Hippocampal functional networking in wakefulness and sleep

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Background: The hippocampal formation (HF+) is part of a system that plays a critical role in the encoding and retrieval of memory [1]. It has repeatedly been shown that consolidation of declarative memories occurs in human NREM sleep, supposedly involving transfer of information from the hippocampus to the neocortex [2,3]. The four major subregions of the HF+ are the cornu ammonis (CA), the dentate gyrus (DG), the subiculum (SUB) and the entorhinal cortex (EC). Anatomically, the SUB is the major source of efferent projections from the hippocampus to the orbitofrontal and infralimbic cortex, as well as to the retrosplenial cortex. The EC is interconnected with temporal, cingulate and insular cortices, whereas no direct neocortical connections have been reported for CA and DG. The goal of this work was to determine unique spontaneous connectivity maps of these hippocampal subregions and their alteration throughout NREM sleep.

Methodology:
Simultaneous EEG/fMRI resting state data (1.5T) were collected in 25 subjects during wakefulness and different NREM sleep stages. Polysomnographically verified epochs of at least 5 minutes of a unique sleep stages were extracted from the fMRI data, comprising Wake (27 epochs), Stage 1 (24), Stage 2 (24) and Slow Wave Sleep (18). Seed correlation analysis of hippocampal subregions and the entorhinal cortex (Fig.1) were performed using SPM5.

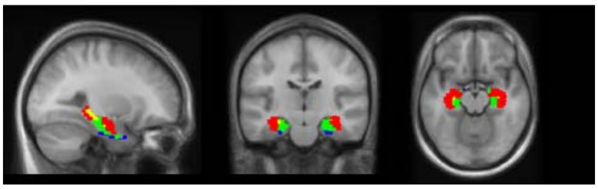

Figure1. Cytoarchitectonical maps defining HF+ subregions and entorhinal cortex seeds. Cornu ammonis (red), dentate gyrus (yellow), subiculum (green) and entorhinal cortex (blue) [6].

Principal findings
In line with previous studies, we confirmed HF+ integration into the default mode network (DMN) during wakefulness. In addition, we observed reduced connectivity of the HF+ with the DMN during NREM sleep [4]. During sleep stage 2, HF+ functional connectivity maps show increased correlation with temporal, insular, cingulate and occipital cortical areas. These altered patterns of functional connectivity in NREM sleep stages were most pronounced in the subiculum. The CA and FD show little connectivity to the neocortex.

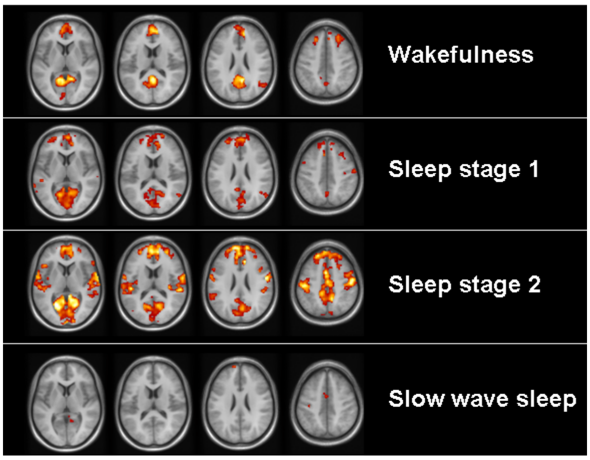

Figure 2. Subiculum connectivities during wakefulness, S1, S2, SWS. $p<0.0001$ cluster corrected.

Conclusions/significance: We provide first evidence of human hippocampal connectivity patterns across wakefulness and NREM sleep stages. Integration of HF+, especially of the subiculum, in the DMN, may represent wakeful memory processes. During sleep, increased connectivity to neocortical brain areas, gated by the subiculum, may reflects a neural correlate of memory consolidation, which has been hypothesized to be synchronized by sleep spindle activity. In fact, the anatomical regions that show higher connectivity with HF+ during stage 2 than wakefulness partly coincide with the ones correlated with fast sleep spindles [5]. Surprisingly, the strongest effects were observed in sleep stage 2, rather than in slow wave sleep, which is commonly viewed as the most important NREM sleep stage for memory consolidation. In summary, resting state fMRI experiments may further our understanding of sleep related memory consolidation.

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