**Impact of sleep pressure, circadian phase and the ADA polymorphism on cerebral correlates underlying working memory performance**

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Objectives: A functional polymorphism in adenosine deaminase (ADA) modulates behavioural susceptibility to variations in sleep pressure as well as circadian sleep-wake regulation. Here we explored whether it also acts on sleep pressure- and circadian phase-dependent cerebral correlates underlying working memory performance.

Methods: Twelve G/A-and 12 G/G-allele carriers underwent a 40- hours sleep deprivation (SD) and multiple nap (NP) protocol. Bloodoxygen- level-dependent (BOLD) activity was assessed during an n-back task scheduled to the end of the biological day and night. Genotype-specific analyses focused on comparisons of (1) NP vs SD, and (2) day vs night during NP.

Results: Performance was worse during SD particularly at night (Pall < 0.05), but similar for both genotypes. The impact of sleep

pressure condition on task-related BOLD activity was modulated by genotype: G/A-allele carriers decreased activity from NP to SD (1) in frontal, anterior cingulate and right temporal regions (Pcorr < 0.05), a pattern not present in G/G-allele carriers. Concomitantly, frontal BOLD activity decreased in G/A-, but not in G/G-allele carriers from day- to nighttime [(2), Pcorr < 0.05], encompassing an area modulated by sleep pressure (1) specifically in the G/A-genotype.

Conclusions: Our results indicate an increased susceptibility to sleep pressure variations in G/A-allele carriers at the cerebral level. They further point towards a stronger circadian modulation in taskrelated frontal BOLD activity in this genotype. Interestingly, a part of these frontal regions overlaps with an area varying according to sleep pressure levels, suggesting a genotype-specific common interface of circadian and homeostatic influences during working memory performance.