

## The physiological role of circadian rhythms in memory

### **ABSTRACT:**

#### **Background**

Circadian disruption impacts on cognition as seen in shift-work and manipulation of sleep-wake cycles in humans and rats. However, the functional interactions between Suprachiasmatic Nucleus (SCN) and memory-related regions, such as the Hippocampus (HIPP), have never been defined.

#### **Aims**

We aimed at characterizing the structural connectivity between the SCN and the hippocampus during a circadian shift protocol in rodents.

#### **Method**

Whole-brain functional connectivity was modeled by combining  $^{14}\text{C}$ -2-deoxyglucose functional imaging and PLS Regression (Dawson et al, 2014) on male rats (13-week-old) under a normal circadian cycle or after 4 cycles of repeated phase shifts and recovery sessions (Craig et al, 2008).

#### **Results**

Upon analysis of 67 brain regions, we found alterations in the metabolic activity of SCN and the HIPP, Medial Entorhinal Cortex (MEC), Perirhinal Cortex and Dorsal Raphé (DR). We then modeled the relationship between the activity of these seed regions and the remainder regions measured. A total of 127 functional connectivity interactions were impacted by the circadian shift, particularly a hypofunction of the MEC and related projections, and a hyperconnection of the DR and associated pathways.

Moreover, the shifted animals displayed a reduced performance in the Novel Object Recognition and Pattern Separation Task, whereas the performances in the Morris Water Maze and the Y-maze were preserved.

Relevant anatomical projections were traced by resorting to transsynaptic antero- and retrograde viral vectors, between the SCN and the HIPP, that revealed the Septum as a putative hub of circadian information onto the HIPP.

#### **Conclusions**

Altogether, these connectivity patterns suggest that circadian disturbance may induce adaptive mechanisms to preserve cognitive performance upon circadian insult.

#### **Keywords**

Circadian; cognition; memory

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### **Published Work:**

Dias, M., Marques-Morgado, I., Coelho, J. E., Ruivo, P., Lopes, L. V., & Remondes, M. (2021). Transection of the superior sagittal sinus enables bilateral access to the rodent midline brain structures. *eNeuro*, 8(4): 0146-21.2021. doi: 10.1523/ENEURO.0146-21.2021

Reis, C., Madeira, S. G., Lopes, L. V., Paiva, T., & Roenneberg, T. (2020). Validation of the Portuguese Variant of the Munich Chronotype Questionnaire (MCTQ(PT)). *Frontiers in Physiology*, 11: 795. doi: 10.3389/fphys.2020.00795

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