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The Changing REM Sleep Signature of Posttraumatic Stress Disorder

Commentary on Mellman et al. A relationship between REM sleep measures and the duration of posttraumatic stress disorder in a young adult urban minority population. SLEEP 2014;37:1321-1326.

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There has been remarkably little agreement about the phenomenology and pathophysiology of the sleep disturbance in posttraumatic stress disorder (PTSD). This presents a significant deterrent to the introduction of more effective treatments for the insomnia and recurrent nightmares that severely disrupt the sleep of most individuals with PTSD. The study by Mellman and colleagues[1] in the current issue of *SLEEP* takes us a next step in understanding the mechanisms of disturbed sleep in PTSD.

In the absence of a consensus on sleep architecture abnormalities in PTSD, there is nevertheless strong evidence for altered REM sleep function.[2,3] Interestingly, fragmented, preserved, and enhanced REM sleep continuity all have been observed following trauma.[4-7] In the process of reconciling these seemingly discrepant findings, Mellman et al.[1] provide an important reminder that PTSD is one outcome of an extended response to traumatic stress and that the time elapsed post-trauma must be carefully considered in explaining polysomnographic findings in PTSD. Their ingenious approach to investigating the development of sleep changes following trauma, while not a "gold standard" longitudinal design, has yielded important insights. The finding, in a nonclinical community sample of young adults, that REM sleep percentage and REM segment length both were positively correlated with PTSD duration, as assessed retrospectively by patient interview, and that REM sleep latency correlated negatively, leads to a view of PTSD pathogenesis in which REM sleep plays a prominent, perhaps central, role. Mellman et al. suggest that the increases in REM sleep percentage and segment continuity over time could reflect an adaptive process that aids in recovery from PTSD. This hypothesis, they note, fits well with evidence that REM sleep is important in the successful processing of emotional memories.[8-10] A necessary corollary, it can be argued, is that the reconstituted REM sleep observed years after traumatization in chronic PTSD may be pathological and, in fact, evidence of maladaptation to stress; this follows from a presumption, not shared by all, that the recurrent nightmares that torment PTSD sufferers emerge largely from REM sleep.[3,7] In psychoanalytic terms, the repeating "traumatic dream" would indicate a failure, not a success, of the dream mechanism.[11]

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It is important to consider the increase in REM sleep continuity with time following trauma in the context of the PTSD treatment literature. The alpha-adrenoceptor antagonist prazosin is arguably the most effective pharmacotherapy for the nightmare disturbance in PTSD.[12,13] Taylor et al.[14] reported that prazosin increased total REM sleep time and average REM sleep episode duration in a civilian group with PTSD, suggesting that prazosin's action may depend on a normalization of REM sleep continuity. It is possible that prazosin recruits, and in fact strengthens, the same neuropharmacological mechanisms promoting REM sleep continuity that Mellman et al.[1] invoke in their model of natural recovery from PTSD.

A comprehensive description of the dynamics of REM sleep changes after exposure to a traumatic stressor must include phasic, as well as tonic, REM sleep measures. REM density (number of rapid eye movements/REM sleep time) does not figure into the model proposed by Mellman et al.[1] However, in earlier work, with accident victims, Mellman et al.[15] reported an increase in REM density shortly after trauma exposure, with no relation between increased rapid eye movement activity and the likelihood of developing PTSD. The meta-analysis of Kobayashi et al.[16] involving 20 polysomnographic studies of established PTSD found an increased REM density. Particularly because work in animals has implicated REM sleep phasic activity in the processing of fearful stimuli,[8,9] it is important to consider the possibility that severe psychological stress initiates processes in REM sleep phasic event generators that promote successful adaptation to trauma, or, alternatively, the development of PTSD. On the basis of a study of fear conditioning in rats, DaSilva et al.[17] suggested that failure to mount a strong phasic REM sleep response in the early aftermath of a stressful experience might relate to the increase in REM sleep phasic activity that has been observed in humans with chronic PTSD.

Mellman et al.[1] make an important contribution in addressing the possible role of a depressive comorbidity in the sleep changes that are observed following psychological traumatization. Largely because PTSD was a late entrant to the field of sleep research in mental disorders, because PTSD is often comorbid with depression,[18] and because heightened "REM sleep pressure" is the best characterized polysomnographic finding in depression,[19] interpretations of REM sleep changes in PTSD have invariably been required to demonstrate that comorbid depression is not the cause. In Ross et al.,[7] polysomnographic data from men with chronic PTSD were analyzed by thirds of the night to show increases in REM sleep percentage and REM density throughout the sleep period; this result was compared to the shifts in the distributions of REM sleep and

rapid eye movements to earlier in the night, which is characteristic of major depressive disorder.[19] In Mellman et al.,[1] the positive correlation between REM sleep percentage and PTSD duration remained significant after removing participants with major depression. Like PTSD, depression has been conceptualized as a disorder of "dysphoric hyperarousal."[20] With the recent introduction by the National Institutes of Health of neurobehavioral research classified by Research Domain Criteria (RDoC), including Arousal and Regulatory Systems,[21] new insights into the functional significance of REM sleep in PTSD, as well as depression and other mental disorders, are certain to be achieved.

In the National Comorbidity Survey,[18] the prevalence of PTSD in women was twice that in men. However, females are underrepresented in the extant polysomnographic literature on PTSD, and with the exception of the study by Breslau et al.,[5] nonclinical community samples with a significant proportion of women have not been investigated. Such problems have led the NIH to renew its emphasis on including females in biomedical research.[22] The work of Mellman et al.[1] with an urban minority population of both sexes exemplifies the type of clinical investigation that ultimately will identify REM sleep mechanisms operative in the aftermath of trauma. Defining the changes in REM sleep may be essential to distinguishing adaptive from maladaptive responses to traumatic stress.

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