Spindles and brain activity in the spindle frequency range during human stage 2 sleep

Abstract No:

6053

Authors:

Andreas Ioannides[1], Lichan Liu[1], Yuko Urakami[2], George Kostopoulos[3]

Institutions:

[1]Lab for Human Brain Dynamics, AAI Scientific Cultural Services Ltd, Nicosia, Cyprus, [2]National Rehabilitation Center for Persons with Disabilities, Tokorozawa, Japan, [3]Neurophysiology Unit, Department of Physiology, University of Patras, Patras, Greece

Introduction:

Sleep stages are usually defined through quantification of the presence of large graphoelements in the EEG, i.e. NREM stage 2 (NREM2) is defined by the presence of spindles and K-complexes. These large graphoelements appear similar in the EEG as paroxysmal events, and there is more than a suspicion that the same underlying mechanisms may generate the large sleep graphoelements and some forms of epileptic activity [1]. We used whole night sleep MEG recordings to study the quiet (core) periods without large graphoelements of each sleep stage that until then received little attention [2]. The core period of each sleep stage was characterized by changes in activity compared to the awake state in well-defined brain areas either over a wide frequency band (dominated by low frequencies, below the alpha band) or in the gamma band (25 – 90 Hz). The most striking change was the gamma band in the Left medial Dorsal Prefrontal Cortex (L-mDPFC) that was consistently higher during sleep than in the awake state and increased from NREM2 to NREM4 and culminated with highest activity during REM sleep [2]. Recent findings implicate damage to this area in insomnia [3] and in consolidation and other memory related functions [4].

There is a growing interest in NREM stage 2 sleep [5] and specifically sleep spindles. Spindles are often implicated in memory consolidation [6] and more recently as indicators for the integrity of brain function and possibly recovery after stroke and brain injury [7,8]. We report here our recent results for activity during NREM2 in the spindle frequency range (11 – 16 Hz) in normal subjects and stroke patients.

Methods:

The whole head MEG hardware at the Brain Science Institute, RIKEN was used to record the MEG signal from four normal subjects [2]. For each subject and for each of the sleep stages NREM1-4, REM and for the awake state with eyes closed before sleep (ECW) 10 noise-free, 4-second long segments of data without any large graphoelements were identified. The data were analyzed with magnetic field tomography (MFT) [9], producing an independent tomographic estimate of activity for each timeslice of MEG data. Statistical analysis of the MFT solutions identified for each sleep stage brain areas with significant changes of activity compared to ECW. Separate computations were made for wide band activity (dominated by low frequencies, below the alpha band) and for the activity in the gamma band (25 – 90 Hz). Here, we focus on the activity during NREM2 in the spindle range of frequencies (11 – 16 Hz), separately for sleep spindle periods and for the quiet (core) periods.

Results:

During sleep spindles the activity in the 11 – 16 Hz band is widely distributed with hot spots around the central sulcus, parietal and prefrontal cortex, anterior and motor cingulate. We observe the same pattern of spindle activity in the contra-lesional hemisphere of stroke patients but reduced spindle activity in the ipsi-lesional hemisphere. Frequency and amplitude, cortical activation source strengths of spindles reduce after brain injury, and significantly increase in relation to the recovery of cognitive functions [8]. In normal subjects the 11-16 Hz activity during the core NREM2 periods is confined to parts of the thalamus, limbic system and in the same L-mDPFC area that has the highest

gamma band activity during REM sleep (Fig. 1).

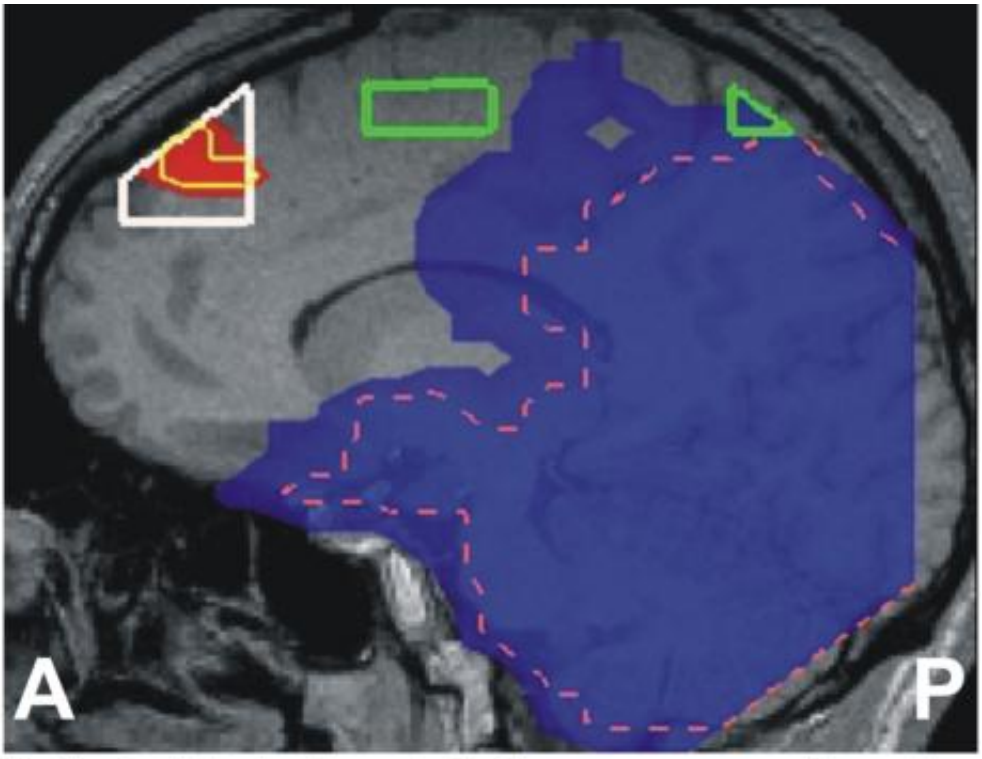

Fig.1: Activity in the spindle frequency range shown in a left paramedical sagittal plane. The red area highlighted by a yellow outline is the area with higher activity in the spindle band during quiet (core) periods of NREM2 sleep compared to the ECW. The blue area highlighted by a red dashed outline is the area with lower activity. The white and green outlines delineate the areas with high gamma band activity during REM identified in our earlier work [2]. All results show overlap of statistically significant changes in activity in all subjects. Note that the area with high activity in the spindle band during NREM2 is entirely within the L-mDPFC area (white contour).

Conclusions:

The large and easily recognizable graphoelements in NREM2 may be paroxysmal-like responses of subtler activity during the more quiet NREM2 core periods. We speculate that further study of the core periods of NREM2 may throw light on the role of spindles and may also provide useful clues about the state of the damaged brain and specifically lead to biomarkers for recovery after stroke and brain injury.

Acknowledgment:
This study is partially funded the European Commission under the 7th Framework Programme under grant agreement no 287720 (ARMOR).

Perception and Attention:

Sleep and Wakefulness

Abstract Information

References

[1] Kostopoulos, G,K. (2000) Spike-and-wave discharges of absence seizures as a transformation of sleep spindles: the continuing development of a hypothesis. Clin Neurophysiol. vol 111, Suppl 2:S27-S38.

[2] Ioannides, A.A., Kostopoulos, G.K., Liu, L.C., Fenwick, P.B.C. (2009) 'MEG identifies dorsal medial brain activations during sleep', NeuroImage, vol. 44, pp 455-68.

[3] Koenigs, M., Holliday, J., Solomon, J., Grafman, J. (2010), Left dorsomedial frontal brain damage is associated with insomnia. The Journal of Neuroscience, vol 30, pp16041-3.

[4] van Kesteren, M.T.R. , Rijpkema, M., Ruiter, D.J., and Fernandez, G. (2010), 'Retrieval of associative information congruent with prior knowledge is related to increased medial prefrontal activity and connectivity', The Journal of Neuroscience, vol 30, pp15888 –15894.

[5] Nir, Y., Staba, R., Andrillon, T., Vyazovskiy, V., Cirelli,C., Fried, I., and Tononi, G. (2011), 'Regional Slow Waves and Spindles in Human Sleep' , Neuron 70, pp153–69.

[6] Fogel, S.M., Smith, C.T. (2011), 'The function of the sleep spindle: a physiological index of intelligence and a mechanism for sleep-dependent memory consolidation', Neurosci Biobehav Rev. vol 35, pp 1154-65.

[7] Urakami, Y. (2008), 'Relationships between sleep spindles and activities of cerebral cortex as determined by simultaneous EEG and MEG Recordings', J Clin Neurophysiol vol 25, pp13-24.

[8] Urakami, Y. (2012), 'Relationship between sleep spindles and clinical outcome in patients with traumatic brain injury: a simultaneous EEG and MEG', Clin EEG and Neuroscience Jan. 2012 (in press).

[9] Ioannides, A.A., Bolton,J.P.R., and Clarke,C.J.S. (1990), 'Continuous probabilistic solutions to the biomagnetic inverse problem', Inverse Problem vol. 6, pp 523-542.