



Original Article

REM sleep characteristics of nightmare sufferers before and after REM sleep deprivation

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ARTICLE INFO

Article history:

Received 23 September 2008

Received in revised form 9 December 2008

Accepted 12 December 2008

Available online 14 December 2009

Keywords:

Parasomnias

Nightmares

REM sleep deprivation

REM sleep propensity

REM density

First night effect

ABSTRACT

Objectives: To examine whether disrupted regulation of REM sleep propensity is implicated in nightmare (NM) pathophysiology.

Background: Heightened REM propensity induced by REM sleep deprivation is belied by increases in REM %, REM density and the dreamlike quality of dream mentation during post-deprivation recovery sleep. Compromised regulation of REM sleep propensity may be a contributing factor in the pathophysiology of frequent NMs.

Methods: A preliminary study of 14 subjects with frequent NMs (≥ 1 NM/week; 27.6 ± 9.9 years) and 11 healthy control subjects (< 1 NM/month; 24.3 ± 5.3 years) was undertaken. Subjects completed home sleep/dream logs and underwent three nights of polysomnographic recording with REM sleep deprivation on night 2. Group differences were assessed for a battery of REM sleep and dream measures on nights 1 and 3.

Results: Several measures, including #skipped early-night REM periods, REM latency, REM/NREM cycle length, early/late REM density, REM rebound, late-night REM% and dream vividness, suggested that REM sleep propensity was abnormally low for the frequent NM group throughout the 3-day study.

Conclusions: Findings raise the possibility that REM anomalies recorded from NM sufferers sleeping in the laboratory environment reflect a disruption of one or more endogenous regulators of REM sleep propensity.

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1. Introduction

The relatively few studies having addressed the pathophysiology of idiopathic nightmares (NMs) consider NMs to be a disturbance of autonomic activity during REM sleep. One early investigation of a mixed sample of idiopathic and post-traumatic NM patients [1] concluded that NM episodes are accompanied by autonomic changes such as elevated heart rate (HR), respiration rate and eye movement density [1]. Our group [2] replicated only the facts that NM episodes occur during REM sleep and are accompanied by elevated HR, but not by changes in respiration or eye movement density. In a second PSG study [3] we found no differences between NM sufferers and controls who slept in the laboratory on measures of REM sleep latency, REM efficiency and REM density.

An alternative view is that the fundamental REM sleep disturbance in NMs is a disruption of REM sleep propensity (REM 'pressure') which, in turn, leads to intermittent autonomic irregularities. REM propensity, as measured by REM% or REM time, is typically

lowest early in the sleep interval, increases across the night, and reaches a high point in the morning—when most NMs are reported to take place [4]. This normal variation of REM propensity over time is determined by at least three endogenous factors: (1) an ultradian (90-min) REM-NREM oscillator, (2) a circadian process linked to core body temperature with a morning ($\sim 8:00$ am) acrophase, and (3) a sleep-dependent process that increases gradually across the night [5]. Any of these factors may be disrupted by exogenous influences such as sleep deprivation, altered work schedules, jet lag, medications, or illness. For example, if healthy human subjects are deprived of REM sleep early in the night, REM propensity will be disproportionately increased later in the night [6]. The latter manifests as atypically high levels of REM% or REM attempts [7] and an increase in the dreamlike quality of REM sleep and hypnagogic dreaming [8] among other changes. In rats, REM sleep deprivation has been seen to heighten emotional drive, i.e., aggressivity [9]. Thus, it may be that abnormally high REM propensity—brought about by disruption of any of the three endogenous regulating factors—underlies the occurrence of NM episodes in susceptible individuals. Moreover, experimentally increasing REM propensity with REM sleep deprivation, forced desynchrony [10] or other procedures may be means of provoking NMs during recovery sleep

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and rendering their physiological signs more accessible to laboratory study.

In the present experiment, we assessed whether measures of REM propensity before and after a partial REM sleep deprivation procedure would differentiate subjects afflicted with frequent NMs from those with few NMs. We anticipated that frequent NM sufferers would have higher levels of REM propensity on pre-deprivation measures and that deprivation would increase these levels to a greater degree—perhaps even eliciting NM episodes in the laboratory. In short, we anticipated that increases in REM propensity would serve as a biomarker of idiopathic NM pathology.

2. Methods

2.1. Subjects

Individuals with frequent NMs ($n = 14$) and healthy comparison subjects with infrequent NMs ($n = 11$) were recruited by media advertisements and through contacts with laboratory staff. The groups were comparable in age and gender composition (see Table 1). Subjects were not seen in a clinical context, were not currently following psychotherapy, were not seeking treatment and were not given extensive psychiatric evaluations. During intake, none reported having neurological, psychiatric or sleep disorders, and none reported having prior traumatic experiences. Two NM subjects reported taking medications known to affect sleep. One who suffered from severe migraine headaches took the beta-blocker propranolol (Inderal). The other, who suffered from fibromyalgia and hypothyroidism, took a combination of amitriptyline (Elavil), bupropion (Wellbutrin), clonazepam (Rivotril), quetiapine (Seroquel) and levothyroxine (Synthroid). These two subjects were retained for statistical comparisons except for the post hoc analyses of non REM-skipping subjects, as both were observed to skip early-night REM periods (see later section). Subjects in the NM group reported recalling at least 1 NM/week for at least 6 months; subjects in the control (CTL) group reported recalling less than 1 NM/month. The protocol was approved by the hospital

Ethics Review Board. Subjects were aware they would be paid \$25 per laboratory recording night as well as their parking and breakfast expenses. After a complete description of the study procedures was given, written informed consent was obtained.

2.2. Home sleep/dream log

Prior to sleeping in the laboratory, subjects were provided with definitions in which bad dreams (emotionally negative dreams) were distinguished from nightmares (emotionally negative dreams that wake you up) on the basis of whether an awakening from sleep was triggered. They then completed daily home logs in which they rated various qualities of their sleep and dreams, wrote out their dreams and indicated whether they had been awakened by them. Most subjects (NM: 11; CTL: 8) completed logs for at least 6 days; 2 others from each group completed them for 4 and 5 days respectively; one subject from each group did not complete this task.

Two log items assessed how well subjects had slept (0 = very poorly; 9 = very well) and how rested they felt in the morning (0 = very poorly; 9 = very well). Five items assessed dream recall clarity, vividness of colors, dreamed anxiety, personal impact of the dream and the inhibition/ineffectiveness of dreamed actions (0 = no report to rate; 1 = not at all; 9 = very). Logs were subsequently evaluated by a judge blind to group membership who classified reports as either dreams (mainly positive affect), bad dreams (mainly negative affect) or nightmares (mainly negative affect with awakening) based upon subjects' emotional ratings and their reports of whether they had woken up after the dream.

2.3. Laboratory procedures

Subjects slept for three consecutive nights in a comfortable, sound-shielded room, including baseline (N1), REM deprivation (N2) and REM recovery (N3) nights. On arriving for N1, subjects completed the Beck Depression Inventory (BDI) [11], the State Trait Anxiety Inventory-State subscale (STAI-S) [12], the Symptom

Table 1

Clinical characteristics and subjective ratings on home sleep/dream logs for subjects with frequent nightmares and controls.

	Nightmares ($N = 14$)		Controls ($N = 11$)		t/χ^2	p
	Mean	(SD)	Mean	(SD)		
Age	27.6	(9.9)	24.3	(5.3)	0.996	0.330
Gender (M:F) ^a	5:9		3:8		0.653	1.000
Beck Depression Inventory ^b	10.9	(7.56)	2.9	(2.07)	2.892	0.008
Spielberger State Anxiety ^c	39.2	(12.40)	28.4	(3.78)	2.656	0.014
SCL-90-R Global Severity Index ^d	61.2	(10.82)	48.7	(10.22)	2.874	0.009
SCL-90-R Positive Symptom Total ^d	59.5	(8.80)	49.0	(11.07)	2.599	0.016
Impact of Event Scale-Revised	26.1	(17.91)	n/a			
Nightmare Distress Questionnaire	38.3	(6.99)	n/a			
<i>Home sleep/dream log</i>						
Sleep: how well ^e	4.34	(1.85)	6.62	(1.29)	-3.311	0.003
Sleep: how rested ^e	3.78	(1.89)	5.62	(1.60)	-2.469	0.022
Number reporting nightmares ^a	9/13		2/10		5.490	0.036
Nightmares reported/week	1.63	(1.70)	0.20	(0.44)	2.572	0.018
Number reporting bad dreams ^a	11/13		8/10		0.772	1.000
Bad dreams reported/week	1.97	(1.46)	1.68	(1.59)	0.444	0.661
Dream recall ^f	5.43	(1.51)	4.63	(1.33)	1.334	0.197
Dream vividness ^f	4.78	(1.65)	3.57	(1.37)	1.887	0.073
Dream anxiety ^f	5.15	(1.92)	2.40	(1.34)	3.853	0.001
Dream inhibition/ineffectuality ^f	4.32	(1.90)	1.84	(1.47)	3.415	0.003

^a Fisher exact test (two-tailed).

^b $n = 10$ CTL subjects for this questionnaire.

^c Scores transformed $\log(1 + x)$, $n = 13$ NM subjects for this questionnaire.

^d T -scores calculated from male and female non-patient B norms.

^e Response scale: 0 = very poorly; 9 = very well, $n = 13$ NM subjects and $n = 10$ CTL subjects.

^f Response scale: (0 = no recall) 1 = not at all; 9 = very, $n = 13$ NM subjects and $n = 9$ CTL subjects; n/a = test not administered.

Checklist 90-Revised (SCL90-R) [13] and a revised version of the Sleep Disorders Questionnaire [14] (SDQ-R; not reported here). NM subjects completed the Nightmare Distress Questionnaire [15], a 13-item instrument measuring the suffering and distress caused by NMs and the Impact of Event Scale-Revised (IES-R) [16,17] in reference to a stressful event. All subjects were fitted with polysomnography electrodes and allowed to sleep undisturbed until the scheduled morning awakening. Audio-visual surveillance was constant throughout the night.

On N2, subjects were deprived of REM sleep by enforced awakenings (80-dB, 500-Hz, 0.5-s tone) from every REM sleep episode after the second, beginning 5 min after appearance of the first rapid eye movement of each episode. They were asked to report and rate sleep mentation and then allowed to return to sleep. This relatively mild deprivation procedure was employed because more severe REM deprivation causes, in many subjects, multiple REM attempts later in the night and requires repeated awakenings [6]; these severely disrupt sleep continuity and are difficult to control in the comparison group.

On N3, subjects were administered a sleep onset mentation sampling procedure [8] during which their EEG was monitored for sleep onset substages 4 and 5 [18]. These substages are associated with spontaneous dreamlike imagery [19] that intensifies with increased REM propensity [8]. When five continuous seconds of either substage were identified, subjects were signalled with a tone and asked to report and rate their mentation on two 9-point scales for *visual intensity* and *dreamlike quality* (1 = none at all; 9 = extremely). They were then allowed to return to sleep. Awakenings were repeated until eight samples had been collected and subjects then slept undisturbed until morning. Mentation ratings for all of a subject's samples containing imagery (at least one instance of hallucinated sensory experience or thought) were averaged.

2.4. Sleep recordings

Subjects were fitted with a 14-channel recording montage that included four referential EEG channels from the international 10–20 electrode placement system (C3, C4, O1, O2), four channels for left/right and vertical/horizontal eye movements, four EMG channels for chin and right side forearm extensor, leg tibialis and forehead corrugator muscle activities, one cardiac channel for bipolar ECG, and one respiration channel for nasal thermistance.

Tracings were scored and artifacts removed by trained polysomnographers applying standard criteria and using Harmonie v6.0b [20] software. An inhouse program was used to output standard sleep stage variables and the following REM sleep measures: *REM latency*, *REM/NREM cycle length*, *#REM periods*, *REM%*, *REM% by thirds of night*. Additionally, *#skipped early-night REM periods* were determined using inhouse criteria [21] that required a trained judge to determine if the sleep hypnogram suggested absence of an expected REM period at the descending arc of the first two stage 2–3–4 sequences. Further, *REM density* was scored from the EOG channels by a trained polysomnographer using a subset of 11 NM and 10 CTL subjects for both early night (cycles 1 or 2) and late night (cycle 3 or 4) REM periods. Three NM subjects who skipped early-night REM periods were dropped from the early-night REM density analyses. *REM density* was calculated as $\# \text{individual eye movements} / \# \text{seconds elapsed in the REM period}$ [22].

2.5. Statistical analyses

Subject characteristics and psychopathology questionnaires were compared using independent *t*-tests. Most N1 and N3 measures were compared using 2×2 ANOVAs with group (NM, CTL) as a between-groups factor and night (N1, N3) as a repeated mea-

sure factor. REM% was assessed in greater detail by adding third of the night (first, second, third) as a second repeated measure factor to this ANOVA and using a $\log(\text{REM}\% + 1)$ transform to correct distributions in some cells. When Levene tests indicated significant ($p < 0.05$) group differences in homogeneity of variance for either N1, N3 or both combined (and thus proscribed the use of an ANOVA), effects involving group were evaluated independently using two-tailed *t*-tests with separate variance estimates. Chi-square tests were used to assess frequency distributions of skipped early-night REM periods. *p*-Values were set at 0.05 for each analysis.

3. Results

3.1. Subject characteristics

As shown in Table 1, the NM group scored higher than the CTL group on depression ($p = 0.008$) and state anxiety ($p = 0.014$). The NM group also scored higher on the SCL-90-R Global Severity ($p = 0.009$) and Positive Symptom ($p = 0.016$) scales. Also shown in Table 1, more NM than CTL subjects reported at least one NM on the home log task ($p = 0.036$), and the mean number of NMs/week was higher for the NM than for the CTL group ($p = 0.018$). Of the 4 NM subjects not reporting NMs, one reported 4 and one reported 5 bad dreams/week respectively, i.e., 1–2 SD above the group mean. The two others reported NM distress scores (30, 35) and/or IES-R scores (26, 12) that were large enough to warrant keeping them in the NM group. While NM and CTL groups rated pre-laboratory dream recall clarity ($p = 0.197$) and vividness ($p = 0.073$) as relatively similar, the NM group rated dreams as being more anxious ($p = 0.001$) and containing more inhibition/ineffectuality ($p = 0.003$) than did the CTL group. The NM group also reported sleeping worse ($p = 0.003$) and feeling less rested in the morning ($p = 0.022$) than did the CTL group.

The mean NM distress score of the NM group (38.3 ± 7.0 ; range: 28–52) was higher than that of idiopathic NM patients (34.8 ± 6.8) reported in a previous study from our group [3] and more similar to that of the post-traumatic NM sufferers in that study (39.9 ± 7.4). The IES-R scores of our current NM group were marginally elevated (26.1 ± 17.9) relative to the different clinical cut-offs of 25, 30 and 33 suggested by previous authors [17,23]. Four of our NM subjects scored above these cut-offs (i.e., IES-R scores = 34, 34, 52, 65); nonetheless, the events they rated concerned non-traumatic events such as spousal conflict and school-related problems.

3.2. General sleep characteristics

NM and CTL groups differed only marginally on one NREM sleep measure (Table 2); a marginal group main effect ($F_{1,23} = 2.935$, $p = 0.100$) indicated that the NM group ($M = 15.46 \pm 9.18$) had fewer awakenings than did the CTL group ($M = 20.59 \pm 9.99$). This difference was evident for N1 ($F_{1,23} = 8.609$, $p = 0.007$) but not for N3 ($F_{1,23} = 0.630$, $p = 0.435$). As expected, however, night main effects were observed for almost all sleep measures; %Stage 1 and %Stage 3–4 were the only exceptions.

3.3. REM sleep deprivation and rebound effects

As shown in Fig. 1, the REM deprivation procedure successfully reduced REM% for the NM group from $17.8\% \pm 7.80$ on N1 to $13.1\% \pm 5.84$ on N2 ($F_{1,23} = 11.550$, $p = 0.002$). REM% was similarly reduced for CTL subjects from $19.0\% \pm 4.16$ on N1 to $13.2\% \pm 4.27$ on N2 ($F_{1,23} = 14.227$, $p = 0.001$). No group differences in REM% were observed for either night.

Table 2

General sleep architecture and REM sleep measures assessed for subjects with frequent nightmares and controls in the group (nightmare, control) × night (night 1, night 3) ANOVA design.

	Nightmares (N = 14)		Controls (N = 11)		Group × night effect		Group effect p	Night effect p
	Night 1 Mean (SD)	Night 3 Mean (SD)	Night 1 Mean (SD)	Night 3 Mean (SD)	F	p		
<i>General sleep architecture measures</i>								
Total sleep time (min)	428.7 (57.6)	382.3 (63.1)	412.3 (45.0)	370.2 (70.3)	0.021	0.887	0.457	0.007
Sleep efficiency (%)	95.0 (5.1)	97.2 (2.6)	94.8 (4.5)	97.9 (1.1)	0.200	0.659	0.847	0.020
Awakenings (#) ^a	17.3 (7.7)	13.6 (10.4)	25.8 (8.3)	15.4 (8.8)	0.239	0.630	0.100	0.003
Wake after sleep onset (min) ^a	21.1 (23.4)	10.8 (11.6)	22.5 (22.6)	8.0 (4.7)	0.112	0.741	0.795	0.001
Sleep latency (min) ^a	15.3 (10.6)	7.4 (4.9)	12.8 (9.0)	6.0 (3.4)	0.035	0.853	0.505	0.000
Latency to persistent sleep (min) ^a	23.6 (16.5)	12.0 (8.5)	19.1 (12.9)	7.9 (5.5)	0.044	0.836	0.335	0.000
Latency to Stage 2 (min) ^a	20.4 (11.6)	11.0 (5.5)	18.3 (12.4)	8.9 (4.8)	0.010	0.920	0.470	0.000
Latency to Stage 3–4 (min) ^a	16.4 (10.2)	13.1 (7.8)	17.7 (8.8)	12.6 (3.0)	0.008	0.929	0.549	0.016
Awake (%) ^a	4.7 (5.0)	2.7 (2.7)	5.1 (4.6)	2.1 (1.1)	0.279	0.603	0.831	0.004
Stage 1 (%) ^a	6.8 (4.2)	6.2 (4.1)	6.1 (2.9)	4.1 (2.0)	0.920	0.347	0.444	0.103
Stage 2 (%)	54.7 (9.4)	48.6 (10.1)	53.0 (4.8)	47.4 (8.3)	0.019	0.891	0.640	0.003
Stage 3–4 (%)	20.7 (7.6)	22.7 (7.7)	21.8 (6.7)	21.0 (8.0)	0.866	0.362	0.915	0.682
<i>REM sleep measures</i>								
Latency to REM (min)	131.6 (64.6)	73.4 (33.5)	70.7 (12.4)	49.3 (18.0)	2.248	0.147	0.000 ^a	0.000 ^b
REM/NREM cycle duration (min)	115.3 (29.4)	87.6 (15.8)	84.8 (8.8)	80.0 (7.5)	3.781	0.064	0.000 ^a	0.000 ^b
REM periods (#)	3.6 (0.9)	3.8 (1.1)	4.8 (0.8)	4.2 (1.1)	2.390	0.136	0.007	0.451
Early REM density (#/sec of REM)	0.131 (0.060)	0.078 (0.042)	0.126 (0.089)	0.067 (0.047)	0.073	0.790	0.781	0.000
Late REM density (#/sec of REM)	0.159 (0.112)	0.145 (0.075)	0.224 (0.122)	0.112 (0.046)	4.451	0.048	0.634	0.014
REM (%)	17.8 (7.8)	22.5 (7.2)	19.0 (5.7)	27.4 (5.8)	3.363	0.079	0.226	0.000
REM efficiency (%)	80.2 (15.0)	83.7 (12.8)	86.3 (7.8)	83.2 (10.4)	2.891	0.103	0.548	0.915
REM fragmentation (#stage shifts within REM period) ^c	13.7 (7.6)	14.7 (6.7)	14.2 (4.2)	17.5 (6.2)	0.092	0.765	0.302	0.133

^a Mann–Whitney test.

^b Wilcoxon matched pairs test.

^c Variable $\log(X + 1)$ transformed for statistical comparisons.

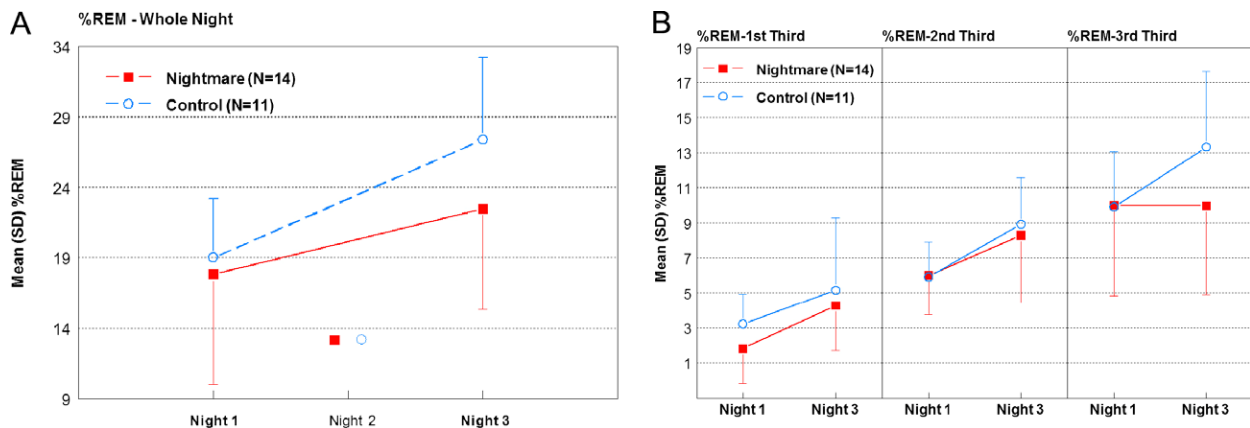


Fig. 1. REM sleep as a percent of total time asleep (REM%) for the whole night and separated by thirds of the night. (A) Partial REM deprivation produced moderate decreases in REM% sleep on night 2 for both NM ($M = 13.1\% \pm 5.84$; $F_{1,23} = 11.550$, $p = 0.002$) and CTL ($M = 13.2\% \pm 4.27$; $F_{1,23} = 14.227$, $p = 0.001$) groups. Also, night 1 to night 3 REM rebound was lower for the NM than for the CTL group (see text). (B) NM subjects showed evidence of REM rebound only in the 1st third of the night ($p = 0.003$), whereas CTL subjects showed REM rebound only in the 2nd ($p = 0.018$) and 3rd ($p = 0.050$) thirds of night 3, when REM sleep is normally most prevalent and most intense.

Also shown in Fig. 1, a differential REM rebound effect was indicated by two findings. First, a marginal group (NM, CTL) × night (N1, N3) interaction ($F_{1,23} = 3.363$, $p = 0.079$) revealed that REM% increased less from N1 (17.8%) to N3 (22.5%) for the NM group ($F_{1,23} = 12.82$, $p = 0.0016$) than it did for the CTL group (19.0% to 27.4%; $F_{1,23} = 31.628$, $p = 0.00001$), i.e., NM subjects displayed less of a REM rebound on N3. Second, also shown in Fig. 1, in the first third of N3, the NM group showed an increase in REM% relative to N1 ($F_{1,23} = 10.748$, $p = 0.003$), whereas the CTL group did not ($F_{1,23} = 1.249$, $p = 0.275$). For the second and third thirds of the night, the NM group showed no N1-to-N3 REM% rebound (2nd third: $F_{1,23} = 2.490$, $p = 0.128$; 3rd third: $F_{1,23} = 0.083$, $p = 0.776$) whereas the CTL group did (2nd third: $F_{1,23} = 6.525$, $p = 0.018$; 3rd third: $F_{1,23} = 4.245$, $p = 0.050$).

3.4. #Skipped early-night REM periods, REM latency, REM/NREM cycle duration, #REM periods

Four measures reflected changes in the timing and duration of the REM/NREM cycle on N1, N3 or both among NM subjects. First, of the 14 initial N1 REM periods that were expected for the NM group, 7 (50.0%) were skipped; of the 11 initial N1 REM periods expected for the CTL group, only 1 (9.1%) was skipped ($\chi^2_{(25)} = 4.738$, $p = 0.042$, Fisher exact test, two-tailed). Three of the 7 NM subjects also skipped the second expected REM period and one NM subject skipped a REM period on N3. Second, as shown in Table 1 and Fig. 2A, REM latency was longer for the NM than for the CTL group both on N1 ($F_{1,23} = 9.410$, $p = 0.005$) and N3 ($F_{1,23} = 4.600$, $p = 0.043$). Further, REM latency was longer on N1 than on N3 for

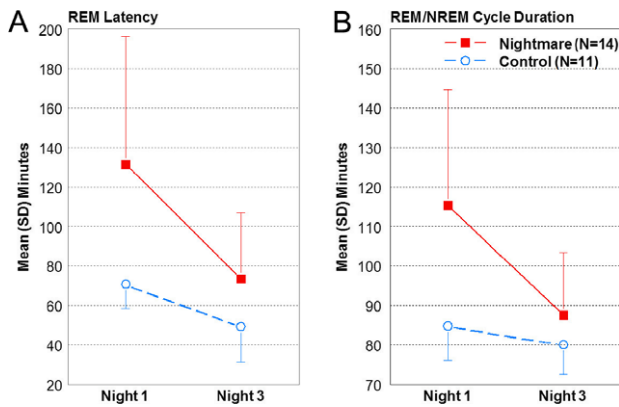


Fig. 2. Latency to onset of REM sleep and REM/NREM cycle duration during baseline (night 1) and recovery (night 3) sleep. (A) REM latency was longer for the NM than for the CTL group both on night 1 ($p = 0.005$) and night 3 ($p = 0.043$). (B) REM/NREM cycle duration was longer for the NM than for the CTL group on night 1 ($p = 0.003$) but not on night 3 ($p = 0.158$; however, see text for additional analyses).

the NM group ($F_{1,23} = 12.754$, $p = 0.002$) but not for the CTL group ($F_{1,23} = 1.351$, $p = 0.257$). Third, as shown in Table 1 and Fig. 2B, REM/NREM cycle durations were longer for the NM than for the CTL group on N1 ($F_{1,23} = 10.986$, $p = 0.003$) but not on N3 ($F_{1,23} = 2.126$, $p = 0.158$). Again, cycle durations were longer on N1 than on N3 for the NM group ($F_{1,23} = 12.580$, $p = 0.002$) but not for the CTL group ($F_{1,23} = 0.297$, $p = 0.591$). Fourth, as shown in Table 1, the NM group had fewer REM periods than did the CTL group on N1 ($F_{1,23} = 12.905$, $p = 0.002$) but not on N3 ($F_{1,23} = 0.855$, $p = 0.365$). But neither N1-N3 comparison within groups differed significantly for this measure.

Because the skipping of early REM periods might bias the previous measures of REM latency, REM/NREM cycle duration and #REM periods, comparisons for the latter were repeated for only those subjects who had not skipped any REM periods (NM: $N = 7$; CTL: $N = 10$). This resulted in removal of the two subjects taking medications. Results were largely the same (see Table 3). REM latency was longer for NM than for CTL groups on N1 ($p = 0.032$) and marginally on N3 ($p = 0.118$). REM/NREM cycle duration was longer for NM than for CTL groups on N1 ($p = 0.010$) and N3 ($p = 0.025$). #REM periods was lower for NM than CTL groups on N1 ($p = 0.017$) but not N3 ($p = 0.851$). Note that removal of subjects who skipped REM periods produced a marked reduction in standard deviations for the NM group on all three measures.

3.5. REM density

As shown in Fig. 3, early-night REM density was similar for the two groups on both nights and decreased significantly from N1 to

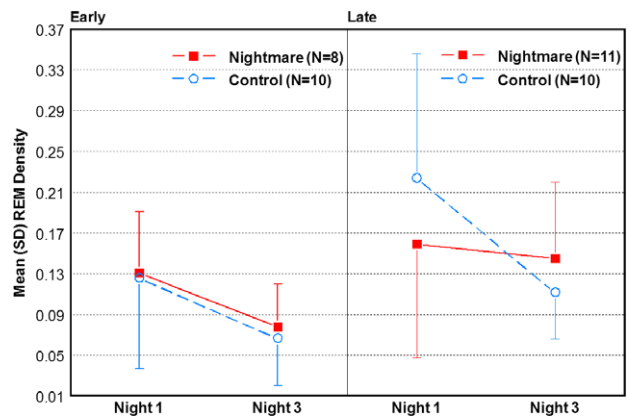


Fig. 3. Mean (SD) eye movement density for early- and late-night REM sleep. A group \times night interaction for late-night REM density ($F_{1,19} = 4.451$, $p = 0.048$) indicates that a night 1 to night 3 decrease in REM density seen for the CTL subjects was absent for NM subjects. Early-night REM sample size for the NM group is smaller because results from three REM sleep 'skippers' who had no early-night REM periods were not available.

N3 for both NM ($F_{1,16} = 9.704$, $p = 0.007$) and CTL ($F_{1,16} = 15.125$, $p = 0.001$) groups. But a significant group \times night interaction for late-night REM density ($F_{1,19} = 4.451$, $p = 0.048$) revealed that late-night density for the NM group did not decrease from N1 to N3 ($F_{1,19} = 0.187$, $p = 0.670$) as it did for the CTL group ($F_{1,19} = 11.073$, $p = 0.004$). Nonetheless, NM and CTL groups did not differ significantly for either N1 or N3 contrasts. Within-nights, N1 REM density increased from early- to late-night by only 21.4% for the NM group ($F_{1,18} = 1.868$, $p = 0.189$) but by 77.8% for the CTL group ($F_{1,18} = 7.637$, $p = 0.013$); N3 REM density increased about equally for the two groups, i.e., 46.2% for the NM group ($F_{1,17} = 19.124$, $p = 0.0004$) and 40.2% for the CTL group ($F_{1,17} = 5.890$, $p = 0.027$).

3.6. Intensity of sleep mentation

The NM group had a lower average visual intensity of SO imagery ($M = 4.18 \pm 2.06$) on N3 than did the CTL group ($M = 5.73 \pm 1.11$; $F_{1,22} = 4.951$, $p = 0.037$). Nevertheless, dreamlike quality of the imagery was similar for the NM ($M = 3.91 \pm 1.82$) and CTL groups ($M = 4.60 \pm 2.16$; $F_{1,22} = 0.73$, $p = 0.404$).

4. Discussion

Our expectation that NM subjects would display signs of increased REM propensity before and after REM sleep deprivation was not supported by the present findings. Rather, a considerable

Table 3
REM sleep measures assessed for subjects with and without frequent non-traumatic nightmares who did not skip any REM periods: Group (nightmare, control) \times night (night 1, night 3) ANOVA design.

	Nightmare subjects ($N = 10$)		Control subjects ($N = 7$)		Group \times night effect		Group effect p	Night effect p
	Night 1 Mean (SD)	Night 3 Mean (SD)	Night 1 Mean (SD)	Night 3 Mean (SD)	F	p		
Latency to REM (min) ^a	67.8 (8.1)	49.8 (18.9)	83.5 (17.6)	82.0 (37.1)	1.321	0.057	0.057	0.150
REM/NREM cycle duration (min)	84.2 (9.1)	80.7 (7.6)	100.0 (13.0)	94.3 (15.0)	0.102	0.754	0.004	0.182
REM periods (#)	4.9 (0.7)	4.1 (1.1)	4.0 (0.6)	4.0 (1.0)	1.544	0.233	0.115	0.2331
Early REM density (#/sec of REM)	0.106 (0.041)	0.058 (0.024)	0.126 (0.089)	0.067 (0.047)	0.206	0.657	0.613	0.001
Late REM density (#/sec of REM)	0.127 (0.052)	0.157 (0.080)	0.224 (0.122)	0.112 (0.046)	8.881	0.009	0.439	0.105
REM (%)	19.0 (4.4)	27.8 (6.0)	22.0 (8.0)	25.5 (6.8)	6.000	0.027	0.891	0.000
REM efficiency (%)	86.9 (7.9)	83.9 (10.7)	86.4 (10.5)	88.1 (11.0)	1.787	0.201	0.697	0.698
REM fragmentation (#stage shifts within REM period) ^a	14.7 (4.1)	17.5 (6.5)	13.6 (7.3)	14.9 (8.1)	0.049	0.827	0.331	0.344

^a Variable was $\log(X + 1)$ transformed for statistical comparisons.

number of our REM sleep measures converged in supporting the opposite conclusion. NM subjects had signs of lower than normal REM propensity for pre-deprivation sleep and, to a lesser extent, during recovery sleep as well. So although our use of PSG and pre/post REM deprivation measures to identify and enhance markers of NM pathophysiology did not produce the anticipated results, they did reveal anomalies in REM propensity that are relevant to the etiology of idiopathic NMs. These findings suggest that the application of REM deprivation together with first- and third-night PSGs provides a methodological advantage over the more standard, undisturbed second-night PSGs we used in our previous study [3].

Together, the present findings suggest that the REM propensity of NM subjects remained ubiquitously low both early and late in the sleep period and for the 3-night duration of the protocol. An absence of early-night REM periods in half of NM subjects suggests there was a reduced drive for initiating or maintaining REM sleep early on N1. A reduction in the intensity of sleep onset dreaming also implicates a diminution in early-night REM propensity on N3. Further, a dampening of the normal within-night increase in REM density [24] on N1 (NM: 21.4% vs. CTL: 77.8%) and a reduced REM% rebound in the latter two-thirds of N3 both suggest that REM propensity was diminished for NM subjects late in the sleep period. Finally, abnormally long REM latencies and REM/NREM cycles on both N1 and N3, as well as a lower number of total REM periods on N1—independent of the ‘skipping’ of early REM periods—all suggest a diminished propensity for initiating and maintaining REM sleep that spanned the three nights of the protocol.

This convergence of findings is most parsimoniously attributed to REM propensity remaining low for NM subjects throughout the 3-night protocol, despite our attempts to increase it experimentally with REM deprivation. Although REM deprivation was successful in increasing REM% for NM subjects on N3, this rebound effect was less apparent and shorter-lasting than it was for CTL subjects. In fact, the REM% rebound of NM subjects appears to have disappeared by the second third of the recovery night.

Although it may be tempting to conclude from these results that increased REM propensity does not contribute to the occurrence of NMs, it should be kept in mind that the samples of sleep we collected in the laboratory may not be representative of these subjects’ typical sleep. The fact that anxious subjects, among whom NM subjects should be included, frequently display abnormal sleep on the first recording night (see discussion of the ‘first night effect’ later) is consistent with this point. These first night anomalies for REM sleep variables have even been documented to last up to four nights [25]. Additionally, the fact that no actual NM episodes were reported during PSG recordings, an observation reported by several authors [1,26,27], also suggests that the NM subjects’ sleep was not entirely representative. This lack of representativeness may mean that, for still unexplained reasons, the suspected intensification of REM propensity was temporarily absent during our PSG recordings. Other approaches may be necessary to raise REM propensity even further and document the suspected pathology with more precision. This might include ambulatory recordings of home sleep, including actual NM episodes, use of longer laboratory adaptation periods (e.g., four nights rather than one) and the application of more exhaustive REM sleep deprivation procedures (e.g., all REM periods of the night).

Despite the obvious need for additional replication studies, the present findings force us to consider the possibility that the sleep of NM subjects outside of the laboratory is also characterized by periods of abnormally low REM propensity. Abnormally low periods of REM propensity might arise from a disruption of any of the ultradian, circadian or sleep-dependent endogenous factors known to regulate REM propensity. For example, a marked desynchrony between the circadian and sleep-dependent components might result in a recurrently periodic alternation between abnor-

mally reduced and abnormally elevated extremes in REM propensity. Such an explanation is supported by evidence that experimentally delaying the sleep-dependent timing of REM sleep so that its peak occurs closer to the circadian acrophase of REM propensity produces dream content that is more vivid, dreamlike and bizarre than if it occurs closer to the circadian nadir [10,28]. But it is not clear from such an explanation why only REM propensity reductions should manifest during PSG recordings in the laboratory. A second possibility is that the sleep-dependent component of REM propensity is reduced by pre-sleep novelty or stress to a greater degree for NM subjects than it is for control subjects. If this is the case, then NMs might be a function of situational and individual difference factors that are known to influence REM propensity. To illustrate, learning [29] and alcohol ingestion [30] both increase REM density, while acute pre-sleep stress [24] and low sleep propensity [31] both decrease it. Similarly, REM% is increased by recent learning and by dispositional factors such as neuroticism [6], with high neuroticism subjects reporting more NMs and showing lower post-deprivation REM% than low neuroticism subjects [32]. The fact that our NM subjects displayed elevated indicators of anxiety and general psychopathology as well as reduced post-deprivation REM% is thus consistent with a high neuroticism profile that should be investigated further.

A final possibility is consistent with a growing literature demonstrating that abnormal autonomic functioning—reduced heart rate variability (HRV), in particular (for review see [33])—is characteristic of a wide spectrum of anxiety disorders, such as PTSD [34] and panic disorder [35], conditions that are frequently comorbid with intense NMs. HRV is also abnormal in REM sleep behaviour disorder [36] which, too, is characterized by vivid NMs. Thus, closer study of anxiety reactions among NM sufferers may clarify how low REM propensity might be preferentially associated with autonomic dysregulation in this population.

It is noteworthy that many common medications have a potent suppressant effect on REM propensity. A comprehensive review of drug effects on nightmares [37] concluded that REM suppression is a major effect of many nightmare-inducing medications such as beta-blockers; 12 of 23 clinical trials considered in the review were consistent with this conclusion.

4.1. Nightmares, REM propensity and the first night effect

From a descriptive point of view, findings for N1 of our study are consistent with the notion that NM subjects manifest a more extreme first night effect (FNE) than do CTL subjects. The FNE is well documented [38–41] to involve primarily REM sleep changes such as those differentiating our two groups: skipped early REM periods [38,42], prolonged REM latencies [38,43,39], longer REM/NREM cycles [41] and fewer REM periods [42]. Some REM sleep changes can require up to four nights to habituate, but this is the case only for latencies to REM periods 2 and 3, without adjustment for skipped REM periods [25]. Nonetheless, because the FNE is mainly a descriptive category whose cause remains unknown, its explanatory value for the present findings is limited. Some researchers have noted associations between the FNE and anxiety [40,44], suggesting a possible functional role for REM sleep, and others [41,45] have proposed outright that FNE reflects functional adaptability of the CNS to external change. Our NM subjects reported anxious and inhibited home dreams, scored high on state anxiety and showed a suppression of the normal within-night increase in REM density similar to that induced by pre-sleep anxiety [24], findings all broadly consistent with such views. On the other hand, published relationships between FNE and anxiety are inconsistent; one group [46] reported that high state anxiety subjects had no obvious FNE. It therefore remains unclear whether FNE is in fact a response to anxiety, whether it plays a functional regula-

tory role and whether this functional response is exaggerated for NM subjects.

Rather, a 'pervasive low REM propensity' explanation accounts not only for the N1 findings but also for some discrepant N1 and N3 findings that are not readily explained by the FNE interpretation. Specifically, the fact that no change in REM% occurred for the NM group on N1, even though REM% is the most sensitive [45] and most consistently reported FNE indicator [38,41,42,45], tends to discount the 'more extreme FNE' explanation of the NM group differences. Also, the findings that group differences in REM latency, REM/NREM cycle duration, REM% and sleep mentation vividness were also found on N3 support the notion that low REM propensity outlasts the first night among NM subjects sleeping in the laboratory. It is important to note that our finding that REM density decreases, rather than increases, as a function of REM deprivation (Fig. 3), i.e., it decreases from N1 to N3 for both NM and CTL groups, which is consistent with findings in the literature. One night of total sleep deprivation in older subjects actually suppresses REM density while other REM propensity measures (REM%, REM latency, sleep onset REM periods) increase [47] (see also [48]). Other studies have found that REM deprivation induced by repeated awakenings, as in the present study, produces no significant rebound in REM density [25,49]. Such findings suggest that REM density may be a less sensitive marker of REM propensity than REM%, REM latency or skipped early REM periods.

5. Conclusions

This preliminary study did not confirm expectations that NM subjects would exhibit higher than normal REM propensity—even following REM sleep deprivation. However, the findings did demonstrate clear differences between groups that suggest alternative hypotheses for future investigation; in particular, decreased REM propensity is a pathophysiological factor in NM production that may be due to disruption of endogenous regulators of REM propensity or to subject differences in anxiety and the FNE. Results also highlight that the skipping of early-night REM periods may be a sensitive measure of REM propensity and that subjects should be screened for REM suppressant medications. An important limitation of the study is that subjects were not seeking treatment for nightmares and so may not necessarily be representative of the population of clinical nightmare sufferers. It is possible that our subjects, unlike clinical patients at large, had developed successful strategies for coping with their frequent nightmares.

Conflict of interest declaration

The research was supported by grants to Tore Nielsen from the Canadian Institutes of Health Research (FRN – 57836) and the Natural Sciences and Engineering Research Council of Canada (RGPIN – 312277-05).

Acknowledgements

We thank Dominique Petit and Philippe Stenstrom for help with data collection and proofreading.

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