**Aging-related modification of sleep pattern in orexin-knockout narcoleptic mice**

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**Background**: Narcolepsy type-1 (NT1) is a lifelong sleep disease with a typical onset during adolescence and young adulthood. NT1 is characterized by the impairment of the orexinergic system which entails an altered sleep pattern. Orexin-knockout (KO) mice largely mirror the human narcoleptic phenotype, importantly improving its understanding and the development of new therapies. Since the wake-sleep cycle of both human and mice physiologically changes with aging, this study aims to compare sleep patterns between KO and wild type (WT) control mice at different ages.
**Methods**: Four groups of age-matched (YO=16 weeks; OLD=87 weeks) mice (KO-YO, n=8; KO-OLD, n=13; WT-YO, n9; WT-OLD, n=12) were implanted with electrodes for discriminating wakefulness, rapid-eye-movement sleep (REMS), and non-REMS (NREMS). Ten days later, recordings were performed for 48h with the mice undisturbed and freely moving. Sleep patterns were automatically assessed on 4s epochs with a validated algorithm (PMID: 25092499). Statistical analysis was performed by 2-way ANOVA (with genotype and age as factors) with significance set at $p<0.05$.
**Results**: We found no significant genotype x age interaction in any of the analyzed sleep variables. Significant main effects of genotype indicated that, compared to WT mice, KO spent more time in NREMS, less time in wakefulness, had a shortened REMS latency, and had more wake-sleep fragmentation with more wakefulness bouts of shorter duration and more NREMS bouts of similar duration compared to WT mice.
Aging had no significant main effect on NREMS mean bout duration or on percentage of this state over 24h whereas it significantly increased the number of NREMS and wakefulness bouts. Moreover, we found a significant reduction in the wakefulness mean bouts duration and in the percentage of time spent in this state over the 24h in OLD compared to YO mice.
Finally, only KO mice showed sleep-onset REMS periods (representing cataplexy-like states in rodents) but aging had no effect on the occurrence rate of these events.
**Conclusions**: We reported for the first time the effects of age on sleep in KO and WT mice. Our data suggest that the sleep phenotype caused by orexin deficiency in KO mice is substantially preserved with aging.