Neuronal excitation/inhibition balance is set by the need for sleep and the biological clock

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Introduction:

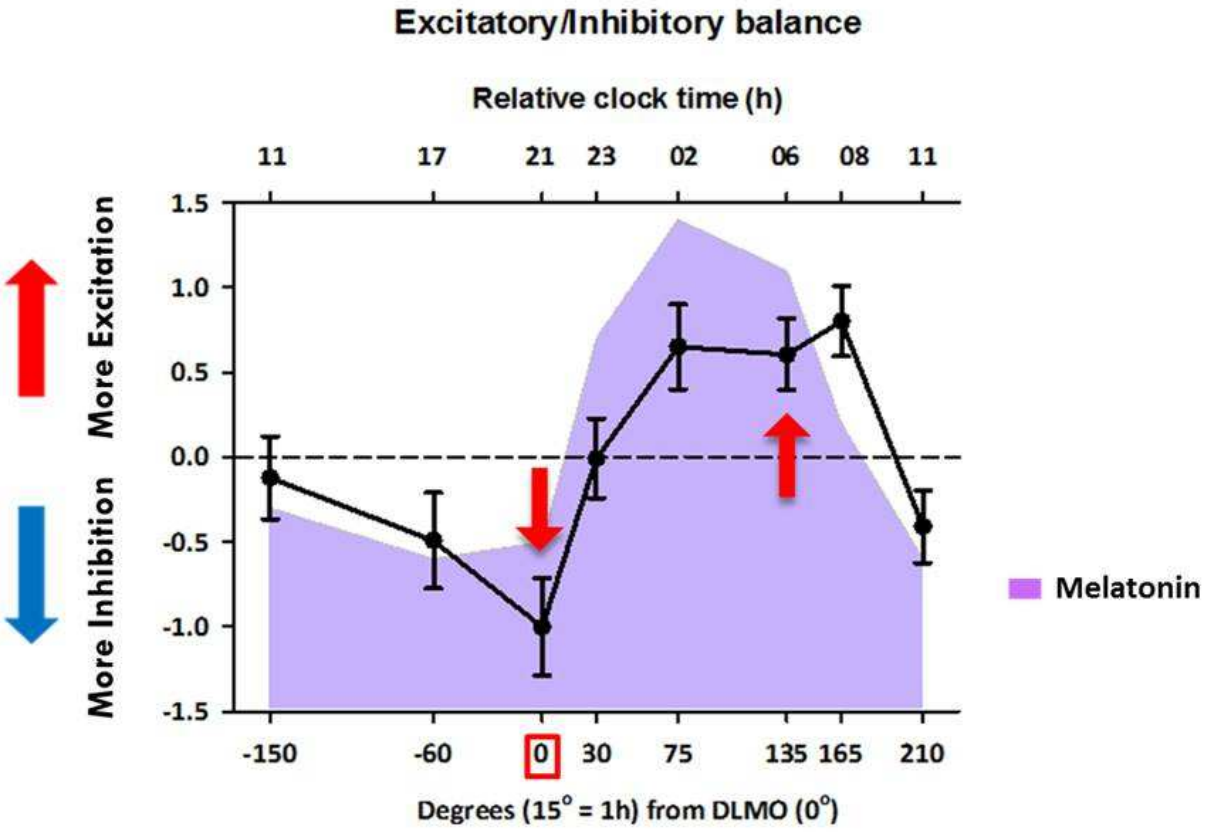
Animal [Vyazovskiy et al., 2011] and human [Huber et al., 2012] data indicate that neuronal excitability linearly increases with time awake. However, recent animal data posit that synaptic efficacy and morphology depend on time of day and on the biological clock [Liston et al., 2013]. Collectively, these data point to uncertainties about how brain dynamics are orchestrated by sleep- and biological clock-dependent processes. Dynamic Causal Modelling for electroencephalography (DCM-EEG) provides a validated non-invasive framework for inferences on in vivo neuronal architectures that generate electrophysiological measures, based on physiologically plausible priors [Friston et al., 2003; Moran et al., 2015]. Here, our aim was to apply DCM-EEG to the EEG evoked responses evoked by Transcranial Magnetic Stimulation (EEG-TMS) over the prefrontal cortex (PFC, highly sensitive to sleep pressure [Finelli et al., 2000]), to investigate the dynamics of human neuronal excitation/inhibition as a function of sleep need and of the biological clock.

Methods:

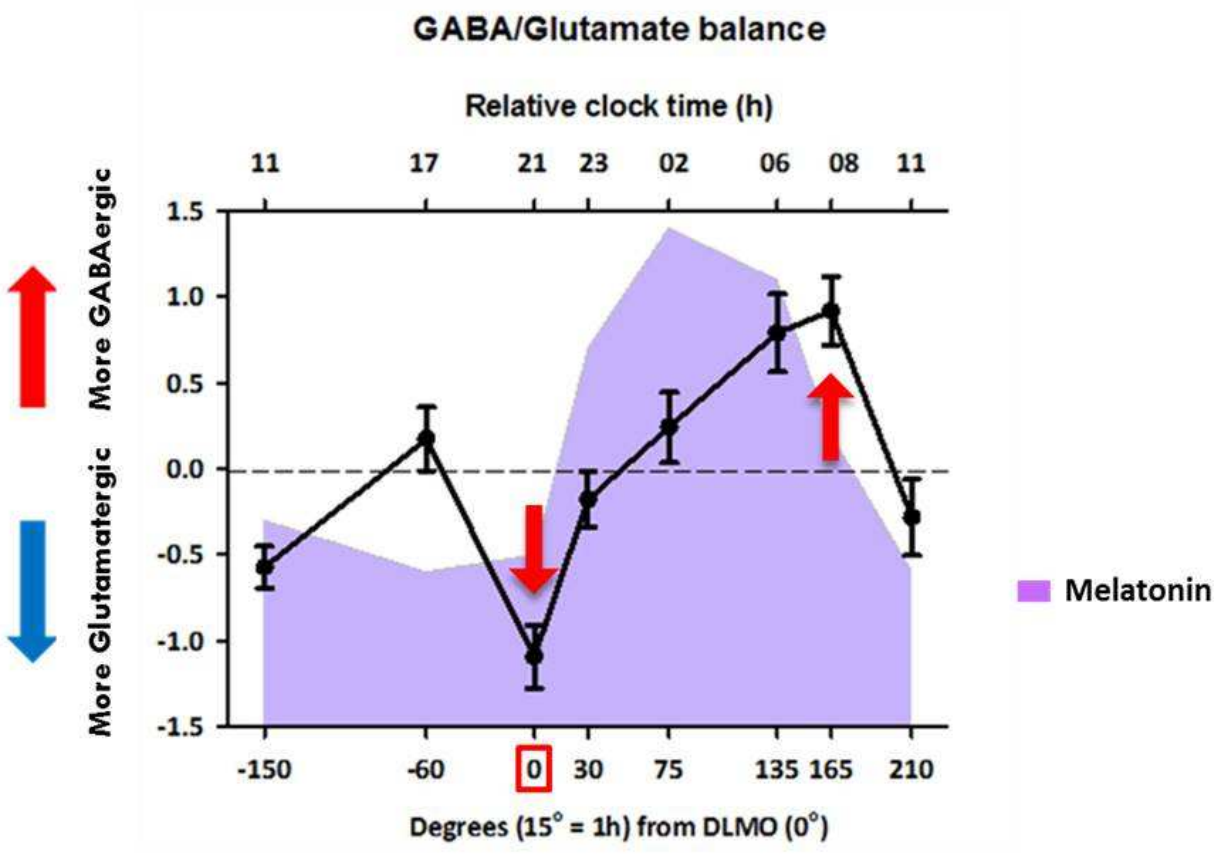
Twenty-two healthy young men (18-30 years) underwent 8 EEG-TMS recording session (each one including more than 250 trials), during 28h of sustained wakefulness, under strictly controlled constant routine conditions. Following visual inspection of the data and standard preprocessing steps, we used DCM-EEG from the SPM software package (http://www.fil.ion.ucl.ac.uk/spm/) to infer excitation/inhibition and GABA/Glutamate drives within the 4 different neuronal subpopulations of the stimulated area in the PFC.

Results:

Results indicate that excitatory and inhibitory drives between these neuronal subpopulations significantly varied across 28h of sustained wakefulness, with relatively more inhibition during the evening, when the biological clock is known to maximally fight sleep need, and relatively more excitation during the biological night, when wakefulness was extended beyond the normal waking day (Fig.1). In a similar vein, DCM-EEG estimates of GABAergic and glutamatergic drives significantly varied across the protocol, with relative decrease and increase GABAergic, respectively, in the evening and during the biological night (Fig.2), when individuals were sleep deprived. Importantly, regression analyses revealed that these DCM-EEG estimates of excitation/inhibition balance within a cortical layer were significantly related to changes in cortical excitability, neuronal synchronization (EEG oscillations) and cognitive performance.



·Fig. 1. Time-course of DCM inference of excitation/inhibition drives under normal wakefulness and sleep deprivation.



·Fig. 2. Time-course of DCM inference of GABAergic/Glutamatergic drive under normal wakefulness and sleep deprivation.

Conclusions:

Collectively, these data suggest that excitation/inhibition balance, which is fundamental to neuronal function [Isaacson et al., 2011], is not stable across time and depends on both biological clock and sleep-dependent processes. Our results also support that mesoscopic changes in excitation/inhibition balance set, at least in part, the decrease in cognitive performance observed during sleep deprivation. Ultimately, the data provide a unique window onto the hidden neuronal milieu that orchestrates the temporal organization of human brain function.

Brain Stimulation Methods:

Non-invasive Magnetic/TMS

TMS

Imaging Methods:

EEG

Modeling and Analysis Methods:

EEG/MEG Modeling and Analysis [2]

Perception and Attention:

Sleep and Wakefulness [1]

Keywords:

Cortical Columns

Electroencephaology (EEG)

Sleep

Transcranial Magnetic Stimulation (TMS)

Other - Sleep-dependent processes ; Biological systems

[1|2]Indicates the priority used for review

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Yes

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Internal Review Board (IRB) or Animal Use and Care Committee (AUCC) Approval. Please indicate approval below. Please note: Failure to have IRB or AUCC approval, if applicable will lead to automatic rejection of abstract.

Yes, I have IRB or AUCC approval

Please indicate which methods were used in your research:

EEG/ERP

TMS

Computational modeling

Which processing packages did you use for your study?

SPM

Provide references in author date format

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