Sleep Modulation in Control and Epileptic Mice Through Ambient Temperature Regulation

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Introduction:
Sleep is altered in most neural disorders including Alzheimer's disease, Parkinson's, and epilepsy. This may present as reduced sleep depth, altered proportions of rapid eye movement sleep (REM), and non-REM sleep (NREM), and other phenomena. In epilepsy, poor sleep can trigger seizures, which further disrupt sleep. We therefore speculate that improving sleep quality could alleviate seizures. To this end, we characterized the effects of acute changes in cage temperature Ta on sleep in a mouse model of chronic epilepsy.

Methods:
With IACUC approval, adult male C57BL/6 mice (n=4) were injected with pilocarpine to induce chronic epilepsy; unimplanted mice (n=10) served as controls. After spontaneous seizures were documented, each animal was instrumented for continuous EEG/EMG monitoring. A thermostatic system elevated Ta to 30°C from 7 a.m. to 9 p.m. (light period) on alternate days for 3-4 weeks with reversal to baseline (23°C) at other times. Control mice were exposed to 23°C and 30°C on different days. Vigilance state was scored in 4s epochs as Wake, REM, or NREM; NREM was further divided into light and deep sleep. Seizures were detected from the EEG. Sleep metrics were estimated and compared for elevated Ta versus baseline.

Results:
Control mice spent more time in NREM and REM and less in Wake at 30°C than at baseline ($p<0.05$). Mean NREM bout duration increased significantly with a reduction in the number of bouts. Likewise, epileptic mice spent more time in NREM and less time in Wake ($p<0.05$) at 30°C, but NREM bouts increased significantly ($p<0.001$) with Ta in number rather than duration. Deep sleep increased significantly in epileptic mice but not in controls. Thus, while sleep increases with Ta in control and epileptic mice, NREM sleep becomes more fragmented in epileptic mice but with a greater proportion of deep sleep. Seizure rate increased with Ta in two animals but decreased for the other two; neither change was significant.

Conclusions:
Sleep changes significantly with Ta in both control and epileptic mice. Our ongoing work investigates strategies for dynamic sleep modulation, which could serve as a simple adjunctive therapy for epilepsy.

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