Sleep May Be Targeted in Treatment of PTSD

BY DIANA MAHONEY

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Boston Sleep disturbances may be an important target for treating post-traumatic stress disorder, according to Dr. R. Bruce Lydiard of the Medical University of South Carolina in Charleston.

Persistent, severe posttraumatic nightmares, REM sleep fragmentation, insomnia, excessive nocturnal periodic limb movements, and sleep-disordered breathing are frequently experienced by individuals with PTSD, Dr. Lydiard said. Although these sleep complaints often are not formally diagnosed, they may be viewed as secondary symptoms of PTSD, “the evidence suggests that after a traumatic event, sleep disruption appears before the onset of PTSD and may be a risk factor for PTSD,” he proposes.

Polysomnographic data from 21 individuals with traumatic injuries showed that the number of REM periods and the shorter duration of REM periods within 1 month after the traumatic event were predictive of PTSD symptom severity 6 weeks later (Am J Psychiatry 2002;159:1696-701).

Neurobiologically, the association makes sense, Dr. Lydiard said. “Sleep is regulated in part by brain areas in which PTSD-related changes occur,” he said. “Consistent evidence that targeting sleep in PTSD and sleep dysfunction may be biologically linked.”

Imaging studies suggest that exposure to trauma-related stimuli leads to hyperactivation in the amygdala and decreased activation in the medial prefrontal cortex/anterior cingulate cortex and hippocampus, with the magnitude of the activation correlating with the clinical severity of PTSD symptoms. Polysomnographic investigations in patients with PTSD and sleep disturbances have revealed increased REM density, reduced REM duration, and increased motor activity, Dr. Lydiard said.

Together with clinical reports, “these data provide the basis for REM sleep dysregulation as a core feature of PTSD,” Dr. Lydiard said, whereby increased activity in the amygdala and decreased inhibitory input from the medial prefrontal cortex lead to a persistently overactive noradrenergic system. “As a result, the usual rhythm of REM sleep is disrupted, and REM sleep is fragmented,” he said.

Based on this model, investigators have hypothesized that targeting noradrenergic signaling during or near REM episodes may normalize REM sleep, which in turn might improve PTSD sleep disturbances and, potentially, other PTSD symptoms, Dr. Lydiard said.

The alpha adrenergic antagonist prazosin has shown promise in multiple case and chart reviews, open-label trials, and placebo-controlled studies. In one trial of 40 veterans with PTSD sleep disturbance, patients who were randomized to receive a nightly dose of prazosin—originally marketed as an antihypertensive agent—reported significant improvements in sleep quality and significant reductions in trauma nightmares, as well as a better overall sense of well-being and improved daily functioning (Bioll, Psychiatry 2007;61:928-34).

In the various studies, the therapeutic benefit of prazosin has been achieved within 1-2 weeks “with dosages as low as 1 mg nightly,” Dr. Lydiard said.

In addition to improving sleep measures, prazosin may be useful for other indications. “Prazosin also may be beneficial in schizophrenia in adults and children,” he said. In a small study of PTSD subjects whose nightmares were well controlled with the drug, the addition of small daytime doses lessened patients’ reactivity to trauma cues during the day, he said (Bioll Psychiatry 2006;59:577-81).

This finding “adds to the growing body of evidence that targeting sleep in PTSD is clinically relevant.”

Although some evidence exists to support the use of other adrenergic agents such as clonidine or another α-adrenergic agonist, as well as the anticonvulsant gabapentin—in PTSD, “large, randomized controlled trials are needed to clarify the role” of all these agents, Dr. Lydiard said.

Additional studies also are warrant- ed, he said, to investigate nonpharmacological approaches to improving PTSD sleep disturbance, such as the use of imagery rehearsal therapy, which has demonstrated efficacy in small studies (J Trauma Stress 2009;22:236-9).

Dr. Lydiard disclosed having received honoraria from Reed Medical Education, the logistics collaborator for the Massachusetts General Hospital Psychiatry Academy.