**Sleep-loss related decrements in night-time vigilance performance: cerebral correlates and the impact of genetic vulnerability**

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Objectives: Sleep-loss-dependent modulation of cognition-related cortical and subcortical brain activity was suggested to be affected by a polymorphism in the clock gene PERIOD3 (PER3). Here we investigated the impact of differential sleep pressure levels and PER3 on cerebral correlates underlying vigilance performance during late night, when circadian sleep promotion is maximal.

Methods: Fifteen homozygous carriers of the long repeat allele (PER35/5) and 14 homozygous carriers of the short repeat allele (PER34/4) underwent a 40-h sleep deprivation (SD) and a 40-h multiple nap protocol (NP). Blood-oxygen-level-dependent (BOLD) activity was assessed with fMRI during a 10-min Psychomotor Vigilance Task (PVT) at the end of the biological night (3 h prior habitual wake-time).

Results: PVT reaction times were slower in SD than NP (P < 0.05); but similar for both genotypes (P > 0.05). PER3 modulated BOLD activity such that activation in attention-related brain regions (e.g., inferior frontal gyrus (IFG), anterior cingulate, inferior parietal and thalamic regions, Pcorr < 0.05) increased in PER34/4carriers from SD to NP, but mostly decreased in PER35/5 carriers. Seed-based connectivity analysis pointed to a stronger connectivity between a brainstem region (part of reticular formation) with the thalamus and left IFG in PER34/4 carriers. Further, a time-on-task-dependent activity increase in the thalamus under SD was present only in PER34/4 carriers (Pcorr < 0.05).

Conclusions: Cerebral coping mechanisms with sleep-loss related vigilance decrements in the late night are affected by a PER3 polymorphism. Higher activations of arousal-promoting brain areas suggest a stronger wake-promotion in the more resilient genotype (PER34/4) in general and also with increasing time-on-task.