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Influence of a genetic variation of adenosine deaminase on individual susceptibility to variations in sleep pressure

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Objectives: A genetic variation in the adenosine metabolizing enzyme adenosine deaminase (ADA) is associated with interindividual differences in sleep depth and subjective sleepiness. Here we investigated whether this polymorphism also modulates the response to a sleep homeostatic challenge, achieved by sleep satiation (nap protocol, NP) and deprivation (total sleep deprivation, SD), respectively.

Methods: So far, 8 heterozygous G/A allele carriers (6 f, 2 m) and 10 homozygous G/G allele carriers (7 f, 3 m) underwent a 40-h SD and a 40-h NP (10 alternating cycles of 160 min of wakefulness and 80 min of sleep) protocol under constant posture conditions. The two groups did not differ according to age (25 years+3.71), Body Mass Index, sleep quality and chronotype. Subjective sleepiness (Karolinska Sleepiness Symptom Checklist, KSSCL) was assessed regularly throughout wakefulness. In order to analyse the response to variations in sleep pressure, differences in KSSCL-values were calculated between NP and SD. Polysomnographic recordings during the naps were visually scored according to standard criteria.

Results: We observed a significant interaction in subjective sleepiness for the factors genotype, sleep pressure level (i.e. NP versus SD) and time (P < 0.05). During the biological night, heterozygous individuals indicated significantly higher subjective sleepiness in the SD compared to homozygous participants. Moreover, differences in subjective sleepiness between SD and NP occurred at nighttime in subjects with the G/A-genotype, while they appeared later and less pronounced in the G/G allele carriers (P < 0.05). Furthermore, heterozygous individuals spent more time in wakefulness and stage 1 and had more movement time during the naps in the sleep satiation condition (P = 0.07), particularly during the first biological day.

Conclusion: Our data corroborate the implication of ADA in the homeostatic regulation of sleepiness and sleep. Moreover, our results indicate a more sensitive response in subjective sleepiness to challenges in homeostatic sleep pressure (low and high) in individuals with the G/A- compared to G/G-genotype. This susceptibility was also mirrored in the sleep structure under low sleep pressure, as indexed by greater difficulties to initiate and maintain sleep in G/A compared to the G/G allele carriers. The circadian dynamics of the observed heightened sensitivity in subjective and physiological variables remains to be further investigated.