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## SLEEP-DEPENDENT HIPPOCAMPAL SLOW ACTIVITY CORRELATES WITH WAKING MEMORY PERFORMANCE IN HUMANS

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**Objectives:** The positive effect of post-learning sleep on memory consolidation as well as the relationship between sleep-related memory processes and the hippocampal formation are increasingly clarified topics in neurobiology (1). However, the possibility that individual-specific (= trait-like) hippocampal sleep signs are related to the level of waking memory functioning remained unexplored. In a recent study we found 2 prominent rhythmic components in the background EEG activity of human parahippocampal-hippocampal (pHip-Hip) structures during sleep: a < 1 Hz oscillation characteristic for deep NREM sleep (stages 3 and 4) and a 1.50-3.00 Hz oscillation in REM sleep (2). Here we report a retrospective study investigating the relationship between pHip-Hip electrophysiologic activity patterns during different sleep-waking states and memory performance.

**Methods:** Thirteen patients with a history of medically refractory epilepsy (4 males, 9 females, age between 21 and 61 years, all right-handers) required mesio-temporal corticography to verify the location of a temporal lobe epileptogenic region for deciding surgical treatment. Mesio-temporal corticography was performed with foramen ovale (FO) electrodes during presurgical video-EEG monitoring. FO electrodes are flexible wires introduced through the foramen ovale into the cisterna ambiens and contact the parahippocampal gyrus at four points bilaterally along the axis of the hippocampal formation. Thirty to 100 4 sec epochs were selected for each patient each sleep-waking state, which belonged to the recordings of night 2 or 3. We carefully avoided artifacts and epileptic spikes in all the 32 simultaneously recorded channels. Based on a FFT routine (Hanning window, 0.25 Hz spectral resolution) absolute and relative power of frequency band 0.00-1.25 Hz, 1.50-3.00 Hz, 3.25-4.50 Hz, 4.75-6.25 Hz, 6.50-7.75 Hz, and 8.00-9.50 Hz were calculated from the average spectral power values for each sleep-waking state and each FO electrode of each subject. Memory testing was done days or weeks before the recording procedure. It was part of the preoperative neuropsychological investigation. Intentional learning of 10 auditory presented common Hungarian words during 5 learning trials as well as delayed (30 min.) recall of these words served as a verbal memory test, commonly used in neuropsychological testing procedures. The 18 item pointing scale of the Rey-Osterrieth Complex Figure Test (ROCFT) was used for testing visual memory performances. Pearson correlation coefficients were calculated between power values and memory performances. A correlation was considered relevant when coefficients reached the  $p < .05$  statistical significance value in at least two FO recording points on one side. Partial correlation coefficients controlled the effects of age, years of intractable seizures and semiquantitative MRI-pathology of the left and right hippocampus respectively.

**Results:** Neither of the absolute power values correlated with memory performances. The relative spectral power of the frequency band 0.00-1.25 Hz during deep NREM sleep at the right pHip-Hip region correlated positively with the short- and long term visual memory performance according to the ROCFT. Along the posterior-anterior direction of the hippocampal formation a linear increasing of correlations was observed. The relative power of the frequency band 0.00-1.25 Hz at the left pHip-Hip during phasic REM sleep correlated positively with verbal learning performance (nr. of words recalled at the 5<sup>th</sup> learning trial). The correlations remained significant after the control of age, years of intractable seizures and level of MRI-pathology.

**Conclusions:** The slow (< 1 Hz) oscillation is a basic EEG feature of NREM sleep (3). We suggest that elements of the neural circuitry responsible for the generation of the slow oscillation during deep NREM sleep are shared by mnemonic systems implicated in the performance in the ROCFT. It can be hypothesized that the right pHip-Hip structures' capacity of producing a synchronized, high-amplitude < 1 Hz oscillation is related to the functional power of this structures. Moreover the right-sided predominance of correlations is in accordance with the cerebral lateralization of visual memory. We can only speculate that the 0.00-1.25 Hz slow activity reflects PGO activity during phasic REM sleep in humans and that the asymmetric propagation of PGO waves is related to verbal memory performances. The correlation of verbal memory and hippocampal activity on the left side is in accordance with the neuropsychologic data regarding the cerebral lateralization of verbal memory functions. We conclude that sleep-dependent, phase-specific hippocampal slow activity is a good marker of waking memory functioning.

**References:** (1). Stickgold, R. et al (2001). *Science* 294:1052-1057. (2). Bódizs, R. et al (2001). *Hippocampus* 11(6):747-753. (3). Steriade, M. (2000). *Neuroscience* 101(2):243-276.

**Keywords:** electrocorticography, foramen ovale electrodes, sleep, NREM, REM, visual memory, Rey-Osterrieth Complex Figure Test, verbal learning, slow oscillation, EEG.

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