**Association between sleep regulation and neuroimaging-derived myelin markers**

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**Introduction** Sleep plays a crucial role in brain plasticity, and has been suggested to be involved in myelin organization. Here we assessed the association between sleep homeostatic responses and quantitative MRI-derived myelin content in a sample of healthy young men.

**Methods**: 238 male participants (age: 22.12.7) underwent an in-lab protocol to assess homeostatic responses in slow wave and REM sleep through a modulation of prior wakefulness and sleep duration. The protocol encompassed four conditions: a baseline night (BAS, duration adjusted on participant’s sleep-wake schedule), a 12h sleep extension night (EXT) followed by a 4-h nap and an 8-h sleep opportunity night (sleep saturation; SAT) and a 12h recovery night (REC) following 40-hours sleep deprivation. For each night, four sleep parameters were extracted: sleep slow wave activity at the beginning of the night (SWA0), its overnight exponential dissipation rate (tau), and overnight mean theta and beta power per REM epoch. Participants underwent a multiparameter brain MRI protocol at 3T to extract quantitative maps sensitive to different myelin biomarkers. F-contrasts were calculated to assess whether the modularity of sleep parameters across sleep conditions explains variance in myelin biomarkers. Reported statistics are family-wise-error corrected over the entire brain volume (pFWE <.05).

**Results**: Slow wave sleep duration and SWA0 were modulated across all sleep conditions (REC>BAS>EXT>SAT; all p < 0.001), while REM sleep percentage significantly differed only between SAT and the other sleep contexts (F(3,1257)= 13.676743, p<.001). The modulation of NREM SWA0 was associated with myelin content in the medio-temporal lobe, encompassing the bilateral hippocampus and entorhinal cortex (grey and white matter), while the modulation of REM beta power was associated to myelin content in diffuse thalamocortical tracts and overhead cortices.

**Discussion**: Spectral power in sleep-specific frequency bands across sleep homeostasis contexts is associated with myelin content in the hippocampus and surrounding cortices as well as thalamocortical fibers. The hippocampus has been proposed as a key player for temporal coupling of brain oscillations, while thalamocortical fibers myelination may facilitate the cortical response to sleep-dependent diencephalic activity. As myelin stands for conduction velocity, it could facilitate the modulation of brain electrical oscillations, and putatively also the homeostatic response of sleep.

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