Journal of Contemporary Psychotherapy, Vol. 26, No. 3, 1996

Effects of Trazodone on Sleep in Patients Diagnosed with Post-Traumatic Stress Disorder (PTSD)

J. Wesson Ashford, M.D., Ph.D., and Thomas W. Miller, Ph.D., ABPP

Trauma victims frequently report nightmares with experiences of reliving the stressful event in catastrophic dreams. The following day there are exaggerated startle responses and psychic numbing, followed that evening by a reluctance to go to sleep and insomnia. This study found trazodone to be effective in veteran patients with a diagnosis or symptoms of PTSD including sleep disturbance. Among this group of veterans, 20 of the 21 under 60 and 24 out of 27 over 60 had positive responses to bedtime trazodone doses, in that they slept better, including going to sleep more quickly, having fewer nightmares, and had less anger the next day. These benefits may be due to deepened non-REM sleep early in the night as well as delayed REM-sleep onset.

INTRODUCTION

PTSD Diagnostic Criteria

Psychological traumatization can result in what DSM-IV (APA, 1994) has defined as post-traumatic stress disorder (PTSD). The DSM-IV diagnostic criteria for PTSD require:

(A) exposure to a traumatic event;
(B) persistent reexperiencing of the event;
(C) avoidance of stimuli associated with the event;
(D) symptoms of increased arousal;
(E) duration more than one month; and

Requests for reprints should be sent to Dr. Thomas W. Miller, Professor of Psychology, Murray State University, 435 Wells Hall, Murray, Kentucky 42071.

© 1996 Human Sciences Press, Inc.

(F) a resultant disruption of function.

Included within these criteria are the reexperiencing of the traumatic event in the form of recurrent, distressing dreams, intrusive daytime recollections, and recurrent and dissociative flashback episodes. The clinical diagnostic criterion of increased arousal includes evidence of sleep disturbance and exaggerated startle response. Symptoms of depression, anxiety, and irritability are frequently seen with this disorder.

PTSD and Sleep Phase

The role of sleep disturbance in post-traumatic stress disorder may be of significance for understanding the pathophysiology of the disorder (March, 1990). Two of the major characteristics of PTSD are *reexperiencing* of the traumatic event in recurrent distressing dreams about the event and symptoms of increased *arousal* manifest as difficulty falling asleep. The sleep disturbance and recurrent, distressing dreams are considered by some to be central and long-lasting aspects of PTSD (van der Kolk, Blitz, Burr, Sherry, & Hartmann, 1984).

Ross & Associates (Boss, Ball, Dinges, Kribbs, Morrison, Silver, & Mulvaney, 1994; Ross, Ball, Sullivan, & Caroff, 1989) hypothesize that the central nervous system mechanisms implicated in the pathogenesis and control of PTSD-related nightmares are related to the state of REM sleep. That is, post-traumatic stress disorder and its sequelae might involve either an inappropriate recruitment of essentially normal REM sleep processes or a coming into play of inherently dysfunctional phasic REM sleep mechanisms. These researchers note that the dream disturbance associated with PTSD may be relatively specific for the disorder and dysfunctional REM sleep mechanisms may be involved in the pathogenesis of post trauma dream activity.

The central argument in this hypothesis concerns the similarity of mentation in traumatic nightmares and in normal REM sleep. Mentation occurs throughout sleep, and that which occurs during REM is described as more dream-like and less related to reality (Rechtschaffen, 1973). However, the nightmares or night terrors described by PTSD patients are intensely related to the real memories of the traumatic event and are described as being like re-experiencing the traumatic event (Inman, Silver, & Doghramji, 1990; van der Kolk, et al., 1984), dissimilar to normal REM-like mental phenomena. Therefore, the relation of the PTSD sleep disturbances to REM must be reevaluated, and the possibility considered that traumatic nightmares are not exclusively a REM phenomenon.

van der Kolk, et al. (1984) and Felembaum (1988) have suggested that PTSD nightmares might be related to *pavor nocturnus* which is observed during stages II to IV in children, thus possibly not dependent on the REM-generating mechanism. They both argue that the issue of at which stage the nightmares occur should be resolved by objective polysomnography. Supporting the conceptualization that PTSD nightmares can occur during non-REM sleep state events, dreams related to the traumatic event occur earlier in the evening, when there is more stage III to IV sleep and less REM sleep, than the more typical dreams which are reported later in the evening, when the proportion of REM sleep is high (van der Kolk, et al., 1984; Woodward, Arsenault, Bilwise, & Gusman, 1991). However, PTSD patients may have more REM earlier in the evening, as do depressed patients (Ross, 1994).

In the laboratory, PTSD patients indeed show sleep disturbance (Hefez, Metz, & Lavie, 1987), which may be characterized by a lowering of awakening thresholds from non-REM sleep (Schoen, Kramer, & Kinney, 1984), specifically, stages III and IV (Dagan, Lavie, & Bleich, 1991), accompanied by a lower REM-elicited dream recall rate (Kramer, Schoen, & Kinney, 1984). The key issue appears to be that sleep architecture is disturbed in PTSD. Lower arousal thresholds and REM occur earlier in the evening, thus allowing reality related issues, still active from day-time mentation, to be more vividly perceived and arouse the patient and disturb sleep.

PTSD, SLEEP, AND DEPRESSION

Laboratory studies related to sleep disturbance have shown that the sleep process is characteristically altered with depression and is likely altered with traumatization or other stresses resulting in shortened sleep latency, shortened REM latency, and a shift of REM sleep to the earlier part of the sleep cycle (Ross, 1994; Scharf & Schais, 1990). Polysomnographic research findings in depressed patients have yielded such phenomena as REM reversal and decrease in slow wave sleep activity. The growing body of evidence suggesting a correlation between sleep abnormalities and depression may be expanded to the arena of understanding sleep disturbance within the syndrome of post-traumatic stress disorder. Sleep disruption may be further recognized as an early symptom in the progression to the full development of PTSD (Mellman, Randolph, Brawman-Mintzer, Flores, & Milanes, 1992).

PTSD, SLEEP AND SEROTONIN

In recent years, many behavioral manifestations and several psychiatric disorders have been linked to the neurochemical serotonin. These links are plausible since "serotonergic neurons comprise the most widely expansive neurochemical network in the vertebrate CNS" (Jacobs & Azmitia, 1992). Of particular importance to this discussion is the relation of serotonin to sleep and the state of arousal. Serotonin neurons have a regular one to three per second firing rhythm during alert wakefulness, and this rate decreases during slow sleep and ceases during REM sleep (Jacobs & Azmitia, 1992; McGinty & Harper, 1976). Several observations suggest that PTSD symptoms may be related to this interaction between sleep and serotonin.

(1) PTSD symptoms occur during both the day and the night. Some of the symptoms such as hyperarousal suggest a disruption of sleep/arousal mechanisms which would be intrinsically related to serotonin neuronal activity and sleep processes.
(2) Daytime flashbacks—very vivid memories—can be related to LSD type flashbacks (Van Putten & Emory, 1973), and LSD mechanisms are related to serotonin, and sleep mechanisms, specifically REM sleep. Serotonin neurons cease firing after LSD exposure in a similar pattern as seen during REM sleep (Aghajanian, 1992; Aghajanian, Foote, & Sheard, 1968; Aghajanian & Vander-Maelen, 1982).
(3) Modest beneficial effects on PTSD symptoms have been obtained from medications with serotonergic effects, particularly antidepressants, including *amitriptyline* (Davidson, Kudler, Saunders, Erickson, Smith, Stein, Lipper, Hammett, Mahorney, & Cavenar, 1993), *fluoxetine* (McDougle, Soutwick, Charney, & St. James, 1991), *cyproheptadine* (Brophy, 1991), and *buspirone* (Wells, Chu, Johnson, Nasdahl, Ayubi, Sewell, & Statham, 1991).

Clinical findings have also suggested that some neurotransmitter systems may not be associated to PTSD symptoms:

(1) Many medications have been used to alleviate PTSD symptoms, but most have been unsuccessful (Friedman, 1988). Thus, one noted failure is the neuroleptics in most cases, suggesting that symptoms depending on dopamine neurotransmission are not involved. This lack of benefit from neuroleptics emphasizes the importance of *distinguishing* PTSD from schizophrenia.
(2) Drugs with GABA-agonistic properties have been widely used for the treatment of PTSD. Benzodiazepine treatments have gener-

ally resulted in poor long-term outcomes. Valproic acid (Fesler, 1991) and carbamazepine (Lipper, Edinger, & Stein, 1990) show some promise. While the basis for a potential benefit of these medications is unclear, it should be noted that they generally induce sleep, but disrupt sleep architecture, and produce no striking benefits for PTSD patients. The benefit of these medications may be in suppressing the consolidation of the traumatic memory immediately after the traumatization has occurred.

TRAZODONE, SLEEP AND DEPRESSION

Trazodone hydrochloride, a triazolopyridine derivative, has been shown to be an effective antidepressant which does not necessarily change sleep continuity but increases early night stage III and IV sleep while increasing REM latency and suppressing total REM sleep (Brogden, Heel, Speight, & Avery, 1981). The effects of trazodone on sleep have been evaluated in a number of studies of depressed patients, patients with insomnia, and others (Mouret, Lemoine, Minuit, Benkelfat & Reinardet, 1988; Muratorio, Maggini, Coccagna and Guazzelli, 1974; Scharf & Schais, 1990). Trazodone has a beneficial effect in inducing sleep (Montgomery, Oswald, Morgan, & Adam, 1983), particularly in depressed patients where this drug increases slow wave sleep (Mouret, et al., 1988) and more than doubles stage four sleep (Scharf & Schais, 1990). However, trazodone has the shortest half-life of any anti-depressant and is rarely associated with residual sedation the next day.

Unlike other anti-depressant medications recognized for sedating qualities, trazodone has nearly no anticholinergic or anti-histaminergic side effects. Trazodone does moderately block the alpha-1 adrenoreceptor, though the relation between this effect and sleep change is unclear. Trazodone has an effect on serotonin transmission, but its mode of action is not typical of other serotonin agents. Trazodone is a serotonin$_2$ receptor antagonist (Richelson, 1993), but chronic treatment causes a desensitization of post-synaptic serotonin receptors (Hingtgen, Hendrie & Aprison, 1984). Furthermore, the trazodone metabolite, m-CPP, is a serotonin$_1$ receptor agonist (Caccia, Ballabio, Samanin, Zanini, & Garattini, 1981; Kahn & Wetzler, 1991). Ritanserin, a potent serotonin$_2$ receptor antagonist, has an effect on sleep similar to that of trazodone (Idzikowski, Mills, & James, 1991). Thus, trazodone's effect on sleep is most likely related to its effect on serotonin.

PTSD AND TRAZODONE

This paper proposes that trazodone has a unique beneficial effect for patients with PTSD, due to its therapeutic action in increasing stage III and IV sleep and prolonging REM latency. Despite clinical lore concerning the benefit of trazodone for these patients, there are no studies describing the effectiveness of trazodone on sleep efficacy in PTSD patients. This report presents the subjective effects and efficacy of trazodone on patients diagnosed with post-traumatic stress disorder and who identify sleep disturbance as a critical factor in their diagnostic symptomatology.

METHOD

Subjects

Subjects were all veterans who presented to the VA Medical Center outpatient clinic in Martinez, California, during 1992 with psychiatric diagnoses which included sleep disturbance for whom trazodone was prescribed (by JWA). Among subjects under the age of 60, mostly Vietman combat Veterans, 20 of a total of 24 had received a diagnosis of PTSD, and 10 of the 33 patients who were over the age of 60, mostly Korean War and World War II veterans, were diagnosed with PTSD. However, 23 of the younger patients and 28 of the elderly patients had histories and clusters of symptoms which met or nearly met DSM-IV criteria for PTSD, and most of these patients described combat related nightmares. All subjects had been prescribed numerous other treatments for their symptoms, but the symptoms were still present. About half of the patients were still taking other psychoactive medications: neuroleptics; antidepressants, including fluoxetine, sertraline, doxepin, and parnate; benzodiazepines, including alprazolam, clonazepam, and diazepam; diphenhydramine; and carbamazepine and valproic acid. Illicit drug use was not documented, and patients with known drug abuse were referred to another clinic.

Design and Procedures

All subjects were initially prescribed trazodone 50mg tablets, to be taken as one at bedtime for three nights and then to increase by one tablet every third night until improvement in sleep was noted. If subjects experienced sedation the next day, they were instructed to return to the prior

dose, or if at 50mg, to reduce to 25mg. Patients achieved variable dosages of trazodone ranging from prn orders (25mg) to 500mg at bedtime. Subjects were reevaluated for both clinical symptoms and the presence of sleep disturbance and nightmares at up to two-week intervals over at least a 3 month period. Two younger subjects did not return for follow-up and one older subject did not take the medication.

RESULTS

The results shown in Table 1 indicate improved subjective ratings of sleep, dreams, and nightmares, as well as other day-time symptoms among PTSD diagnosed patients treated with trazodone regardless of age.

Table I. Trazodone Doses, Efficacy, and Ill Effects by Age of PTSD Patients with Sleep Disturbance

	Age		
	Number of Ss Under Age of 60	Number of Ss Over Age of 60	Total
Therapeutic Doses in Milligrams (HS)			
Prn only	1	3	4
50	3	2	5
100	2	10	12
150	0	3	3
200	6	1	7
300	2	3	5
400	2	0	2
450	0	1	1
500	4	3	7
Total Ss who benefited	20	26	46
Ill Effects (and Dose Levels)			
Hiccups (50mg)	1	0	1
Upset stomach (100mg)	1	0	1
Stomach problems (50mg)	0	1	1
Severe insomnia and restless legs (50mg)	0	1	1
Later exacerbation of ulcer (50mg)	0	1	1
Hypotension, bleeding ulcer (50mg)	0	1	1
Sleep worse, MI (50mg)	0	1	1
Unclear benefit (100mg)	0	1	1
Unclear benefit, schizophrenia (200mg)	0	1	1
Stopped for ill effects	2	6	8
Declined to try, no follow-up	2	1	3
Total group	24	33	57

Among the younger subjects who took the trazodone, 20 of 22 (91%) reported beneficial effects. In this group, 19 of 19 subjects with diagnoses of PTSD who returned for follow-up reported improvements and all of these subjects said that their sleep was better. Of these subjects, seven stated they had no more bad dreams. The other 12 subjects made statements ranging from saying that their sleep was helped to saying the nightmares were 75% better. One non-PTSD, non-responder stopped the drug because of an upset stomach, and a possible PTSD patient stopped because of hiccups.

Of the older subjects who took the trazodone, 26 of 32 (81%) reported beneficial effects. In this group, 9 of 10 of the subjects with PTSD diagnoses reported that their symptoms were better; three said they had no more nightmares, and another three said their sleep was better. The other three reported less disturbing thoughts the next day. The PTSD patient who had no benefit from trazodone also had a diagnosis of schizophrenia. Of the 18 older subjects not diagnosed for PTSD but with stress symptoms, one declined to try the trazodone, but 15 reported that their sleep was better, they were rested the next day, or they had fewer violent dreams. Two were able to stop their benzodiazepines. One had to stop the trazodone because of exacerbation of a stomach ulcer, one reported stomach pains (possible ulcer) and a hypotensive reaction, and one had no clear effects from the medication. Of the five non-PTSD patients with no stress history, one reported better sleep and one said he felt more rested the next day, but three did not benefit from the trazodone, one having a severe bleeding ulcer, one reporting restless legs with severe insomnia, and one reporting worsened sleep and later having a myocardial infarction.

Wives of five of the patients remarked that the patients slept better at night and ceased violent nocturnal behavior. While sleep partner report was infrequent, this source of information may be the most meaningful for assessing this problem (Felembaum, 1988).

Three of the younger subjects with diagnoses of PTSD also had diagnoses of schizophrenia, and all three reported increased sleep with trazodone. The one elderly subject with a diagnosis of PTSD who did not respond to the trazodone also had a diagnosis of schizophrenia.

The most serious adverse effect of trazodone noted in this study was one occurrence of a bleeding ulcer in an elderly patient that seemed temporally related to the use of trazodone. Trazodone is known to upset the stomach, and some individuals may be particularly sensitive to this side-effect, even when the medication is taken with food. Among the elderly, there were two complaints of daytime dizziness including one hypotensive episode, but no reports of falls. However, trazodone can be

associated with serious falls because it can cause significant postural hypotension, particularly in the elderly. There were no reports of priapism, though some of the veterans, younger and elderly, reported some improvement in sexual function, and trazodone increases the duration of nocturnal erection (Saenz de Tejada, Ware, Blanco, Pittard, Nadig, Azadzoi, Krane, & Goldstein, 1991). Of note, the trazodone doses were started out at 50mg at bedtime and increased by no more than 50mg every three days, until a beneficial effect was obtained. Slow increase of dose may decrease the likelihood of side-effects, such as postural hypotension, exacerbation of nightmares, or priapism. Patients who responded well to 25mg or 50mg per day were occasionally noted to have had liver damage by blood tests, perhaps accounting for their enhanced sensitivity to the drug. The study found that patients with liver damage seemed more likely to report sedation the next morning.

DISCUSSION

This study provides preliminary evidence that trazodone benefits both sleep and next day function in PTSD patients. The study is limited in being an open trial and having no standardized treatment or assessment of the patients. However, the sample of patients was broad, including elderly patients, and the benefits were striking.

The effect of trazodone on deepening NREM sleep stages and prolonging REM stages would be of direct benefit to PTSD patients if disruption of sleep occurs more specifically during the early part of the night. One possible explanation is that the beneficial effect may be related to a selective effect of trazodone on serotonergic mechanisms. Deepening of slow sleep (decreasing stages I and II, and increasing stages III and IV) and prolonging the REM latency may allow disruptive sleep mentation whether related or unrelated to reality or memories, to occur without disrupting the normal cycles of sleep or conscious recollections. Accordingly, the sleep mentation would follow its normal course of integrating past memories (Epstein, 1988; Freud, 1955), more normal REM-like sleep would occur to integrate recent memories (Karni, Tanne, Rubenstein, Askenasy, & Sagi, 1994; Rotenberg, 1992), and the patient would get a good night's sleep. Trazodone has a short half-life and, when given at bedtime, would not be expected to affect the patient's functioning the next day. Thus, the decrease of PTSD symptoms the day following trazodone treatment may be attributed to either an improved sleep the night before or the proper integration of stressful memories (dream work), allowing the

patient to address and accommodate the traumatic experience in a deeper state of unconsciousness.

Montgomery et al., (1983) found that trazodone enhanced sleep in subjective quality but not in objective duration. The results of their study showed that sleep improved in quality on trazodone significantly during the first and second weeks of intake, though with significant rebound insomnia on the second withdrawal night. They further found that trazodone halved the frequency of arousals interrupting sleep and reduced the time spent in Stage I of the sleep cycle. Trazodone further increased the duration of slow wave sleep stages (Stages III and IV) with a negative rebound following withdrawal. It reduced the time spent in REM sleep with a rebound above baseline levels after withdrawal. Finally, trazodone did not change total sleep duration nor the time required to fall asleep. These effects would account for the benefit to PTSD-related sleep disruption reported here.

Miller and Miller (1989) reviewed several studies assessing the impact of stressful life events on REM sleep. Support is clearly available for the hypothesis that REM sleep does serve a mastery function which aids in the adaptive process of the individual to accommodate to traumatization and stressful life experience. This process involves an awareness of the stressor itself, and if begun in the conscious state, may lend itself to cognitively disputing or reorganizing the disruption caused by the traumatization (Miller, 1989). Several studies (for example Dement & Hall, 1957; Metcalf & Simons, 1981) have demonstrated that pre-sleep experiences of traumatization alter either dream content or dream affect and produce concomitant alterations in some aspects of the sleep cycle including stage III and IV sleep. When one considers the mechanisms of the flashback experience and sleep mentation during non-REM sleep, the hypothesis of elevation of early night sleep depth in PTSD disturbance symptomatology may help to better understand the mechanisms and processing of sleep disturbance within the PTSD syndrome.

Future efforts need to address the biochemical variability affecting sleep dysfunction in PTSD. Ross et al., (1989) and others (for example March, 1990) have suggested that the problem in PTSD may be in the timely recruitment of the entire ensemble of CNS processes that define REM sleep. An alternative hypothesis argues that the fundamental structure and physiology of all sleep behavior may be disturbed. The relation between sleep phase and nightmares might be better revealed by measurements of both REM and non-REM quantities, other physiological functions, and type of REM and non-REM sleep mentation (Woodward, et al., 1991). Also of importance is the study of the impact of traumatization on non-REM activity as affected by sociocultural factors and variables that

affect the accommodation of stressful life events (Dagan, et al., 1991). What emerges is that the effects of trazodone on sleep would suggest that this medication should be specifically studied for its benefit to PTSD patients, especially those with major insomnia associated with trauma-related nightmares.

REFERENCES

Aghajanian, G. K., & VanderMaelen, C. P. (1982). Intracellular recordings from serotonergic dorsal raphe neurons: Pacemaker potentials and the effect of LSD. *Brain Research, 238,* 463-469.

Aghajanian, G. K. (1992). Serotonin and the action of LSD in the brain. *Psychiatric Annals, 24,* 137-141.

Aghajanian, G. K., Foote, W. E., & Sheard, M. H. (1968). Lysergic acid diethylamide: Sensitive neuronal units in the midbrain raphe. *Science, 161,* 706-708.

American Psychiatric Association (1994). Task Force on DSM-IV. *Diagnostic* and *statistical manual of mental disorders* (4th ed.). Washington, DC: American Psychiatric Association.

Brogden, R. N., Heel, R. C., Speight, T. M., & Avery, G. S. (1981). Trazodone: A review of its pharmacological properties and therapeutic use in depression and anxiety. *Biological Psychiatry, 9,* 117-123.

Brophy, M. H. (1991). Case Report: Cyproheptadine for combat nightmares in post-traumatic stress disorder and dream anxiety disorder. *Military Medicine, 156,* 100-101.

Caccia, S., Ballabio, M., Samanin, R., Zanini, M. G., & Garattini, S. (1981). (-)m-Chlorophenyl-piperozine, a central 5-hydroxytryptamine agonist, is a metabolite of trazodone. *Journal of Pharm. Pharmacol., 33,* 477-478.

Dagan, Y., Lavie, P., & Bleich, A. (1991). Elevated awakening thresholds in sleep stage 3-4 in war-related post-traumatic stress disorder. *Biological Psychiatry, 30,* 618-622.

Davidson, J., Kudler, H. S., Saunders, W. B., Erickson, L., Smith, R. D., Stein, R. M., Lipper, S., Hammett, E. B., Mahorney, S. L., & Cavenar, J. O. (1993). Predicting response to amitriptyline in post-traumatic stress disorder. *American Journal of Psychiatry, 150,* 1024-1029.

Dement, W. C., & Hall, J. (1957). Cyclic variations of EEG during sleep and their relationship to eye movements, body motility and dreaming. *EEG Clinical Neurophysiology, 9,* 673-678.

Epstein, A. W. (1988). Obligatory associations: A function of dreaming. *American Journal of Psychiatry, 145,* 365-366.

Felembaum, A. (1988). Polysomnography as an objective diagnostic tool for PTSD. *Psychosomatics, 29,* 139-140.

Fesler, F. A. Valproate in combat-related posttraumatic stress disorder. *Journal of Clinical Psychiatry, 52,* 361-364.

Freud, S. (1955). *The Interpretation of Dreams.* New York: Basic Books.

Friedman, M. J. (1988). Toward rational pharmacotherapy for post-traumatic stress disorder: An interim report. *American Journal of Psychiatry, 145,* 281-285.

Hefez, A., Metz, L., & Lavie, P. (1987). Long-term effects of extreme situational stress on sleeping and dreaming. *American Journal of Psychiatry, 144,* 344-347.

Hingtgen, J. N., Hendrie, H. C., & Aprison, M. H. (1984). Post-synaptic serotonergic blockade following chronic antidepressive treatment with trazodone in an animal model of depression. *Pharmacology, Biochemistry and Behavior, 20,* 425-428.

Idzikowski, C., Mills, F. J., & James, R. J. (1991). A dose-response study examining the effects of ritanserin on human slow wave sleep. *British Journal of Clinical Pharmacology, 31,* 193-196.

Inman, D. J., Silver, S. M., & Doghramji, K. (1990). Sleep disturbance in post-traumatic stress disorder: A comparison with non-PTSD insomnia. *Journal of Traumatic Stress, 3,* 429-437.

Jacobs, B. L., & Azmitia, E. C. (1992). Structure and function of the brain serotonin system. *Physiological Review, 72,* 165-229.

Kahn, R. S., & Wetzler, S. (1991). m-Chlorophenylpiperazine as a probe of serotonin function. *Biological Psychiatry, 30,* 1139-1166.

Karni, A., Tanne, D., Rubenstein, B. S., Askenasy, J. J. M., & Sagi. D. (1994). Dependence on REM sleep of overnight improvement of a perceptual skill. *Science, 265,* 679-682.

Kramer, M., Schoen, L. S., & Kinney, L. (1984). The dream experience in dream disturbed Vietnam veterans. In B. A. Van de Kolk (Ed.), *Post-traumatic Stress Disorder: Psychological and Biological Sequelae* (pp. 81-95). Washington DC: American Psychiatric Press.

Lipper, S., Edinger, J. D., & Stein, R. M. (1990). Sleep disturbance in PTSD. *American Journal of Psychiatry, 147,* 1697-1698.

March, J. S. (1990). Sleep disturbance in PTSD. *American Journal of Psychiatry, 147,* 1697.

McDougle, C. J., Soutwick, S. M., Charney, D. S., & St. James, D. L. (1991). An open trial of fluoxetine in the treatment of post-traumatic stress disorder. *Journal of Clinical Psychopharmacology, 11,* 325-327.

McGinty, D., & Harper, R. M. (1976). Dorsal raphe neurons: Depression of firing during sleep in cats. *Brain Research, 101,* 569-575.

Mellman, R. A., Randolph, C. A., Brawman-Mintzer, O., Flores, L. P., & Milanes, F. J. (1992). Phenomenology and course of psychiatric disorders associated with combat-related posttraumatic stress disorder. *American Journal of Psychiatry, 149,* 1568-1574.

Metcalf, D. R., & Simons, R. C. (1981). Sleep and dreaming. In R. C. Simon & H. Pardes (Eds.), *Understanding Human Behavior in Health and Illness* (pp. 528-537). Baltimore/London: Williams and Wilkins.

Miller, T. W., & Miller, D. T. (1989). Dreaming: The impact of life stress events. *Psychiatric Developments, 4,* 367-373.

Miller, T. W. (1989). Conceptual and theoretical problems in measuring life stress. In T. W. Miller (Ed.), *Stressful Life Events* (pp. 31-50). Madison, Connecticut: International Universities Press.

Montgomery, I., Oswald, I., Morgan, K., & Adam, K. (1983). Trazodone enhances sleep in subjective quality but not in objective duration. *British Journal of Clinical Pharmacology, 16,* 139-144.

Mouret, J., Lemoine, P., Minuit, M. P., Benkelfat, C., & Renardet, M. (1988). Effects of trazodone on the sleep of depressed subjects—a polygraphic study. *Psychopharmacology, 95,* S37-S43.

Muratorio, A., Maggini, C., Coccagna, G., & Guazzelli, M. (1974). Polygraphic study of the all-night sleep pattern in neurotic and depressed patients treated with trazodone. *Modern Problems in Pharmacopsychiatry, 9,* 182-189.

Rechtschaffen, A. (1973). The psychophysiology of mental activity during sleep. In F. J. McGuigan & R. A. Schoonover (Eds.), *The Psychophysiology of Thinking* (pp. 153-205). New York: Academic Press.

Richelson, E. (1983). Antidepressants and brain neurochemistry. *Mayo Clin Proc, 65,* 1227-1236.

Ross, R. J., Ball, W. A., Sullivan, K. A., & Caroff, S. N. (1989). Sleep disturbance as the hallmark of post traumatic stress disorder. *American Journal of Psychiatry, 146,* 697-707.

Ross, R. J., Ball, W. A., Dinges, D. F., Kribbs, N. B., Morrison, A. R., Silver, S. M., & Mulvaney, F. D. (1994). Rapid eye movement sleep disturbance in posttraumatic stress disorder. *Biological Psychiatry, 35,* 195-202.

Rotenberg, V. S. (1992). Sleep and memory. II: Investigations on humans. *Neuroscience and Biobehavioral Reviews, 16,* 503-505.

Saenz de Tejada, I., Ware, J. C., Blanco, R., Pittard, J. T., Nadig, P. W., Azadzoi, K. M., Krane, R. J., & Goldstein, I. (1991). Pathophysiology of prolonged penile erection associated with trazodone use. *The Journal of Urology, 145,* 60-64.

Scharf, M. B., & Schais, B. A. (1990). Sleep laboratory evaluation of the effects and efficacy of trazodone in depressed insomniac patients. *Journal of Clinical Psychiatry, 51,* 13-17.

Schoen, L., Kramer, M., & Kinney, L. (1984). Auditory thresholds in the dream disturbed. *Sleep Research, 13,* 102.

van der Kolk, B., Blitz, R., Burr, W., Sherry, S., & Hartmann, E., (1984). Nightmares and trauma: A comparison of nightmares after combat with lifelong nightmares in veterans. *American Journal of Psychiatry, 141,* 187-190.

Van Putten, T., & Emory, W. H. (1973). Traumatic neuroses in Vietnam returnees. *Archives of General Psychiatry, 29,* 695-698.

Wells, B. G., Chu, C. C., Johnson, R., Nasdahl, C., Ayubi, M. A., Sewell, E., & Statham, P. (1991). Buspirone in the treatment of post-traumatic stress disorder. *Pharmacotherapy, 11,* 340-343.

Woodward, S. H., Arsenault, E. J., Bilwise, D. L., & Gusman, D. F. (1991). Physical symptoms accompanying dream reports in combat veterans. *Sleep Research, 20,* 153.