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**Sleep pressure and a PER3 polymorphism affect blood pressure in healthy young people**

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Background: A variable number tandem repeat polymorphism in the coding region of the clock gene PERIOD3 has been shown to affect several markers of sleep homeostasis as well as the autonomic nervous system such as the cardiac control similar to the effect of sleep deprivation. Here we investigated blood pressure levels under high and low sleep pressure conditions in individuals homozygous for the long (PER3-5/5) or short (PER3-4/4) variant of this polymorphism. Methods: In this on-going project, twenty healthy volunteers (seven men and 13 women;  $25.7 \pm 0.7$  years, BMI  $22.35 \pm 0.44$  kg/m<sup>2</sup>) were selected exclusively on the basis of their PER3 genotype. Ten PER3-5/5 (four men and six women) and 10 PER3-4/4 (three men and seven women) participants underwent a 40-h sleep deprivation protocol (SD, high sleep pressure) and a 40-h nap protocol (NAP, low sleep pressure, alternating cycle of 160 min of wakefulness and 80 min of sleep) under constant conditions in a balanced crossover design, starting at habitual wake time. Blood pressure and heart rate were recorded every 2 h after being in a very controlled postural position for 3 min. Comparisons of repeated measures between genotypes were made with a mixed-model approach. Genotypes as well as time were factors in all analyses. Contrasts were assessed with the LSMEANS statement. Results: Heart rate did not significantly differ between sleep pressure conditions (i.e. SD versus NAP) and between the long and short PER3 variant. However, systolic and diastolic blood pressure increased significantly under SD, particularly during the night ( $P < 0.05$ ). Furthermore, there was a significant interaction between gene and condition during the night period ( $F = 6$ ;  $P = 0.01$ ), such that the PER3-5/5 individuals were more affected by SD (i.e. stronger increase in systolic and diastolic blood pressure) than the PER3-4/4 individuals. Conclusion: Our data show that a state challenge of the sleep homeostat by total sleep deprivation as well as a trait-like challenge, as induced by the PER3 polymorphism can impact on diastolic and systolic blood pressure. Thus, besides sleep structure, behavioural and neuronal responses to sleep deprivation and autonomic cardiac control, this polymorphism may also account for inter-individual differences in blood pressure modulation.

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