

O271

The interaction of homeostatic and circadian regulation of sleepiness depends on a PER3 polymorphism

M. MAIRE¹, C. F. REICHERT¹, V. GABEL¹, A. VALOMON², J. KREBS¹, A. VIOLA¹, W. STROBEL³, V. BACHMANN², H.-P. LANDOLT², S. C. HOLST², C. CAJOCHE¹ and C. SCHMIDT¹

¹Center for Chronobiology, Basel, CH, ²Institute for Pharmacology and Toxicology, Zurich, CH, ³Respiratory Medicine, Basel, CH

Objectives: The variable number tandem repeat polymorphism of the human clock gene PER3 is involved in circadian and homeostatic regulation of human sleep and wakefulness. Here we investigated subjective sleepiness and sleep during naps in homozygous PER3 4/4 and PER3 5/5 allele carriers under high and low sleep pressure conditions. The aim of this study was to further unravel associations between inter-individual differences in the homeostatic and circadian impact on sleep and wakefulness related to this polymorphism. **Methods:** So far, 22 healthy participants (25.1 ± 3.4 year), thereof 12 PER3-5/5 (5 m, 7 f) and 10 PER3-4/4 (4 m, 6 f), underwent both a 40-h sleep deprivation (SD) and nap (NP; 10 cycles of 160-min wakefulness and 80-min naps) protocol. The groups were matched according to sex, age, BMI, sleep quality and chronotype. Subjective sleepiness was assessed at regular intervals during both protocols along with subjective sleep quality after each nap. Polysomnographic recordings during naps were scored visually according to standard criteria. **Results:** Significant effects for genotype · time ($P < 0.05$) and a trend for genotype · sleep pressure ($P = 0.07$) revealed higher sleepiness levels in PER35/5 than in PER34/4 subjects at specific times during SD and NP. PER35/5 carriers were sleepier after 9–16.5 h of scheduled wakefulness ($P < 0.05$) during SD, while during NP they differed after six naps and stated less difficulties to fall asleep in the subsequent nap at the rise of the second biological day ($P < 0.05$). Analysis of total sleep time, sleep efficiency, wakefulness and sleep stages over all naps did not reveal a main effect of genotype. Both groups slept least in the naps during biological evenings (wake-maintenance zone, WMZ) and most during the biological night. However, during the WMZ, PER35/5 carriers slept more than PER34/4 individuals, as indexed by a greater amount of NREM sleep ($P < 0.05$). **Conclusion:** Our data suggest greater subjective susceptibility of PER35/5 than PER34/4 carriers to increases in homeostatic sleep pressure, emerging already after 9 h awake. In conjunction with the finding of more NREM sleep during the nap in the WMZ in PER35/5, as well as the higher sleepiness in the beginning of the second biological day, the data indicate that the reported differential vulnerability to sleep homeostasis in PER35/5 and PER34/4 carriers might be partially mediated by a difference in the strength of the circadian arousal signal.