ADAPTIVE CHANGES IN MEMORY-RELATED BRAIN REGIONS UPON CHRONIC CIRCADIAN MANIPULATION

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Grant 135/18

Background: Circadian disruption impacts on cognition as seen in shift-work and manipulation of sleep-wake cycles in humans and rats (Marquié et al, 2015; Fekete et al, 1985). However, the functional interactions between Suprachiasmatic Nucleus (SCN) and memory-related regions, such as the Hippocampus (HIPP), have never been defined.

Aims: Explore the functional alterations of brain regions related to memory, upon circadian insult in a rodent model.

Method: Whole-brain functional connectivity was modeled by combining ^{14}C-2-deoxyglucose functional imaging and Partial Least Square 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, Perirhinal Cortex and Dorsal Raphé. 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, suggesting a disruption of HIPP-cortical communication with strong remodelling of the connections between cognitive regions. Moreover, the shifted animals displayed reduced performance in the Novel Object Recognition Test, whereas the performances in the Morris Water Maze and the Y-maze were preserved. Trans-synaptic antero- and retrograde tracing using viral vectors also suggested a role of theta rhythm in the interaction between circadian rhythms and cognition. We found anatomical projections between the SCN and the HIPP with a relay in the Septum, that may act as a hub of circadian information onto the hippocampal system.

Conclusions: Altogether, these results indicate a pronounced change in dominant functional circuits after circadian insult. These altered patterns of connectivity suggest an adaptation to a different type of HIPP-cortical communication, from a process dependent on theta oscillations to a form of interaction not mediated by theta rhythm. Further analysis is ongoing to validate this hypothesis.

Keywords: Circadian, Memory, Hippocampus, Cognition

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