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CASE REPORTS

Rapid Eye Movement Sleep Percentage and Duration in Posttraumatic Stress Disorder Vary Dynamically and Inversely With Indices of Sympathetic Activation During Sleep and Sleep Fragmentation

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Posttraumatic stress disorder (PTSD) is associated with activation of the brain fear circuitry. Studies of sleep in PTSD provide a unique window into the relation or connection of sleep physiology and autonomic activation. Serial level 3 home sleep apnea tests (HSATs) (10 HSATs over 1 month) in a patient who was medication free, had PTSD, and had refused positive airway pressure therapy, revealed both percentage of rapid eye movement (REM) sleep (mean \pm standard deviation [SD]: 19.88% \pm 10.11%; range 1.94% to 35.01%) and REM sleep duration (minutes) (mean \pm SD: 73.08 \pm 48.24; range 3.49– 151.59) varied markedly over the 10 HSATs. Both percentage of REM sleep and REM sleep duration correlated negatively with sleep onset latency (r = -.661, P = .037 and r = -.748, P = .013, respectively) and the mean pulse rate during sleep (r = -.667, P = .035 and r = -.771, P = .009, respectively), and positively with sleep efficiency (r = .824, P = .003 and r = .922, P < .001, respectively) and percentage of stage N3 sleep (r = .784, P = .007 and r = .734, P = .016, respectively), an index of parasympathetic tone during sleep. These empirical findings suggest a previously unreported inverse relation of REM sleep with sleep fragmentation and sympathetic activation.

Keywords: arousal, autonomic nervous system, home sleep apnea testing, parasympathetic, posttraumatic stress disorder, PTSD, rapid eye movement sleep, REM sleep, sleep fragmentation, slow wave sleep, stage N3 sleep, sympathetic

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INTRODUCTION

The central role of rapid eye movement (REM) sleep in posttraumatic stress disorder (PTSD) is well recognized.¹⁻⁷ A wide range of REM sleep abnormalities have been reported in PTSD ranging from REM sleep fragmentation to preserved and enhanced REM sleep continuity following trauma.⁷ The development of PTSD after traumatic injury has been associated with REM sleep fragmentation⁶ and it has been proposed that increases in REM sleep percentage and segment continuity reflect an adaptive process that aids in the recovery from PTSD.^{3,7} A higher baseline REM sleep level has been shown to be associated with reduced fear conditioning in humans under experimental conditions.⁸ A meta-analysis of 20 polysomnographic studies of patients with PTSD⁹ observed increased REM sleep density in PTSD and the importance of the phasic component of REM sleep⁷ in PTSD has been stressed.

The following is a case study of a patient with PTSD who agreed to undergo serial home sleep apnea tests (HSATs), consisting of 10 HSATs over a period of 1 month while she was experiencing an acute exacerbation of her PTSD. During this period, the patient refused to take any medications or use positive airway pressure (PAP) therapy. To my knowledge there are no reported prospective studies of serial REM sleep measures during a phase of acute activation of PTSD. Approval to present this case study was obtained from the Office of Research Ethics, University of Western Ontario, London, Ontario, Canada.

REPORT OF CASE

The patient was a 40-year-old woman (height of 5 feet 4 inches, weight 210 pounds), in whom PTSD was first diagnosed at age 32 years. She was referred by her family physician with an acute exacerbation of her PTSD over the previous 6 months. The patient presented with complaints of insomnia, waking up with a sensation that someone was choking her, hypervigilance, acute anxiety, flashbacks, and nightmares about her childhood sexual abuse, following an unexpected encounter with a perpetrator who had sexually abused her over a period of several years during her early childhood. The patient, who did not have a history of traumatic brain injury, reported tinnitus and a heightened sensitivity to sounds in conjunction with exacerbations of her PTSD. Her symptoms were interfering with her ability to work and she had to take medical leave. The patient was fearful that the perpetrator would once again assault her and/or her children, even though she was able to acknowledge that her fears were irrational because she was now an adult who was capable of defending herself. The patient had undergone an in-laboratory level 1 sleep study about 4 months before her consultation, and the following are some of the results of the level 1 sleep study:

- total sleep time: 4 hours, 2 minutes
- sleep onset latency: 13 minutes
- arousal index: 57.5 events/h
- sleep efficiency: 62%

- mean heart rate during sleep: 97 beats/min
- respiratory disturbance index (RDI) of 82.1 events/h
 - 34.4 apnea (33.0 obstructive, 1.2 mixed, 0.2 central)
 - 46.4 hypopnea
 - 1.2 respiratory effort-related arousal events/h
- sleep stages:
 - stage R sleep 0%
 - stage N1 sleep 60%
 - stage N2 sleep 39%
 - stage N3 sleep 0%

After the level 1 study, the patient was unable to tolerate PAP therapy despite several attempts mainly due to feelings of suffocation and restriction.

The patient presented to the practice with moderately severe PTSD symptoms and her Clinician Administered PTSD Scale for DSM-5 (CAPS-5) score was 67 (past month, described elsewhere¹⁰). She completed a battery of questionnaires (described elsewhere¹⁰); her Insomnia Severity Index (ISI) score was 25 (consistent with severe insomnia¹⁰); her overall PTSD Checklist for DSM-5 (PCL-5) score was 71 (cutoff score of 33 used to screen for PTSD¹⁰), with the following cluster scores (number of items per cluster rated as $\geq 2/\text{total no. of items}$) which were both consistent with a PTSD diagnosis: cluster B (Intrusion, total score 19) (5/5); cluster C (avoidance, total score 8) (2/2); cluster D (negative alterations of cognition and mood, total score 25) (8/8); and cluster E (alterations in arousal and reactivity, total 19) (5/6). Prior to the recent exacerbation the patient had successfully managed her PTSD with psychotherapy alone, from her social worker. When the patient was first seen in my practice, she initially insisted that she should be able to manage her symptoms with psychotherapy alone and refused any medications including antihypertensive medications or PAP therapy. She agreed, however, to undergo multiple nights of HSATs (using the WatchPAT 200, Itamar, Caesarea, Israel)¹⁰ and in fact liked the fact that she could monitor her own sleep physiology. The WatchPAT200 is categorized as level 3 by the American Academy of Sleep Medicine and is used unattended in the patient's home.¹⁰ It uses peripheral arterial tonometry (PAT), pulse oximetry, heart rate, and actigraphy to detect obstructive sleep apnea, arousals from sleep, and sleep stages, using the proprietary zzzPAT software (detailed description and validation studies assessing correlation of sleep indices such as RDI, arousals from sleep and sleep staging, between PAT devices and level 1 in-laboratory polysomnography have been described elsewhere¹⁰).

The following are the results of 10 HSATs carried out over a period of 1 month during a period when the patient was treated with only standard psychotherapeutic interventions for emotional regulation and stabilization. The REM sleep variables obtained from the 10 nights of sleep recordings were as follows: mean \pm SD percentage REM sleep: 19.88% \pm 10.11% (range 1.94% to 35.01%) and mean \pm SD REM duration (minutes) 73.08 \pm 48.24 (range 3.49–151.59). **Table 1** provides the means and the minimum to maximum ranges of some of the major sleep physiological variables associated with arousal and autonomic activation during sleep. Patients with PTSD tend to develop some degree of sleep-disordered breathing (SDB) due

to factors such as postarousal ventilatory instability secondary to the autonomic activation, and there usually tends to be a bidirectional relationship between SDB and PTSD severity. In this patient the possible confounding effect of the SDB was accounted for by statistically partialling out the effect of RDI (partial correlation coefficients provided in Table 1). In this exploratory study, the relation between the REM sleep measures and the sleep physiological measures related to arousal and activation was examined with scatter plots (eg, Figure 1 and Figure 2) and Pearson product moment correlations only. The night-to-night variation in the RDI, which was a potentially important confounding factor, was further evaluated by examining the exact study dates for each of the 10 HSATs (Figure 1). Statistical Package for the Social Sciences version 24 (IBM Corp, Armonk, New York, United States) was used for all statistical analyses.

DISCUSSION

PTSD is associated with activation of the brain fear circuitry and autonomic arousal in PTSD has been most consistently associated with functional hypoactivation of the medial prefrontal cortex; this hypoactivation varies positively with the level of arousal, and is associated with hyperactivity of the amygdala which can directly affect sleep physiology including REM sleep.⁴ A study of sleep physiology in a patient with PTSD experiencing an acute exacerbation of their PTSD therefore can provide an unique window into the changes in sleep physiology across a wide range of autonomic nervous system activation. The results from this study (Table 1) suggest that the percentage and duration of REM sleep in PTSD are both negatively associated with the level of sympathetic activation (or positively associated with the parasympathetic tone during sleep) and sleep fragmentation (Table 1, Figure 2) (or positively associated with indices of sleep consolidation) in a dynamic and graded manner. This results in a varying percentage of REM sleep that decreases in relation to increasing sympathetic tone. REM sleep is also positively related to indices of sleep consolidation (which also decreases in relation to increased sympathetic tone and sleep fragmentation). The variation in percentage of REM sleep and duration of REM sleep is likely driven in part by homeostatic factors related to sleep fragmentation and resultant relative sleep deprivation, which are caused by the acute and often recurrent sympathetic activation in PTSD. There tends to be a bidirectional relationship between SDB and PTSD severity, and it is noteworthy that most of the partial correlations stayed significant after controlling for the effect of the RDI (Table 1). After controlling for the RDI, the direct relation between the REM sleep parameters and stage N3 sleep was no longer significant and the mean pulse rate was no longer significantly inversely related to percentage of REM sleep (Table 1). This is likely because the patient had severe sleep apnea that accounted for a significant portion of the autonomic activation that contributed to these relationships. To my knowledge these empirical relationships and the dynamic and negative associations of percentage and duration of REM sleep with indices of sympathetic tone and sleep fragmentation in PTSD have not been previously reported, and further

Duration of REM Sleep

Date of HSAT	REM Sleep (%)	TST (minutes)	SOL (minutes)	Mean Pulse (beats/min)	Awakenings (events/h)	Sleep Efficiency (%)	Stage N3 Sleep (%)	Stage N1 and N2 Sleep (%)	RDI (events/h)
10/07/2015	11.83	347.00	42.00	95	15	64.60	11.94	76.23	45.60
10/16/2015	1.94	180.00	111.00	101	14	42.65	3.34	94.71	61.10
10/21/2015	17.16	370.00	47.00	96	18	64.34	12.57	70.27	52.60
10/22/2015	18.34	387.00	76.00	92	21	66.17	18.60	63.06	37.60
10/24/2015	22.56	334.00	56.00	94	13	66.65	23.91	53.53	21.70
10/27/2015	15.37	315.00	23.00	94	24	63.49	8.24	76.39	46.00
10/28/2015	25.90	444.00	18.00	95	11	78.06	19.79	54.31	28.10
10/29/2015	16.11	152.00	112.00	104	11	38.34	13.17	70.72	37.20
11/02/2015	35.01	433.00	15.00	90	11	83.68	20.20	44.79	28.10
11/05/2015	34.59	396.00	31.00	92	9	81.57	17.81	47.60	35.20
Mean ± SD (Range)	19.88 ± 10.11 (1.94–35.01)	335.80 ± 98.43 (152.00-444.00)	53.10 ± 35.89 (15.00–112.00)	95.30 ± 4.24 (90–104)	14.70 ± 4.88 (9–24)	64.96 ± 14.95 (38.34–83.68)	14.96 ± 6.24 (3.34–23.91)	65.16 ± 15.49 (44.79–94.71)	39.32 ± 12.12 (21.70–61.10)

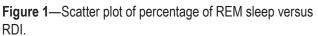
Table 1—Sleep physiological variables related to sleep fragmentation and sympathetic activation and their correlation with percentage of REM sleep and REM sleep duration in a patient with PTSD who underwent 10 HSATs.

	TST (minutes)	SOL (minutes)	Mean Pulse (beats/min)	Awakenings (events/h)	
Percentage of REM Sleep	r = .706, P = .022 (r = .593, P = .093)	r =661, P = .037 (r =591, P = .094)	r =667, P = .035 (r =559, P = .118)	r =458, P = .183 (r =228, P = .555)	
Duration of REM Sleep	r = .831, P = .003 (r = .779, P = .013)	r =748, P = .013 (r =700, P = .036)	r =771, P = .009 (r =707, P = .033)	r =410, P = .239 (r =185, P = .637)	
	Sleep Efficiency (%)	Stage N3 Sleep (%)	Stage N1 and N2 Sleep (%)	RDI (events/h)	
Percentage of REM Sleep	r = .824, P = .003 (r = .744, P = .021)	r = .784, P = .007 (r = .309, P = .419)	r =968, P < .001 (r =958, P < .001)	<i>r</i> =764, <i>P</i> = .010	

Table presents values of sleep physiological variables related to sleep fragmentation and sympathetic activation and their correlation with percentage and duration of REM sleep (including partial correlation obtained after controlling for the effect of the RDI) in a patient with PTSD, who refused positive airway pressure therapy, and was medication free. Correlation values presented as Pearson r (partial r after controlling for RDI) and P values (if assumption that measures are independent is satisfied). The correlation coefficient provides an index of the magnitude of the effect size (population correlations of .10 defined as a small effect, .30 as a medium effect, and .50 as a large effect). HSAT = home sleep apnea test, PTSD = posttraumatic stress disorder, RDI = respiratory disturbance index, REM = rapid eye movement, SD = standard deviation, SOL = sleep onset latency, TST = total sleep time.

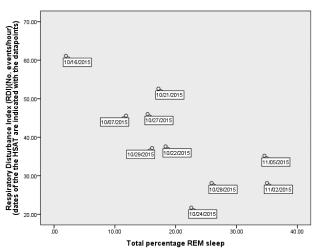
r = .734. P = .016

(r = .390, P = .299)



r = .922. P < .001

(r = .891, P = .001)



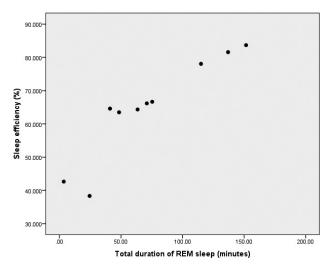
Scatter plot of percentage of REM sleep versus RDI over a period of 1 month in a patient with PTSD who was medication free and had refused positive airway pressure therapy. Pearson r = -.764, P = .010. PTSD = posttraumatic stress disorder, RDI = respiratory disturbance index, REM = rapid eye movement.

Figure 2—Scatter plot of total duration of REM sleep versus sleep efficiency.

r = −.923. P < .001

(r = -.925, P < .001)

r = -.676, P = .032



Scatter plot of total duration of REM sleep versus sleep efficiency over 1 month in a patient with PTSD who was medication free. Pearson r = .922, P < .001. PTSD = posttraumatic stress disorder, REM = rapid eye movement.

empirically support the proposition that increases in REM sleep percentage and segment continuity reflect an adaptive process that aids in the recovery from PTSD.^{3,7}

Both the percentage of REM sleep (mean ± SD $19.88\% \pm 10.11\%$; range 1.94% to 35.01%) and REM sleep duration (mean \pm SD 73.08 \pm 48.24; range 3.49–151.59 minutes) varied significantly over the course of the 1-month period and 10 HSATs. The inverse correlations of both percentage REM sleep and REM sleep duration with direct indices of sympathetic activation during sleep (Table 1) for example, mean pulse rate during sleep and percentage of stage N1 and N2 sleep, suggest that the variation in percentage of REM sleep and REM sleep duration were most likely inversely related to the changes in sympathetic autonomic activation in PTSD (which is also related in a bidirectional manner to the RDI). This may explain the relatively wide range of REM sleep measures⁷ that have been previously reported in PTSD, possibly reflecting the varying levels of autonomic activation in the various study participants at different time points.⁷ The direct and robust correlations of percentage of REM sleep (Pearson r = .784, P = .007) and REM sleep duration (Pearson r = .734, P = .016) with percentage of stage N3 sleep is quite remarkable and suggests a strong positive relation between the REM sleep indices and stage N3 sleep, which is an index of the parasympathetic tone during sleep. To my knowledge this relationship has not been previously reported. In this patient with severe sleep apnea, the sympathetic activation underlying this relationship was largely related to the RDI, as the correlations between REM sleep indices and stage N3 sleep were no longer significant after the effect of the RDI was statistically partialled out (Table 1). Similarly, the previously unreported strong and negative correlations of both percentage of REM sleep (Pearson r = -.968, P < .001) and REM sleep duration (Pearson r = -.923, P < .001) with stage N1 and N2 sleep further support the relation between the REM sleep indices and the parasympathetic tone during sleep, as does the inverse relation of the REM sleep indices with the RDI (Table 1).

A high sympathetic tone tends to be associated with greater sleep fragmentation. The results further indicate a strong positive association of both percentage of REM sleep (Pearson r = .824, P = .003) and REM sleep duration (Pearson r = .922, P < .001; **Figure 2**) with sleep efficiency, a direct measure of sleep consolidation. To my knowledge this strong and robust empirical relation has not been previously demonstrated and supports earlier observations.^{3,6,7} The negative correlations of the REM sleep indices with number of awakenings per hour (**Table 1**) were not statistically significant; it is possible that because the patient was acutely distressed by the thought of being attacked by the perpetrator, additional factors related to her overall level of hypervigilance, in addition to REM sleep, played a role in the actual number of awakenings per hour that were experienced during the acute PTSD exacerbation.

The results of this study possibly shed some light on the apparently wide range of REM sleep-related findings in PTSD,⁷ as REM sleep indices in PTSD may vary inversely with the level of sympathetic activation in the patient and appear to be dynamically and positively related to the sleep physiological indices of parasympathetic tone and sleep consolidation. The relationships observed in this case study (**Table 1**) are most likely bidirectional and mediated by the underlying sympathetic nervous tone. It was not possible to examine the relation of REM sleep density⁹ and phasic REM sleep in this patient with the WatchPAT200.¹⁰ Phasic REM sleep is associated with sympathetic activity and it would be important to examine its relation to the indices of sympathetic activation and sleep consolidation that are addressed in this case report. These initial findings need to be followed up with future studies using level 1 polysomnography.

ABBREVIATIONS

CAPS-5, Clinician Administered PTSD Scale for DSM-5 DSM, Diagnostic and Statistical Manual of Mental Disorders HSAT, home sleep apnea test ISI, Insomnia Severity Index PAP, positive airway pressure PAT, peripheral arterial tonometry PCL-5, PTSD Checklist for DSM-5 PTSD, posttraumatic stress disorder RDI, respiratory disturbance index REM, rapid eye movement SD, standard deviation

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DISCLOSURE STATEMENT

The author has seen and approved the manuscript. The author reports no conflicts of interest.