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PTSD SLEEP RESEARCH: AN UPDATE

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A decade has passed since publication of the first *Research Quarterly* devoted to sleep disturbance in PTSD. Since then, important advances have been made in PTSD sleep research and many areas bearing upon it. Animal and human studies now confirm the existence of functional relationships between fear and sleep systems in the brain. Understanding these connections should lead to testable models of the specific effects trauma and PTSD impose on the sleep system. This decade has also seen continuing evolution in the assessment and treatment of PTSD-related sleep disturbances. An efficient group treatment aimed at reducing trauma-related nightmares has performed well in two controlled trials. The first randomized controlled trial of prazosin for the amelioration of intractable nightmares has been completed in combat veterans with PTSD. Another new clinical research front has been opened by studies reporting excess rates of obstructive sleep apnea in PTSD. The following annotated bibliography is intended to guide the reader to key papers in these three domains.

Sleep/fear system interactions. Prior to the last decade, efforts to understand fear and sleep systems in the brain proceeded more or less independently. Convergence was inevitable in light of the fact that both systems are fundamentally engaged in arousal modulation and intersect at brain regions such as the nucleus locus coeruleus. Neuroanatomic studies have now shown that the amygdala, the principal integrator for fear-related afferent and efferent information, projects directly to cholinergic nuclei in the brainstem that initiate REM sleep, trigger "REM phasic events" (such as rapid eye movements; Semba & Fibiger, 1992), and arbitrate REM-to-wake transitions (Datta & Siwek, 1997). Direct and indirect manipulations of the amygdala influence REM sleep in rats (Morrison et al., 2000). Rats sleeping in environments where they have received electrical shocks exhibit reduced REM sleep (Sanford et al., 2003). There is also converse evidence that downregulation of amygdala function can result in better sleep. In one study, rhesus macaques that had been chemically amygdalectomized exhibited both more sleep overall and a higher percentage of REM sleep than controls, a pattern opposite to that produced by amygdala stimulation in rats (Benca et al., 2000). In summary, an understanding of the interactions between sleep and fear systems in the brain is

emerging that may lead to a new heuristic framework for future investigations of PTSD-related sleep disorders. It may also serve as a guide for reviewing the extant literature in the field.

The insight that some PTSD-related sleep disturbances might arise from dysregulation of brainstem nuclei regulating REM sleep actually predated the neuroanatomic observations noted above. Ross's theoretical review advancing this possibility ushered in the modern era of PTSD sleep research (Ross et al., 1989). (It was also around this time that DSM-based diagnosis became a consistent feature of studies of sleep in PTSD.) In his paper, Ross proposed not only that REM phasic events should be exaggerated in PTSD, but also that the same changes at the level of the brainstem might underwrite trauma-related nightmares and exaggeration of the startle response. Exaggeration of REM phasic events in the sleep of PTSD patients, including more rapid eye movements (Mellman et al., 1997; Ross et al., 1994b) and more and longer leg myoclonic bursts (Ross et al., 1994a), has been reported. While encouraging, these studies have relied upon small samples, and the predicted correlations between phasic events levels, trauma-related nightmares, and exaggerated startle remain to be tested. Because of the potential for close analogy to an active animal literature, further work on REM phasic events in human PTSD is highly desirable. While the studies to date have relied on labor-intensive manual counts of phasic events, the use of computer-based sleep analysis methods should facilitate future studies.

Additional features of the REM sleep of PTSD sufferers, such as its percentage of total sleep, latency from sleep onset, and "fragmentation," may also be considered for evidence of modification compatible with upregulated input from the amygdala. Taking the last of these first, two recent studies with very different methodologies have provided evidence that REM sleep is more frequently interrupted in PTSD patients than in controls. In a study of acute trauma, Mellman et al. (2002) found that the post-trauma sleep of patients who would later develop PTSD was characterized by shorter average REM period durations. In a large community-based random sample of persons with predominantly remitted PTSD, Breslau found an excess of REM-to-wake and REM-to-stage-one transitions (Breslau et al., 2004). Such findings are intriguing from a number of perspectives. As both studies found evidence of REM "fragmentation" in samples that did not meet criteria for PTSD at the time sleep

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From the Editor

I experienced mixed feelings during the preparation of this issue, which is the final issue of 2004, our 15th year of production. (The National Center for PTSD celebrated its 15th birthday this past August.) I am proud of what we have accomplished. I've learned so much from the Guest Editors who have contributed their time over the years to prepare authoritative bibliographies on a wide range of topics in trauma—for example, sleep, in the current issue, and torture, personality, and resilience in recent issues. I'm grateful to them for helping me to increase my knowledge about topics that were new to me. I'm also grateful to the *Quarterly's* staff, who have extended themselves in so many ways to help Guest Editors and keep production on schedule.

But I'm also sad because this is my last issue as Editor. I'll be moving on to new opportunities in the National Center and beyond. Fran Norris, Ph.D., a psychologist here at the Executive Division of the National Center for PTSD, will be the new Editor. Many of you know Fran for her work on disasters and epidemiology, and may even recall that she was a Guest Editor recently. I'm confident that the *Quarterly* will be in good hands under her leadership.

Starting in 2005, I'll look forward to receiving each issue just as I hope you do.

Thanks,



was evaluated, they suggest trait vulnerability. Second, the work of Cartwright et al. (1998) suggests that REM fragmentation could disrupt emotional reprocessing of traumatic memories that occurs normatively in REM sleep and functions to reduce their impact on current cognition. This reprocessing may represent one instance of a growing class of memory-enhancing effects now posited to occur during sleep (Stickgold et al., 2001). Lastly, the cholinergic brainstem nuclei receiving input from the amygdala contain both "REM-on" and "wake-on" cells organized in close proximity. In normal sleep, awakenings are more likely to follow REM than other sleep stages (Dijk et al., 2001), a preferential "phase-transition" relationship not accounted for by current "two-process" models of sleep cycling. Thus, REM fragmentation in PTSD may reflect potentiation of a mechanism that functions normatively to produce arousals from sleep, and that is not well understood by sleep science.

REM percent of total sleep and REM latency, the time between sleep onset and the first REM period, are conventionally-scored indices of sleep macroarchitecture reported in all polysomnographic studies of sleep in PTSD. Whereas the framework derived from animal studies predicts REM sleep reduction and perhaps also REM onset delay, roughly equal numbers of laboratory studies have reported REM sleep percent to be increased, decreased, or normal. Studies finding REM increase include that of Engdahl et al. (2000), notable for its use of a relatively large community random sample of elderly veterans with high levels of trauma, moderate PTSD, and low levels of substance abuse by history. Likewise, roughly equal numbers of studies have found REM latency to be normal, reduced, or delayed. Some attention has been paid to the possible impact of comorbid major depressive disorder (MDD), as primary MDD is associated with both abbreviated REM onset and with excess REM sleep. To date, only one study has addressed the comorbidity issue directly, finding no differences between PTSD patients with and without comorbid

MDD in REM latency, REM percent, or REM density (Woodward et al., 1996). It is interesting in this light that a laboratory manipulation that has been termed "chronic mild stress" results in tonic increases in REM percent of sleep in rats (Cheeta et al., 1997). This finding raises the possibility that the amount of REM sleep exhibited by chronic PTSD patients may be responsive to countervailing influences. If fear system input to the sleep system proves to be consistently associated with reduced REM sleep in animal studies, resolution of some of the REM-related ambiguities in the human PTSD literature will acquire higher priority.

One unexpected observation that may point to modulation of sleep behavior by the fear system is a significant reduction in sleep movement time observed in PTSD patients, particularly those with nightmares and/or comorbid panic disorder (Woodward et al., 2002). Movement suppression or "freezing" is a low-threshold behavioral output of the fear system, which, unlike the fight/flight response, is motorically compatible with sleep. Reduced movement during sleep has been observed as well in panic disorder in association with nocturnal panic attacks (Mellman & Uhde, 1989).

Regulation of the amygdala involves input from frontal cortical structures, especially the anterior cingulate, a cortico-limbic region that exhibits abnormalities of both structure and function in PTSD. In humans, PET neuroimaging of different sleep states has shown that the limbic system, in general, and the amygdala and anterior cingulate, in particular, are highly activated during REM sleep (Maquet et al., 1996). The first single-cell neurophysiological investigation of the anterior cingulate in primates has suggested that many units in its ventromedial subdivision (Brodmann's area 25) are quiescent during wake, but tonically active during sleep (Rolls et al., 2003). Together, these data suggest that anterior cingulate/amygdala relations may be relevant to PTSD symptoms during sleep as well as wake.

Nightmares are the most prominent and specific of PTSD-related sleep complaints, and a symptom that researchers are most eager to understand. They remain especially challenging due to their low rate of appearance in the sleep laboratory; nevertheless, progress has been made in studying them using indirect methods. Neylan has now confirmed in two large independent samples that nightmares, and not dysomnia, are correlated with trauma severity (Neylan et al., 1998, 2002). In addition, two independent studies have now shown that trauma-related nightmares, and not ideopathic nightmares, are associated with excess awakenings after sleep onset (Germain & Nielsen, 2003; Woodward et al., 2000). Interestingly, comparisons of subjects with and without histories of trauma-related nightmares have not found differences in REM sleep parameters. Comparisons of such samples using sleep neuroimaging methods may be more revealing.

New treatments for PTSD-related nightmares. The original psychotherapeutic treatments for nightmares, both trauma-related and idiopathic, were rarely systematically described. Early systematic approaches were mostly based upon classic desensitization. A new benchmark in this area has been established by the work of Krakow, who has reported multiple trials of imagery rehearsal therapy (IRT) for the reduction of nightmares due to trauma. Two reports concern randomized controlled trials (Krakow, Hollifield et al., 2000, 2001). IRT is delivered in a group format. Three three-hour sessions spaced one week apart are followed by a one-hour follow-up session, three weeks later. In introducing the treatment, post-trauma nightmares are normalized and presented as controllable. Participants then select one nightmare "of lesser intensity" for initial targeted treatment. They write down the nightmare, then change it "any way they wish," and write down the modified version. The efficacy of waking manipulation of the nightmare is conceptualized as flowing from the fact that most dream content is comprised of events from the previous day. Participants are instructed to imaginatively rehearse the revised dream narrative for 5–20 minutes daily over the next week. Effect sizes have typically exceeded 1.0. A small open trial in combat veterans published by an independent group (Forbes et al., 2001) suggests that this approach may also be effective in this hard-to-treat population. Studies of the effects of IRT on objective sleep parameters have not yet been performed.

In view of findings implicating central noradrenergic systems in PTSD, numerous clinical trials have been launched to assess the efficacy of drugs that suppress them directly, or potentiate their regulation. Perhaps the most successful such effort, to date, is that of Raskind, Peskind, and colleagues, who have promoted prazosin for the amelioration of PTSD-related nightmares. This group has now published an archival study, an open-label trial, and a small randomized, double-blind, placebo-controlled trial (Raskind et al., 2003), all with positive results. Prazosin, an alpha-1 adrenergic receptor antagonist, was developed in the early 1970s as a treatment for hypertension, and is now used to treat benign prostatic hypertrophy. From a

research perspective, much remains to be done in order to validate this treatment. As with IRT, the objective effects of prazosin on sleep physiology and behavior in PTSD patients have not been explored. No specific model of prazosin's mechanism of action in reducing trauma-related nightmares now exists, and no studies of the effects of prazosin on the waking or sleeping EEG in humans have been published.

Nefazodone is another medication that has recently interested PTSD sleep researchers, in part because it does not suppress REM sleep and so should not disrupt any beneficial traumatic memory reprocessing that might proceed during that state. Two small open-label trials employing polysomnography have been performed (Gillin et al., 2001; Neylan et al., 2003). Both found moderate symptomatic improvement in PTSD symptoms, though only one found objective improvements in sleep (increased total sleep and increased slow-wave sleep).

PTSD and sleep-disordered breathing. Krakow and colleagues are also responsible for a series of papers indicating that a very high rate (>90%) of undetected comorbidity may exist between sleep-disordered breathing (SDB), PTSD-related nightmares, and PTSD, per se. Most of these studies have relied on psychometric approaches to detecting SDB that have low specificity, but some have also employed objective assessment of SDB (Krakow, Melendrez et al., 2001, 2002; Krakow, Haynes et al., 2004). This group has also shown that treatment of SDB via continuous positive airway pressure (CPAP) is typically associated with substantial relief from PTSD symptoms (Krakow, Lowry et al., 2000). Taken together, these studies challenge the notion that PTSD-related sleep disturbances originate in esoteric interactions between fear and sleep systems. And they raise the attractive prospect that available and well-documented treatments for SDB, such as CPAP, may ameliorate many symptoms of PTSD in many, if not most, cases. Thorough and independent tests of this framework using state-of-the-art polysomnographic and psychometric assessments of SDB are warranted.

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MORRISON, A.R., SANFORD, L.D., & ROSS, R.J. (2000). **The amygdala: A critical modulator of sensory influence on sleep.** *Biological Signals and Receptors*, 9(6), 283-296.

NEYLAN, T.C., LENOCI, M., MAGLIONE, M.L., ROSENLICHT, N.Z., LEYKIN, Y., METZLER, T.J., SCHOENFELD, F.B., & MARMAR, C.R. (2003). **The effect of nefazodone on subjective and objective sleep quality in post-traumatic stress disorder.** *Journal of Clinical Psychiatry*, 64, 445-450.

NEYLAN, T.C., MARMAR, C.R., METZLER, T.J., WEISS, D.S., ZATZICK, D.F., DELUCCHI, K.L., WU, R.M., & SCHOENFELD, F.B. (1998). **Sleep disturbances in the Vietnam generation: Findings from a nationally representative sample of male Vietnam veterans.** *American Journal of Psychiatry*, 155, 929-933.

NEYLAN, T.C., METZLER, T.J., BEST, S.R., WEISS, D.S., FAGAN, J.A., LIBERMAN, A., ROGERS, C., VEDANTHAM, K., BRUNET, A., LIPSEY, T.L., & MARMAR, C.R. (2002). **Critical incident exposure and sleep quality in police officers.** *Psychosomatic Medicine*, 64, 345-352.

ROLLS, E.T., INOUE, K., & BROWNING, A. (2003). **Activity of primate subgenual cingulate cortex neurons is related to sleep.** *Journal of Neurophysiology*, 90, 134-142.

SANFORD, L.D., FANG, J., & TANG, X. (2003). **Sleep after differing amounts of conditioned fear training in BALB/c mice.** *Behavioural Brain Research*, 147, 193-202.

SEMBA, K., & FIBIGER, H.C. (1992). **Afferent connections of the laterodorsal and the pedunculopontine tegmental nuclei in the rat: A retro- and anterograde transport and immunohistochemical study.** *Journal of Comprehensive Neurology*, 323(3), 387-410.

STICKGOLD, R., HOBSON, J., FOSSE, R., & FOSSE, M. (2001). **Sleep, learning, and dreams: Off-line memory reprocessing.** *Science*, 294, 1052-1057.

SELECTED ABSTRACTS

BENCA, R.M., OBERMEYER, W.H., SHELTON, S.E., DROSTER, J., & KALIN, N.H. (2000). **Effects of amygdala lesions on sleep in rhesus monkeys.** *Brain Research*, 879, 130-138. The amygdala is important in processing emotion and in the acquisition and expression of fear and anxiety. It also appears to be involved in the regulation of sleep and wakefulness. The purpose of this study was to assess the effects of fiber-sparing lesions of the amygdala on sleep in rhesus monkeys (*Macaca mulatta*). We recorded sleep from 18 age-matched male rhesus monkeys, 11 of which had previously received ibotenic acid lesions of the amygdala and seven of which were normal controls. Surface electrodes for sleep recording were attached and the subjects were seated in a restraint chair (to which they had been adapted) for the nocturnal sleep period. Despite adaptation, control animals had sleep patterns characterized by frequent arousals. Sleep was least disrupted in animals with large bilateral lesions of the amygdala. They had more sleep and a higher proportion of rapid-eye-movement (REM) sleep than did either animals with smaller lesions or control animals. Based on these results, it seems likely that, in the primate, the amygdala plays a role in sleep regulation and may be important in mediating the effects of emotions/stress on sleep. These findings may also be relevant to understanding sleep disturbances associated with psychopathology.

ENGDAHL, B.E., EBERLY, R.E., HURWITZ, T.D., MAHOWALD, M.W., & BLAKE, J.D. (2000). **Sleep in a community sample of elderly war veterans with and without posttraumatic stress disorder.** *Biological Psychiatry*, 47, 520-525. *Background:* Although sleep disturbances are commonly reported by individuals with PTSD, objective findings have been inconsistent, due in part to small sample sizes, comorbid psychiatric disorders, variations in the recentness of trauma exposure, and the use of PTSD subjects involved in psychiatric treatment. *Methods:* A community sample of elderly males ($n = 59$) exposed to war trauma 28-50 years ago and free from sleep-affecting medications and disorders other than PTSD completed 3 nights of polysomnography. Of these participants, 30 met criteria for current PTSD; three were receiving supportive outpatient psychotherapy. *Results:* Two statistically significant differences were observed: those with PTSD had a higher percentage of rapid eye movement (REM) sleep and fewer arousals from non-REM sleep. The perceptions of sleep quality among the participants with PTSD were lower than the perceptions of non-PTSD participants. Although participants with untreated obstructive sleep apnea and sleep movement disorders were not included in the sample, many cases were detected on initial screening. Treatment resulted in improved sleep and increased feelings of well being. *Conclusions:* Alterations in REM and arousals characterized PTSD in this sample. When comorbid sleep disorders were ruled out, sleep was clinically similar across the groups. Trauma-related sleep disturbances that subjects reported as arising early in the course of the disorder appear to have declined over time.

KRAKOW, B., HAYNES, P.L., WARNER, T.D., SANTANA, E.M., MELENDREZ, D., JOHNSTON, L., HOLLIFIELD, M., SISLEY, B.N., KOSS, M.P., & SHAFER, L. (2004). **Nightmares, insomnia, and sleep-disordered breathing in fire evacuees seeking treatment for posttraumatic sleep disturbance.** *Journal of Traumatic Stress*, 17, 257-268. Eight months after the Cerro Grande Fire, 78 evacuees seeking treatment for posttraumatic sleep disturbances were assessed for chronic nightmares, psychophysiological insomnia, and sleep-disordered breathing symptoms. Within this sample, 50% of participants were tested objectively for sleep-disordered breathing; 95% of those tested screened positive for sleep-disordered breathing. Multiple regression analyses demonstrated that these three sleep disorders accounted for 37% of the variance in posttraumatic stress symptoms, and each sleep disorder was significantly and independently associated with posttraumatic stress symptoms severity. The only systematic variable associated with posttraumatic stress symptoms of avoidance was sleep-disordered breathing. The findings suggest that three common sleep disorders relate to posttraumatic stress symptoms in a more complex manner than explained by the prevailing psychiatric paradigm, which conceptualizes sleep disturbances in PTSD merely as secondary symptoms of psychiatric distress.

KRAKOW, B., HOLLIFIELD, M., JOHNSTON, L., KOSS, M.P., SCHRADER, R., WARNER, T.D., TANDBERG, D., LAURIELLO, J., MCBRIDE, L., CUTCHEN, L., CHENG, D.T., EMMONS, S., GERMAIN, A., MELENDREZ, D., SANDOVAL, D., & PRINCE, H. (2001). **Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: A randomized controlled trial.** *Journal of the American Medical Association*, 286, 537-545. *Context:* Chronic nightmares occur frequently in patients with PTSD but are not usually a primary target of treatment. *Objective:* To determine if treating chronic nightmares with imagery rehearsal therapy (IRT) reduces the

frequency of disturbing dreams, improves sleep quality, and decreases PTSD symptom severity. *Design, Setting, and Participants:* Randomized controlled trial conducted from 1995 to 1999 among 168 women in New Mexico; 95% had moderate-to-severe PTSD, 97% had experienced rape or other sexual assault, 77% reported life-threatening sexual assault, and 58% reported repeated exposure to sexual abuse in childhood or adolescence. *Intervention:* Participants were randomized to receive treatment ($n = 88$) or to the wait-list control group ($n = 80$). The treatment group received IRT in 3 sessions; controls received no additional intervention, but continued any ongoing treatment. *Main Outcome Measures:* Scores on the Nightmare Frequency Questionnaire (NFQ), Pittsburgh Sleep Quality Index (PSQI), PTSD Symptom Scale (PSS), and Clinician-Administered PTSD Scale (CAPS) at 3- and 6-month follow-up. *Results:* A total of 114 participants completed follow-up at 3 and/or 6 months. Comparing baseline to follow-up ($n = 97$ -114), treatment significantly reduced nights per week with nightmares (Cohen $d = 1.24$; $P < .001$) and number of nightmares per week (Cohen $d = 0.85$; $P < .001$) on the NFQ and improved sleep (on the PSQI, Cohen $d = 0.67$; $P < .001$) and PTSD symptoms (on the PSS, Cohen $d = 1.00$; $p < .001$ and on the CAPS, Cohen $d = 1.53$; $P < .001$). Control participants showed small, nonsignificant improvements for the same measures (mean Cohen $d = 0.21$). In a 3-point analysis ($n = 66$ -77), improvements occurred in the treatment group at 3-month follow-up (treatment vs control group, Cohen $d = 1.15$ vs 0.07 for nights per week with nightmares; 0.95 vs -0.06 for nightmares per week; 0.77 vs 0.31 on the PSQI, and 1.06 vs 0.31 on the PSS) and were sustained without further intervention or contact between 3 and 6 months. An intent-to-treat analysis ($n = 168$) confirmed significant differences between treatment and control groups for nightmares, sleep, and PTSD (all $P < .02$) with moderate effect sizes for treatment (mean Cohen $d = 0.60$) and small effect sizes for controls (mean Cohen $d = 0.14$). Posttraumatic stress symptoms decreased by at least 1 level of clinical severity in 65% of the treatment group compared with symptoms worsening or not changing in 69% of controls ($\chi^2(1) = 12.80$; $p < .001$). *Conclusions:* Imagery rehearsal therapy is a brief, well-tolerated treatment that appears to decrease chronic nightmares, improve sleep quality, and decrease PTSD symptom severity.

KRAKOW, B., MELENDREZ, D., JOHNSTON, L., WARNER, T.D., CLARK, J.O., PACHECO, M., PEDERSEN, B., KOSS, M.P., HOLLIFIELD, M., & SCHRADER, R. (2002). **Sleep-disordered breathing, psychiatric distress, and quality of life impairment in sexual assault survivors.** *Journal of Nervous and Mental Disease, 190*, 442-452. Using American Academy of Sleep Medicine research criteria, sleep-disordered breathing (SDB) was assessed in a pilot study of 187 sexual assault survivors with posttraumatic stress symptoms. Nightmares, sleep quality, distress, and quality of life were also assessed along with historical accounts of prior treatments for sleep complaints. Presumptive SDB diagnoses were established for 168 patients. 21 of 168 underwent sleep testing, and all met objective SDB diagnostic criteria. There were no clinically meaningful differences in age, body-mass index, sleep quality, distress, or quality of life measures between 21 confirmed SDB cases and 147 suspected cases not tested. Compared with 19 women without SDB, 168 women with diagnosed or suspected SDB reported significantly worse nightmares, sleep quality, anxiety, depression, posttraumatic stress, and impaired quality of life. Despite suffering from sleep problems for an average of 20 years, which had not responded to repeated use of psychotropic medications or psychotherapy, few of these women had been referred to sleep specialists. SDB appears widespread

among sexual assault survivors seeking help for nightmares. Research is needed to clarify the associations among SDB, distress, and physical and mental health impairment in trauma patients.

KRAKOW, B., MELENDREZ, D., PEDERSEN, B., JOHNSTON, L., HOLLIFIELD, M., GERMAIN, A., KOSS, M.P., WARNER, T.D., & SCHRADER, R. (2001). **Complex insomnia: Insomnia and sleep-disordered breathing in a consecutive series of crime victims with nightmares and PTSD.** *Biological Psychiatry, 49*, 948-953. *Background:* Sleep disturbance in PTSD is very common. However, no previous PTSD studies systematically examined sleep breathing disturbances, which might influence nightmares, insomnia, and PTSD symptoms. *Methods:* 44 consecutive crime victims with nightmares and insomnia underwent standard polysomnography coupled with a nasal pressure transducer to measure airflow limitation diagnostic of obstructive sleep apnea and upper airway resistance syndrome. *Results:* 40 of 44 participants tested positive on objective sleep studies based on conservative respiratory disturbance indices of more than 15 events per hour; 22 patients suffered from obstructive sleep apnea and 18 suffered from upper airway resistance syndrome. *Conclusions:* In an uncontrolled study, insomnia and sleep-disordered breathing were extremely prevalent in this small and select sample of crime victims. Research is needed to study (1) prevalence of sleep-disordered breathing in other PTSD populations using appropriate controls and nasal pressure transducers and (2) effects of sleep treatment on posttraumatic stress symptoms in trauma survivors with comorbid obstructive sleep apnea or upper airway resistance syndrome. In the interim, some PTSD patients may benefit from sleep medicine evaluations.

MELLMAN, T.A., BUSTAMANTE, V., FINS, A.I., PIGEON, W.R., & NOLAN, B. (2002). **REM sleep and the early development of posttraumatic stress disorder.** *American Journal of Psychiatry, 159*, 1696-1701. *Objective:* The potential for chronicity and treatment resistance once PTSD has become established has stimulated interest in understanding the early pathogenesis of the disorder. Arousal regulation and memory consolidation appear to be important in determining the development of PTSD; both are functions of sleep. Sleep findings from patients with chronic PTSD are complex and somewhat contradictory, and data from the acute phase are quite limited. The aim of the present study was to obtain polysomnographic recordings during an acute period after life-threatening experiences and injury and to relate measures of sleep duration and maintenance and the timing, intensity, and continuity of REM sleep to the early development of PTSD. *Method:* 21 injured subjects meeting study criteria received at least one polysomnographic recording close to the time of medical/surgical stabilization and within a month of injury. PTSD symptoms were assessed concurrently and 6 weeks later. Sleep measures were compared among injured subjects with and without significant PTSD symptoms at follow-up and 10 noninjured comparison subjects and were also correlated with PTSD severity. *Results:* There was more wake time after the onset of sleep in injured, trauma-exposed patients than in noninjured comparison subjects. Development of PTSD symptoms was associated with shorter average duration of REM sleep before a stage change and more periods of REM sleep. *Conclusions:* The development of PTSD symptoms after traumatic injury is associated with a more fragmented pattern of REM sleep.

R., & DOMINGUEZ, R. (1997). **A polysomnographic comparison of veterans with combat-related PTSD, depressed men, and non-ill controls.** *Sleep*, 20, 46-51. PTSD overlaps major depression (MD) clinically, but differs with respect to treatment response and some biological markers. Sleep disturbances represent core features of PTSD and are also common in MD. Rapid eye movement sleep (REM) has been postulated to be involved in the pathophysiology of PTSD, and REM abnormalities occur in MD. 25 patients with combat-related PTSD, 16 men with a principal diagnosis of MD, and 10 asymptomatic male controls were compared by polysomnography (PSG) under medication and substance-free conditions. Data were obtained from recordings made after an accommodation night. 1 subject from each group was excluded for significant apnea or limb movements. Sleep efficiency was decreased in the PTSD group compared to the MD and control groups. REM density was comparably increased in PTSD and MD groups, while the amount of REM sleep was reduced in PTSD compared to MD groups. These sleep measures were not significantly associated with co-morbid depression, substance-use disorder histories, or subclinical sleep apnea or limb movements within the PTSD group. These findings support sleep maintenance being impaired in chronic PTSD patients. Increased REM density in PTSD patients was replicated and was comparable to increases in the MD group. Divergence of REM time between these clinical groups suggests the possibility of different underlying mechanisms.

RASKIND, M.A., PESKIND, E.R., KANTER, E.D., PETRIE, E.C., RADANT, A.D., THOMPSON, C.E., DOBIE, D.J., HOFF, D.J., REIN, R.J., STRAITS-TRÖSTER, K.A., THOMAS, R.G., & MCFALL, M.E. (2003). **Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: A placebo-controlled study.** *American Journal of Psychiatry*, 160, 371-373. *Objective:* Prazosin is a centrally active alpha-1 adrenergic antagonist. The authors' goal was to evaluate prazosin efficacy for nightmares, sleep disturbance, and overall PTSD in combat veterans. *Method:* 10 Vietnam combat veterans with chronic PTSD and severe trauma-related nightmares each received prazosin and placebo in a 20-week double-blind crossover protocol. *Results:* Prazosin (mean dose = 9.5 mg/day at bedtime, SD = 0.5) was superior to placebo for the three primary outcome measures: scores on the (1) recurrent distressing dreams item and the (2) difficulty falling/staying asleep item of the Clinician-Administered PTSD Scale and (3) change in overall PTSD severity and functional status according to the Clinical Global Impression of change. Total score and symptom cluster scores for reexperiencing, avoidance/numbing, and hyperarousal on the Clinician-Administered PTSD Scale also were significantly more improved in the prazosin condition, and prazosin was well tolerated. *Conclusions:* These data support the efficacy of prazosin for nightmares, sleep disturbance, and other PTSD symptoms.

ROSS, R.J., BALL, W.A., DINGES, D.F., KRIBBS, N.B., MORRISON, A.R., SILVER, S.M., & MULVANEY, F.D. (1994a). **Motor dysfunction during sleep in posttraumatic stress disorder.** *Sleep*, 17, 723-732. A subjective disturbance of sleep, including the occurrence of repetitive, stereotypical anxiety dreams, is characteristic of PTSD. The phenomenology of the PTSD anxiety dream has seemed most consistent with an underlying rapid eye movement (REM) sleep dysfunction. However, motor behavior reportedly can accompany PTSD dreams, and normal REM sleep typically involves a nearly total paralysis of the body musculature. As a means of understanding this discrepancy, anterior tibialis muscle activity during sleep was studied in a group of

Vietnam combat veterans with current PTSD and in an age-matched normal control group. The PTSD subjects had a higher percentage of REM sleep epochs with at least one prolonged twitch burst; they also were more likely to have periodic limb movements in sleep, during nonrapid eye movement sleep. Both these forms of muscle activation also have been observed in REM behavior disorder (RBD), a parasomnia characterized by the actual enactment of dream sequences during REM sleep. The identification of RBD-like signs in PTSD adds to the evidence for a fundamental disturbance of REM sleep phasic mechanisms in PTSD.

ROSS, R.J., BALL, W.A., DINGES, D.F., KRIBBS, N.B., MORRISON, A.R., SILVER, S.M., & MULVANEY, F.D. (1994b). **Rapid eye movement sleep disturbance in posttraumatic stress disorder.** *Biological Psychiatry*, 35, 195-202. The subjective sleep disturbance in PTSD, including the repetitive, stereotypical anxiety dream, suggests dysfunctional rapid eye movement (REM) sleep mechanisms. The polysomnograms of a group of physically healthy combat veterans with current PTSD were compared with those of an age-appropriate normal control group. Tonic and phasic REM sleep measures in the PTSD subjects were elevated on the second night of recorded sleep. Increased phasic REM sleep activity persisted in the PTSD group on the subsequent night. During the study, an anxiety dream occurred in a PTSD subject in REM sleep. The results are consistent with the view that a dysregulation of the REM sleep control system, particularly phasic event generation, may be involved in the pathogenesis of PTSD. The finding of a specific disturbance of sleep unique to PTSD may have significant implications for the design of effective treatments for PTSD.

ROSS, R.J., BALL, W.A., SULLIVAN, K.A., & CAROFF, S.N. (1989). **Sleep disturbance as the hallmark of posttraumatic stress disorder.** *American Journal of Psychiatry*, 146, 697-707. The reexperiencing of a traumatic event in the form of repetitive dreams, memories, or flashbacks is one of the cardinal manifestations of PTSD. The dream disturbance associated with PTSD may be involved in the pathogenesis of the posttraumatic anxiety dream. Furthermore, the results of neurophysiological studies in animals suggest that CNS processes generating REM sleep may participate in the control of the classical startle response, which may be akin to the startle behavior commonly described in PTSD patients. Speculating that PTSD may be fundamentally a disorder of REM sleep mechanisms, the authors suggest several strategies for future research.

WOODWARD, S.H., FRIEDMAN, M.J., & BLIWISE, D.L. (1996). **Sleep and depression in combat-related PTSD inpatients.** *Biological Psychiatry*, 39, 182-192. The sleep of 27 unmedicated Vietnam combat-related PTSD inpatients was monitored for 3 nights. Depressive comorbidity was considered both as a diagnostic category using DSM-III-R criteria, and as a continuous variable using the Beck Depression Inventory (BDI). Data collected included sleep architecture features that have discriminated unipolar depressives from controls in many prior studies, rapid eye movement (REM) sleep latency, and slow-wave sleep time, as well as two additional indices that have sometimes discriminated depressives from controls in waking studies—baseline heart rate and facial electromyography. Structured Clinical Interview for the DSM-III-R (SCID)-diagnosed PTSD + major depressive disorder (MDD) patients failed to exhibit shorter REM latencies, greater REM percents of sleep, or greater REM densities than PTSD - MDD patients, but did exhibit less slow wave sleep. PTSD + MDD patients also exhibited less facial (mentalis) electromyographic

activity. REM densities and baseline heart rates were equivocal. REM density, baseline heart rate, and mentalis electromyography all correlated with the BDI, the former two positively, the last, negatively. In summary, SCID-diagnosed PTSD + MDD patients failed to exhibit the classic REM sleep architectural modifications associated with unipolar depression, despite the fact that several other psychophysiological indices of dysphoria were detectable in their sleep.

WOODWARD, S.H., LESKIN, G.A., & SHEIKH, J.I. (2002). **Movement during sleep: Associations with posttraumatic stress disorder, nightmares, and comorbid panic disorder.** *Sleep, 25*, 681-688. *Study Objectives:* To corroborate findings from the National Comorbidity study with objective sleep data. *Design:* Retrospective data review. *Setting:* Sleep laboratory, National Center for Post-Traumatic Stress Disorder. *Participants:* Male Viet-

nam Combat Veterans. *Interventions:* N/A. *Measurements and Results:* We reanalyzed laboratory sleep data obtained from subjects undergoing inpatient treatment for posttraumatic stress disorder. Comorbid panic disorder was not associated with a significant worsening of objective sleep in this sample. Posttraumatic stress disorder, comorbid panic disorder, and trauma-related nightmare complaint were all associated with significant and systematic reductions of sleep movement time. Analyses of potential "rescoring" artifacts provided further support for this effect. *Conclusions:* A curvilinear function may describe the relationship between anxiety symptom severity and sleep-movement time in both PTSD and panic disorder. Evidence for movement suppression in association with pathologic levels of human anxiety is consistent with the suppression of movement ("freezing") exhibited by animals under conditions of perceived threat.

ADDITIONAL CITATIONS Annotated by the Editor

BRESLAU, N., ROTH, T., BURDUVALI, E., KAPKE, A., SCHULTZ, L., & ROEHRS, T. (2004). **Sleep in lifetime posttraumatic stress disorder: A community-based polysomnographic study.** *Archives of General Psychiatry, 61*, 508-516.

Used polysomnographic recording to assess sleep in a sample of adult male and female members of a health maintenance organization who had been followed longitudinally for 10 years. The authors failed to find clinically meaningful differences between the 71 individuals with lifetime PTSD and 212 individuals without PTSD or between current versus past only PTSD subgroups.

FORBES, D., PHELPS, A., & MCHUGH, T. (2001). **Treatment of combat-related nightmares using imagery rehearsal: A pilot study.** *Journal of Traumatic Stress, 14*, 433-442.

Administered 6 sessions of imagery rehearsal therapy to 12 Australian Vietnam veterans with PTSD. There were significant improvements in targeted nightmares, as well as symptoms of PTSD and associated problems.

GERMAIN, A., & NIELSEN, T.A. (2003). **Sleep pathophysiology in posttraumatic stress disorder and idiopathic nightmare sufferers.** *Biological Psychiatry, 54*, 1092-1098.

Used polysomnographic recording to assess sleep in 9 nightmare sufferers with PTSD, 11 nightmare sufferers without PTSD, and 13 healthy controls. The PTSD group had more awakenings than the other groups, both of whom had more leg movements during REM and non-REM sleep relative to controls.

GILLIN, J.C., SMITH-VANIZ, A., SCHNIEROW, B., RAPAPORT, M.H., KELSOE, J., RAIMO, E., MARLER, M.R., GOYETTE, L.M., STEIN, M.B., & ZISOOK, S. (2001). **An open-label, 12-week clinical and sleep EEG study of nefazodone in chronic combat-related posttraumatic stress disorder.** *Journal of Clinical Psychiatry, 62*, 789-796.

Assessed laboratory sleep in 12 male veterans with PTSD who were participating in an open-label study of nefazodone. Although symptoms improved during treatment, there were no changes in objective polysomnographic sleep measures.

KRAKOW, B., HOLLIFIELD, M., SCHRADER, R., KOSS, M.P., TANDBERG, D., LAURIELLO, J., MCBRIDE, L., WARNER, T.D., CHENG, D.T., EDMOND, T.E., & KELLNER, R. (2000). **A controlled study of imagery rehearsal for chronic nightmares in sexual assault survivors with PTSD: A preliminary report.** *Journal of Traumatic Stress, 13*, 589-609.

Randomized sexual assault survivors with PTSD to an imagery rehearsal therapy ($n = 87$) or wait list control condition ($n = 82$). At a 3-month follow-up, completed by 54% of the original participants, the group IRT reported decreased severity of nightmares and PTSD relative to the control group.

KRAKOW, B., LOWRY, C., GERMAIN, A., GADDY, L., HOLLIFIELD, M., KOSS, M.P., TANDBERG, D., JOHNSTON, L., & MELENDREZ, D. (2000). **A retrospective study on improvements in nightmares and post-traumatic stress disorder following treatment for co-morbid sleep-disordered breathing.** *Journal of Psychosomatic Research, 49*, 291-298.

Assessed the effect of treatment for sleep-disordered breathing on 23 nightmare sufferers, 15 of whom had PTSD. Among the PTSD participants, there was a median 75% improvement among the 9 who received treatment, whereas there was a median worsening of 43% among the 6 assigned to a waitlist control condition.

WOODWARD, S.H., ARSENAULT, N.J., MURRAY, C., & BLIWISE, D.L. (2000). **Laboratory sleep correlates of nightmare complaint in PTSD inpatients.** *Biological Psychiatry, 48*, 1081-1087.

Assessed heart rate and EEG spectral power during sleep in 56 Vietnam combat veterans with PTSD and 14 nonpatient controls without PTSD, 10 of whom were Vietnam combat veterans. Although heart rate did not differ between groups, there were differences in EEG that varied across sleep stages.

PILOTS UPDATE

Four years ago we published the third edition of the *PILOTS Database User's Guide*. It contained a description of the purpose and scope of the database, instructions for searching PILOTS on the Dartmouth College Information System (DCIS), and a detailed presentation of our indexing vocabulary. Our indexers use this PILOTS Thesaurus to select the descriptors that best reflect the subject-matter of the publications we index in the PILOTS Database; and we advise database users to consult the PILOTS Thesaurus in planning their own literature searches.

We have begun planning a new edition of the *PILOTS Database User's Guide*. The database has a new host, BiblioLine, whose interface and search procedures differ substantially from those of DCIS. We described these briefly in the Fall 2003 *PTSD Research Quarterly*, and those who needed further information can use the tutorials and help screens provided by BiblioLine. But we are concerned that users new to the PILOTS Database might not realize that the access and search instructions provided in the current *User's Guide* are no longer valid.

The publication of a new *PILOTS Database User's Guide* allows us to improve the explanations and instructions we provide to database users. As we prepare the text, we test it out on searchers of varying degrees of expertise and experience, and incorporate their comments into successive drafts. In this way we try to anticipate, and forestall, problems that our users may encounter. But if there is anything about the layout, structure, or terminology of the current edition of the *User's Guide* that renders it frustrating or ineffective, this is the time to call it to our attention.

We are also eager to receive suggestions for revising the PILOTS Thesaurus. Traumatic stress studies is a rapidly growing, continually changing field. New developments and new concepts challenge our ability to link the information needs of database users with the publications that will fulfill them. Even well-established terms will continually acquire new synonyms and new shades of meaning.

As we use the existing Thesaurus in our indexing, we keep a list of new terms that are candidates for inclusion in the next revision. Those we do not choose are considered

for use as "entry terms" — terms listed in the Alphabetical Index to the PILOTS Thesaurus with links to the proper descriptors to use in indexing and searching.) We also keep track of terms whose utility is questionable or whose relationship to other descriptors warrants reexamination.

We arrange our list of descriptors into eight hierarchies, each of which represents a particular approach to describing the content of a document. The following examples of possible changes in our indexing vocabulary may convey some idea of the decisions we shall have to make.

Potential new terms in the *Stressors* hierarchy would include Death of Public Figure, Deprogramming, Mass Murder, Parental Alcoholism, Parental Drug Abuse, Poverty, School Violence, Sibling Abuse, and Trafficking.

New categories of *Affected Persons*, include Cuban Americans, Diplomatic Personnel, Expatriates, Grandparents, Human Rights Workers, Interpreters, Judges, Mentally Ill, Psychiatric Outpatients, Security Guards, Shelter Residents, Transgendered Persons, and Transsexuals.

In the *Effects* hierarchy we are considering terms such as Attributional Style and Memory Functioning. We also need to examine the relationships among the concepts of Flashbacks, Hallucinations, and Reexperiencing.

New *Assessment* terms under consideration include Acute Stress Disorder Assessment Instruments and Dissociation Assessment Instruments.

We have already added Energy Psychotherapy to the *Treatment* hierarchy, and we are also considering Lateral Visual Stimulation, Peer Counseling, School Based Treatment, Testimony Therapy, and Therapeutic Exercise.

In the *Scientific Research* hierarchy, should we merge Neurosciences and Neurobiology into a single descriptor? Under Policy Issues we might add Child Sexual Abuse Accommodation Syndrome to the descriptors used only in a forensic context. Books for Adolescents and Books for Children are possible new *Literary Formats* to be used.

The upcoming revision of the *PILOTS Database User's Guide* will be the last for several years, so this would be an excellent time to make suggestions for its improvement.

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