**Cortical excitability dynamics of during sleep deprivation set PVT performance**

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**Objectives:** Alertness and vigilance are regulated by the subtle interaction of circadian and sleep homeostasis processes. However, brain mechanisms that underlie how this interaction impacts on alertness and vigilance remain scarcely understood, particularly at the neuronal level. Here we assessed the relationship between excitability of human cortical neurons and performance to a Psychomotor Vigilance Task (PVT), which probes sustained attention and phasic alertness, during extended wakefulness.

**Methods:** Twenty-two healthy men (18-30y) followed 28-h sleep deprivation under constant routine conditions. During the protocol, they underwent 8 transcranial magnetic stimulation (TMS)-EEG sessions and 12 cognitive task sessions, in which they performed the PVT. Cortical excitability was inferred from the amplitude of the first TMS-evoked EEG potentials component over the prefrontal cortex, a brain region sensitive to sleep deprivation. We computed a linear regression between cortical excitability and PVT performance [median (MedRT), mean (MRT), slowest (SRT), fastest (FRT) reaction times and intermediate reaction times (INT; between fastest and slowest)].

**Results:** Analyses indicate a significantly positive regression between the overnight variation of cortical excitability, i.e. changes from morning after habitual sleep to the morning after sleep deprivation (27-h of wakefulness) and global PVT measures averaged across all cognitive task sessions (MedRT, MRT, INT and SRT; *r*>.18; *p*<.05). Collectively, our data show that higher changes in cortical excitability are associated to slower reaction times across all PVT variables analyzed.

**Conclusions:** Our data suggest that changes cortical excitability during prolonged wakefulness modulate overall performance to a vigilance task.

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