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THETA OSCILLATIONS DURING REM SLEEP SYNCHRONIZE BEHAVIOR AND NEURAL ACTIVITY IN THE DEVELOPING MOTOR SYSTEM

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Introduction: Myoclonic twitches are abundantly produced during REM sleep in skeletal muscles across the body. In infant rats, movements are produced by the red nucleus (RN), with the RN both sending motor commands and receiving sensory feedback from twitches. The RN's role in producing twitches contrasts with that of primary motor cortex (M1), which does not generate motor commands at early postnatal ages. Instead, M1 functions as a sensory structure, processing sensory feedback from self-generated movements, including twitches. By postnatal day (P) 12, the RN (but not M1) also begins to exhibit a continuous theta rhythm (~6 Hz) during REM sleep that promotes sensorimotor integration with other brain areas. Given that the RN and M1 collaborate to control movement in adult rats, we hypothesized that theta emerges in M1 after P12, at which time theta synchronizes M1 and RN activity.
Methods: To determine if and when theta synchronizes activity in the RN and M1, we recorded local field potentials and unit activity in the RN and the forelimb region of M1 in unanesthetized preweanling rats at P12 and P20. Rats were head-fixed but were able to locomote and cycle freely between sleep and wake.
Results: Neurons in the RN and M1 continued to respond to twitches through P20. Further, as predicted, we observed the developmental emergence of REM-associated theta oscillations in M1 by P20 that were coherent with theta in the RN. Additionally, neural activity was phase-locked to theta; surprisingly, twitches were also phase-locked to theta, with twitches being more likely during the troughs of the oscillation. Finally, the temporal relationship between twitch-related activity in the two structures depended on the phase of theta, with twitch-related activity in M1 lagging behind twitch-related activity in the RN in the rising phase of theta. However, in the falling phase of theta, twitch-related activity in the RN and M1 showed similar time courses.
Conclusion: These results show how theta during REM sleep promotes the developmental integration of behavior with neural activity in the RN and M1. Because synchronous activity strengthens synaptic connectivity, and theta synchronized twitch-related activity in the RN and M1, these results also implicate twitches and twitch-related activity in the development of somatotopically precise functional connectivity between the RN and M1.
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LOSS OF NEURONS IN THE INTERMEDIATE NUCLEUS IS RELATED TO PERTURBED SLEEP-WAKE RHYTHMS IN OLDER ADULTS

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Introduction: The ventrolateral preoptic nucleus (VLPO) is composed of neurons that are maximally active during sleep. In animal studies, VLPO lesion decreased the amount of sleep but only marginally attenuated circadian rhythm. The human intermediate nucleus (IN) is believed to be the homologue of the VLPO. Neuronal loss in IN has found to be associated with increased sleep fragmentation in older adults. We investigated whether IN neuronal loss is also associated with perturbed sleep-wake rhythms in humans.
Methods: We studied 50 deceased participants [age at death: 88.9±6.1 (mean±SD; female: 33 (66%)] from the Rush Memory and Aging Project, who had actigraphy assessment 1.6±1.3 years (range: 0.1-5.1 years) before death. Post-mortem immunohistochemical and stereological analysis was performed to quantify the count of galanin-immunoreactive neurons (Gal+) in the IN of them. Actigraphy data were used to calculate amplitude, acrophase, interdaily stability, and intradaily variability of the 24-h activity rhythms. Linear regression models were used to determine the associations of the four measures of sleep-wake rhythms with the GAL+ neuron counts, adjusting for age at death and sex. Further covariates considered included sleep fragmentation (derived from actigraphy) and the time interval between actigraphy assessment and death.
Results: The number of Gal+ neurons in IN was positively associated with interdaily stability and amplitude, and negatively associated with intradaily variability. Specifically, for one-SD decrease in Gal+ neurons, interdaily stability decreased by 0.06±0.02 (mean±standard error; equivalent to 40% SD of interdaily stability; p=0.009), amplitude decreased by 5.8±2.3 (equivalent to 35% SD of amplitude; p=0.014), and intradaily variability increased by 0.12±0.04 (equivalent to 36% SD of intradaily variability; p=0.009). Longer time interval between actigraphy and death showed a trend to attenuate these associations although not statistically significant (all p>0.1). These observations also remained statistically significant after adjusting for sleep fragmentation.
Conclusion: Neuronal loss in the IN was linked with perturbed sleep-wake rhythms in older adults. Further investigations are warranted to examine whether the observed associations are mediated by reduced sleep quantity or other aspects of sleep quality.
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SLEEPING WELL OR SLEEPING POORLY: CLUES FROM BRAIN NEUROCHEMISTRY

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Introduction: Sleep problems are prevalent throughout the population, but little is known about the brain mechanisms that differentiate good and poor sleepers. We studied the association between brain neurochemistry, as measured by proton magnetic resonance spectroscopy (1H-MRS), and sleep quality as measured by actigraphy. We hypothesized that better sleep quality would be predicted by brain metabolites indicative of greater neuronal health, neural inhibition, and reduced levels of excitatory neurotransmitters.
Methods: 24 healthy adults (12 females25.4±5.6 years) wore an actigraph for seven consecutive days to collect Time in Bed (TIB), Total Sleep Time (TST), Sleep Efficiency (SE), Sleep Onset Latency (SOL), and Wake After Sleep Onset (WASO), and underwent 1H-MRS neuroimaging at 3T. Metabolite data from the medial prefrontal cortex (mPFC), dorsolateral prefrontal cortex (dlPFC), and medial