femtowatt photo detector, a vacuum port to evacuate the sphere, and a computer connected to the camera and photodetector. Scattered light will be measured by the photodetector. The camera will continuously measure the laser beam power. If scattering or absorption are detected, the air will be removed from the sphere. Participants will be asked to direct their attention toward and then away from the laser beam inside the sphere in 40 alternating 25-30 second epochs. Sound and light feedback will be given. IONS double-slit experiment data will be analyzed for detectable light attenuation effects.

Results: This experiment is currently underway and results will be available in early 2018. The PI, Loren Carpenter, is planning to present the results at the 2018 BIAL meeting in Oporto.

Conclusions: Awaiting results.

Keywords: PK, Psychokinesis, Photon, Mind-matter, Light

Publications: 2017 IONS Conference presentation

E-mail contact: lcarpenter@noetic.org

FUNDAÇÃO
Bial

À Av. da Siderurgia Nacional • 4745-457 Coronado (S. Romão e S. Mamede) • Portugal
Tel. + 351 22 986 6100 • Fax + 351 22 986 6199 • fundacao@bial.com • www.fundacaobial.com

12º Simpósio da Fundação Bial

Constituída em 1994 pelos Laboratórios BIAL, em conjunto com o Conselho de Reitores das Universidades Portuguesas, a Fundação BIAL tem como missão incentivar o conhecimento científico do Ser Humano, tanto do ponto de vista físico como espiritual.

Entre as suas atividades destaca-se a atribuição de Prémios no âmbito da investigação médica e biomédica: o **Prémio BIAL de Medicina Clínica** (nos anos pares) e o ***BIAL Award in Biomedicine*** (nos anos ímpares).

A Fundação BIAL promove também um programa bianual de **Apoios à Investigação Científica**, na forma de concursos, nas áreas da Psicofisiologia e da Parapsicologia.

Desde 1996, de dois em dois anos, organiza o **Simpósio "Aquém e Além do Cérebro"**, um espaço de debate que reúne os investigadores apoiados pela Fundação e alguns dos mais prestigiados especialistas mundiais nas áreas das Neurociências e da Parapsicologia.

O livro de atas que agora se publica é uma compilação dos textos das palestras apresentadas no 12º Simpósio "Aquém e Além do Cérebro", dedicado ao tema "Potenciar a Mente". Contém também os *abstracts* de alguns dos trabalhos de investigação financiados pela Fundação BIAL, apresentados neste encontro em sessões de posters e em comunicações orais. A versão online destes *abstracts* está disponível em www.fundacaobial.com.

Instituição sem fins lucrativos, considerada de utilidade pública pelo Governo português, a Fundação conta com os altos patrocínios do Senhor Presidente da República, do Conselho de Reitores das Universidades Portuguesas e da Ordem dos Médicos, sendo atualmente uma instituição de referência entre a comunidade científica internacional, particularmente no âmbito da investigação em Neurociências.

The BIAL Foundation was created in 1994 by Laboratórios BIAL in conjunction with the Council of Rectors of the Portuguese Universities. BIAL's Foundation mission is to foster the scientific knowledge of the human being from both the physical and spiritual perspectives.

*Among its activities, it is worth mentioning the Awards in the fields of medical and biomedical research: the **Prémio BIAL de Medicina Clínica** (in even years) and the **BIAL Award in Biomedicine** (in odd years).*

*The BIAL Foundation also promotes biannually a programme of **Grants for Scientific Research**, in the form of calls, in the areas of Psychophysiology and Parapsychology.*

*Every two years, since 1996, the Foundation organizes the **"Behind and Beyond the Brain" Symposium** - a discussion forum that brings together grant-holders and several world-renowned experts in the fields of Neuroscience and Parapsychology.*

The Proceedings that are now being published include the texts of the lectures presented during the 12th Symposium "Behind and Beyond the Brain" dedicated to the theme "Enhancing the Mind". It also includes the abstracts of some of the research projects supported by the BIAL Foundation and presented at this meeting in poster sessions and oral communications. The online version of these abstracts is available at www.fundacaobial.com.

The Foundation is a non-profit-making institution, considered as a public utility by the Portuguese Government and includes among its patrons the Portuguese President, the Council of Rectors of the Portuguese Universities and the Portuguese Medical Association. Today it is an institution of reference within the international scientific community, particularly in Neuroscience research.

FUNDAÇÃO Bial

Instituição de utilidade pública
Institution of public utility