Are Human Cortical Slow Oscillations During NREM Sleep Traveling Waves or Are They Synchronized Across the Cortex?

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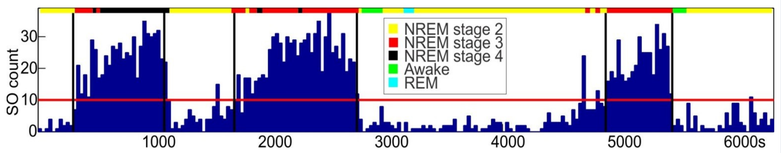
Introduction

The slow oscillation (SO) is a fundamental cortical operating mode of NREM sleep. It consists of a DOWN state with a strong outward K current in layers 2/3 and very low firing, alternating at ~1Hz with an active UP state when most cells fire at near waking levels. SO organizes other rhythms such as sleep spindles and high-frequency activity and may be implicated in declarative memory consolidation. It has been claimed, based on referential scalp EEG, that all slow oscillations begin focally and then spread through the cortex at a rate of ~2-7 m/s. However, the large cortical lead fields of referential EEG limit the ability of such recordings to reliably localize highly distributed activity, and both synchronous and traveling SO are reported in animal studies. The lead fields of MEG planar gradiometers are smaller and generally confined to the underlying cortex. We examined the propagation of slow oscillations using gradiometer recordings and related them to slow oscillations in simultaneously recorded scalp EEG.

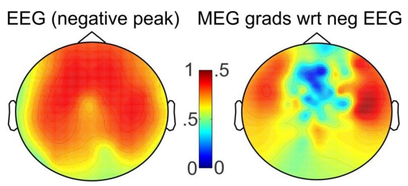
Methods

Slow-wave sleep was recorded in six healthy subjects using 204 MEG planar gradiometer sensors and 60 EEG sensors. An automatic SO detection algorithm identified SO peak times in all channels throughout the entire recording. An automatic SWS detection algorithm limited the subsequent analysis to NREM stages 3 and 4. The remaining detections were clustered across sensors in small windows (300ms for EEG; 200ms for MEG) around EEG peaks.



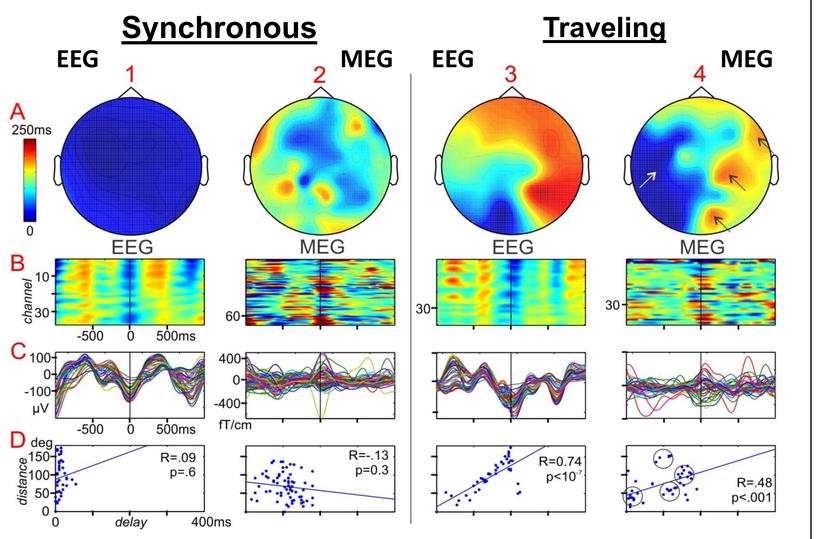
Validation of AASM guideline-based automatic MEG slow wave detection (blue histogram, 30s bins) **with an expert R&K hypnogram**.

The SO origin was defined for each cluster as the sensor with the earliest detection. Propagation delays and distances were calculated for each cluster with respect to the origin, and the correlation coefficient between them, R, quantified propagation patterns. R values with $p < 0.05$ indicate that the relationship between propagation distance and delay is linear and the SO is a traveling wave.



Probability of detecting SO. MEG map is average of Grad1 and Grad2, detections within ±100ms of the EEG peak.

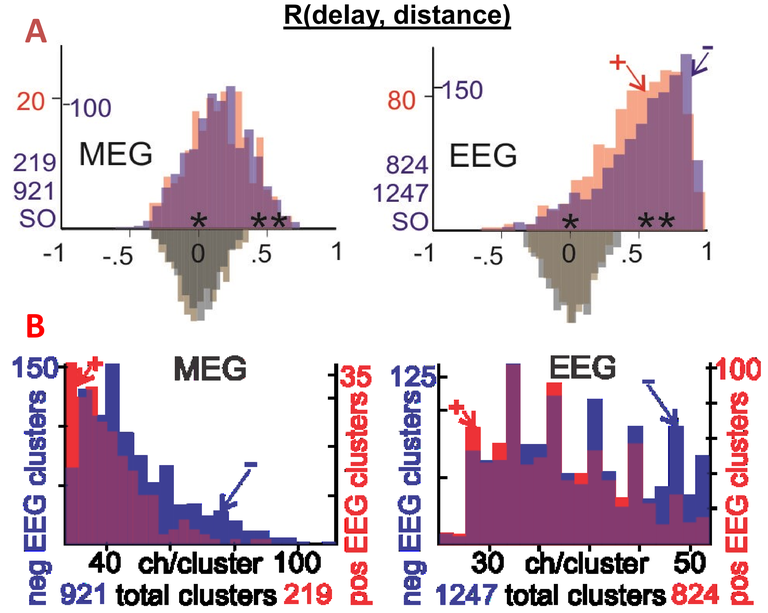
Two Types of Slow Oscillations



According to either EEG (1,3) or MEG (2,4), SO can be either stationary (1,2) or traveling (3,4) waves. **A**. Topoplots of the latency to peak from the earliest channel in 2 example DOWN states. **B**. Sensor amplitude vs time (negative=blue). **C**. Sensor waveforms. **D**. Angular distance vs delay. Circles in 4D and arrows in 4A denote apparent spatiotemporal clusters of DOWN state onsets in MEG, suggesting that 'travelling' waves may actually be 'saltatory.'

All SO Detected During SWS

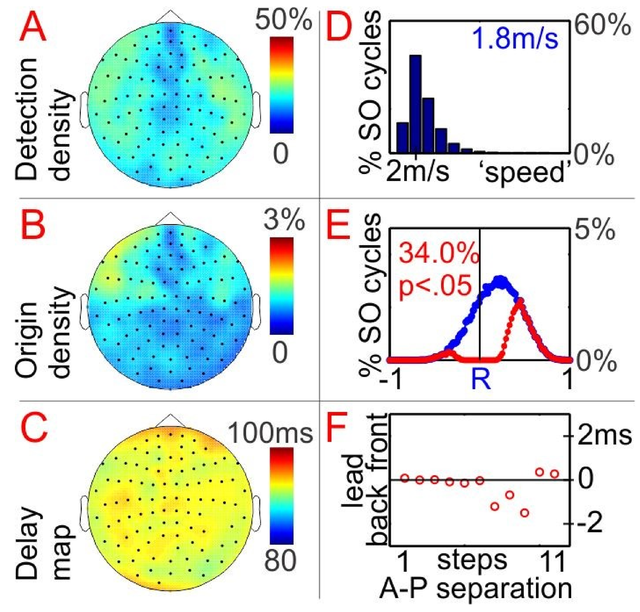
R(delay, distance)



A. Greater probability of MEG SO during EEG DOWN states than UP states, and greater correlation (R) of distance vs delay for DOWN states than UP states. Fewer of the EEG UP states (219/824) than EEG DOWN states (921/1247) had MEG SO associated with them (Chi2, p<.01). A greater regularity of EEG spread during the DOWN state is indicated by greater R values during negative peaks (-), as compared to positive (+) (Kolmogorov-Smirnov p<.01). The overall distributions were significantly different after randomizing sensor locations (descending histograms, KS p<.01). **B. More channels (ch) are involved in DOWN states (-) than UP states (+)**. (KS p<.01)

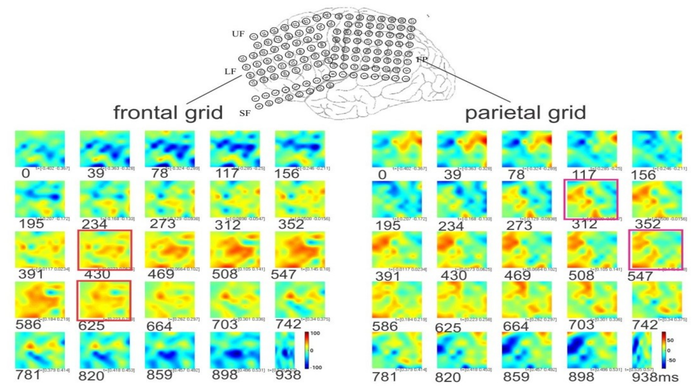
Grand Average (6 subjects)

Characteristics of SO in MEG



Future Directions

Synchronous SO in ECoG



Conclusions

Our data clearly show that the human sleep slow oscillation can be either traveling or synchronous. This finding is contrary to the standard model of slow oscillation propagation and suggests there may exist two mechanisms for generating the slow oscillation. One intriguing possibility is that a cortico-cortical mechanism underlies the traveling SO and a thalamocortical mechanism underlies the synchronous SO. This leads to several interesting questions: What thalamocortical network and intrinsic biophysical factors produce the synchronous SO? Do the different SO modes perform different functions?