Title : Sleep homeostasis and the circadian timing system set the dynamics and excitability of neuronal ensembles

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Cognitive brain function is regulated by the interplay between sleep homeostasis and the circadian timing system. The macroscopic brain correlates involved in this interaction are being uncovered, but microscopic cellular-level mechanisms remain largely unknown. We recorded neuronal responses to TMS pulses using hdEEG in 22 healthy young individuals over a stringent 29h constant routine protocol during which participants performed cognitive test batteries. Dynamic causal modelling and neural mass modelling were applied to infer connectivity between pyramidal (PC) and stellate cells (SC) and inhibitory interneuron (II), as well as glutamate and GABA functions. Cortical excitability was computed from the slope and amplitude of the evoked responses recorded at scalp level and inferred at the brain surface. Mean firing rate, excitatory drive form SC to both II and PC as well as inhibitory feedback drives of II and SC showed a significant time modulation. The temporal changes in all these variables were best explained by an interaction between a linear and sinusoidal function. Similarly, cortical excitability changed with time awake and dynamics was matched by a linear-sinusoidal interplay. Finally, regression analyses indicated that changes in neural system organization and excitability were related to variations in performance and subjective feeling as well as with slow wave activity during previous baseline sleep. These results demonstrate that the temporal changes in the organization of the different cortical layers reflect the interplay between sleep homeostasis and the circadian clock. The data further suggest the theses neuronal changes set non-linear variations in cortical excitability and behavior.