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129S1/SvlmJ mouse model of impaired fear extinction shows abnormal sleep architecture
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Background: Post-traumatic stress disorder (PTSD) is a psychiatric disorder that may develop after exposure to a traumatic event. However, it remains unclear why only about 10–20% of trauma victims develop the disease in the later course. Sleep disturbances in particular constitute a hallmark of PTSD, but it is not known whether impaired sleep is a secondary symptom or a core feature. Sleep has been strongly implicated in memory consolidation, and emerging evidence suggests that in PTSD sleep disturbances interfere with fear memory processing, most likely by impairing fear memory extinction.

Methods: To address the assumption that disturbed sleep per se contributes to the development of PTSD we evaluated circadian sleep/wake behavior of 129S1/SvlmJ (S1) mice, which have a well-documented deficit in fear extinction, and a C57BL/6N (BL6) control group. Electroencephalogram (EEG) and electromyogram (EMG) activities were recorded chronically prior to and following contextual fear conditioning. Animals were also assessed for fear expression during exposure to the aversive unconditioned stimulus (US) consisting of a footshock, and during a recall session.

Results: Our results revealed that baseline sleep/wake behavior of S1 mice differed significantly from that of BL6 mice, especially in the active period. Here, S1 animals spent significantly more time sleeping with increased amounts of non-rapid eye movement sleep (NREMS) and rapid eye movement sleep (REMS). In line with these findings also sleep fragmentation was distinct from that in BL6 mice. Contextual fear conditioning seemed to affect sleep/wake behavior in both groups differently. Most interestingly, after exposure to the aversive stimulus BL6 animals showed an elevation in REMS in the inactive period, while REMS amount in S1 mice appeared to be unaffected. Moreover, also changes in spectral power densities following the fear conditioning protocol were significantly different in S1 and BL6 mice, pointing to a poorer sleep quality in S1 mice.

Discussion: Our findings strongly suggest that altered baseline sleep and an impaired adaptation of sleep behavior after exposure to an aversive stimulus might interfere with fear memory processing in the S1 mouse model. This in turn may predispose these animals towards the development of a pathological PTSD-like phenotype. Generally, our data are in line with the recent theory that impaired sleep, and in particular altered REMS behavior, prior to and in the early aftermath of a trauma may represent a risk factor for PTSD. Therefore, we propose that further evaluation of such sleep disturbances in humans may provide a vantage point for the development of prognostic and early diagnostic biomarkers of PTSD to identify high-risk individuals and facilitate immediate treatment of trauma-exposed persons.

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