Fluctuations between sleep and wakefulness: Wake-like features indicated by increased EEG alpha power during different sleep stages in nightmare disorder

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ABSTRACT

Although a growing body of research indicates that frequent nightmares are related to impaired sleep regulation, the pathophysiology of nightmare disorder is far from being fully understood. We examined the relative spectral power values for NREM and REM sleep separately in 19 individuals with nightmare disorder and 21 healthy controls, based on polysomnographic recordings of the second nights' laboratory sleep. Nightmare subjects compared to controls exhibited increased relative high alpha (10–14.5 Hz) and fronto-central increases in high delta (3–4 Hz) power during REM sleep, and a trend of increased fronto-central low alpha (7.75–9 Hz) power in NREM sleep. These differences were independent of the confounding effects of waking emotional distress. High REM alpha and low NREM alpha powers were strongly related in nightmare but not in control subjects. The topographical distribution and spectral components of REM alpha activity suggest that nightmare disordered subjects are characterized by wake-like electroencephalographic features during REM sleep.

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1. Introduction

Nightmares are intense and highly unpleasant mental experiences that occur usually – but not exclusively – during late-night Rapid Eye Movement (REM) sleep and often provoke abrupt awakenings (ICSD-II, 2005). Nightmares affect approximately 4% of the adult population on a weekly basis (Spoormaker, Schredl, & van den Bout, 2006). Even though nightmares are often co-morbid with a wide variety of mental complaints (Levin & Nielsen, 2007), research indicates that frequent nightmares are more appropriate to be conceptualized as a specific sleep disorder that are independent in its origins from waking psychopathological symptoms (Coolidge, Segal, Coolidge, Spinath, & Gottschling, 2010; Lancee, Spoormaker, & van den, 2010; Spoormaker et al., 2006). Frequent nightmares are related to impaired subjective sleep quality in different age-groups and populations (Li et al., 2011; Li, Zhang, Li, & Wing, 2010; Schredl, 2010), and negatively toned dreams are more frequent among subjects with different sleep disorders (Schredl, 2009a,b; Schredl, Schafer, Weber, & Heuser, 1998) in whom nightmares seem to increase the severity of sleep complaints (Krakow, 2006; Schredl, 2009a,b).

In consistence with questionnaire-based findings, early polysomnographic studies reported altered sleep architecture and sleep fragmentation in subjects with frequent nightmares (Fisher, Byrne, Edwards, & Kahn, 1970; Newell, Padamadan, & Drake, 1992). In addition, a recent study that also controlled for the confounding effects of co-morbid waking symptoms of depression and anxiety found decreased sleep efficiency, reduced slow wave sleep (SWS) and increased nocturnal awakenings in a group of young nightmare sufferers (Simor, Horváth, Gombos, Takács, & Bódizs, 2012). Others found enhanced periodic leg movements in nightmare sufferers with and without post-traumatic stress disorder suggesting that increased arousal and accompanying motor activation characterize the pathophysiology of nightmare disorder (Germain & Nielsen, 2003). Enhanced arousal during sleep was also evidenced by increased sympathetic (cardiac) activation in a group of nightmare subjects after a REM deprivation procedure (Nielsen et al., 2010).

A more recent study found altered sleep microstructure in nightmare sufferers during Non-REM (NREM) sleep (Simor, Bódizs, Horváth, & Ferri, 2013) revealed by the Cyclic Alternating Pattern (CAP) analysis that quantifies and categorizes electroencephalographic (EEG) oscillations corresponding to recurrent activation

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events and transient states of unstable sleep depth (Terzano et al., 1985). More specifically, nightmare subjects in comparison to controls exhibited increased arousal responses comprised of desynchronized, high or mixed frequency activities and a reduced amount of synchronized, low frequency oscillations during spontaneous recurrent events of instability in NREM sleep and these differences were independent of the effects of anxious and depressive symptoms, indexed by psychometric tests. Desynchronized arousal responses that are generated usually at posterior sites and incorporate alpha (8–13 Hz) and beta (13–30 Hz) frequency bands shift the cortex toward a more alert brain state, while the generally antero-posterior propagation of slow (0.25–2 Hz) synchronized oscillations reflects the "effort" of the cortex to preserve sleep depth by reinforcing the thalamic-basal forebrain gate against arousing impulses (Parrino, Ferri, Bruni, & Terzano, 2012). Therefore, these findings indicate that nightmare disorder is characterized by inefficient sleep regulation and increased arousal responses that reduce the threshold for awakening.

Interestingly, although nightmare disorder is considered to be a REM parasomnia (ICSD-II, 2005), anomalies in sleep continuity have been reported mainly during NREM sleep (Simor et al., 2013, 2012). Nevertheless, it is feasible that the above studies based on the visual scoring of sleep EEG could not capture the subtle alterations in the structure of neural oscillations during REM sleep. Power spectral analysis provides a fine-grained and sensitive examination of the electrophysiological oscillations during sleep, which seems to be an efficient tool to detect sleep alterations in different pathological conditions (Armitage, 1995; De la Fuente, Tugendhaft, & Mavroudakis, 1998; Feige, Scaal, Hornyak, Gann, & Riemann, 2007; Krystal, Edinger, Wohlgemuth, & Marsh, 2002; Lindberg et al., 2003; Moritz et al., 2002; Philipsen et al., 2005; Poulin, Stip, & Godbout, 2008). To the best of our knowledge, no previous studies have investigated the electrophysiological features of a whole night sleep in nightmare disorder. Therefore, our aim was to describe the EEG spectral profile of NREM and REM sleep in a group of nightmare subjects in comparison with that of controls.

2. Materials and methods

2.1. Participants

Participants (all native Hungarians) were selected from a large pool of undergraduate students from the Budapest University of Technology and Economics and Semmelweis University. Nightmare (NMs) and control subjects (CTLs) were enrolled after a stringent selection procedure described previously in detail (Simor et al., 2012). In brief, the enrollment was based on subjects' scores on three different dreaming-related questionnaires: the Dream Quality Questionnaire (DQQ) (Bódizs, Simor, Csóka, Bérdi, & Kopp, 2008), the Hungarian version of the Van Dream Anxiety Scale (VDAS-H) (Simor et al., 2009) and two seven-point Likert scales, one assessing the frequency of awakening nightmares, and the other assessing the frequency of bad dreams without awakenings (0 – almost never; 1 – once or twice a year; 2 – every 2–3 month; 3 – once in a month; 4 – twice a month; 5 – once a week; 6 – more than once a week). NMs were selected on the basis of the International Classification of Sleep Disorders, 2nd edition (2005) criteria and Levin and Nielsen's (2007) model of disturbed dreaming, including disturbed dreamers without abrupt awakenings. Subjects reporting one or more nightmares with awakening and/or bad dreams without awakening per week in the retrospective questionnaires were assigned to the NMs group, while individuals having less than two nightmares and/or bad dreams during the previous year were assigned as CTLs. Those subjects who reported the onset of negative dream experiences in relation to a traumatic event or indicated that the content of their dreams were related to a prior trauma (such as physical attack, accident, sudden death of a close relative, etc.) were excluded from the study. 21 NMs and 23 CTLs took part in polysomnographic examination; however, two NMs left the experiment after the first (baseline) night and two of the CTLs' recordings were considered too noisy for spectral analyses. Therefore, 19 NMs (10 males; $M_{age} = 20.87 \pm 1.57$) and 21 CTLs (11 male; $M_{age} = 21.57 \pm 1.47$) were included in the present study. There was no significant age difference between the two groups ($U(38) = 146$; $Z = -1.48$; $p = 0.138$). NMs scored higher on the Negative Dream Affect Scale of the DQQ ($M_{NMs} = 8.12$; $SD_{NMs} = 1.91$ vs. $M_{CTLs} = 4.03$; $SD_{CTLs} = 1.77$; $t(38) = -7.25$; $p < 0.0001$) and on the VDAS-H ($M_{NMs} = 20.58$; $SD_{NMs} = 7.5$ vs. M_{CTLs}: $0.23 \pm SD_{CTLs} = 0.62$; $t(18.22) = -11.73$; $p < 0.0001$; equal variances not assumed),

indicating at least moderately severe dream disturbances (Bódizs, Sverteczki, & Mészáros, 2008; Simor et al., 2009).

None of the subjects reported prior neurological, psychiatric or sleep disorders or prior history of any chronic disease. The study protocol was approved by the Ethical Committee of the Semmelweis University. The subjects received monetary compensation for their participation in the sleep laboratory investigations. Written informed consent was obtained.

2.2. Procedure

Polysomnographic recordings were performed in the sleep research laboratory of the Semmelweis University for two consecutive nights. (The first night served as the adaptation night.) Subjects were not allowed to drink alcohol or take drugs (except contraceptives) on the day and the previous day of the examination. They were asked to avoid napping and consuming caffeine in the afternoon of the sleep recordings. The timing of lights off was between 11.00 PM and 1.00 AM depending on each participant's preferred bedtime. Morning awakenings were scheduled after 9 h of undisturbed sleep unless participants woke up earlier spontaneously. Five of the NMs reported negatively toned dreams in the laboratory.

In the morning – in order to measure subjective sleep quality – subjects were asked to complete the Hungarian adaptation of the Groningen Sleep Quality Scale (GSQS) (Simor, Köteles, Bódizs, & Bárdos, 2009). The one-dimensional 14-item questionnaire measures the extent of subjective sleep fragmentation.

In order to control for the confounding effects of waking emotional distress on sleep EEG the Hungarian versions of the Spielberger Trait Anxiety Inventory (STAI-T) (Spielberger, Gorsuch, & Lushene, 1970) and the short Beck Depression Inventory (BDI-H) (Rózsa, Szádoczky, & Füredi, 2001) were assessed. The STAI-T is a widely used self-report instrument that differentiates between the temporary condition of state anxiety and the longstanding quality of trait anxiety. We used the 20-item Hungarian version of the STAI-T to assess general levels of anxiety (Sipos, Sipos, & Spielberger, 1994).

The 9-item BDI-H is a one-dimensional scale assessing different symptoms of depression including social withdrawal, indecision, sleep disturbance, fatigue, intense worry about bodily symptoms, loss of work performance, pessimism, lack of satisfaction and self accusation (Rózsa et al., 2001).

2.3. Polysomnography

On both nights, subjects were fitted with 19 EEG electrodes (Fp1, Fp2, F3, F4, Fz, F7, F8, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2) according to the 10–20 electrode placement system (Jasper, 1958) as well as with two EOG electrodes (bipolar channel) monitoring vertical and horizontal eye-movements; EMG electrodes (bipolar channels) for the chin and for the anterior tibialis muscles, two ECG electrodes according to standard lead I; in addition to the thoracic and abdominal respiration sensors. Gold-coated Ag/AgCl EEG cup electrodes were fixed with EC2 Grass Electrode Cream (Grass Technologies, USA) and referred to the mathematically-linked mastoids. Impedances were kept below 8 kΩ. Signals were collected, prefiltered (0.33–1500 Hz, 40 dB/decade anti-aliasing hardware input filter), amplified and digitized with 4096 Hz/channel sampling rate (synchronous) with 12 bit resolution by using the 32 channel EEG/polysystem (Brain-Quick BQ 132S, Micromed, Italy). A further 40 dB/decade anti-aliasing digital filter was applied by digital signal processing which low-pass filtered the data at 450 Hz. Finally, the digitized and filtered EEG was undersampled at 1024 Hz.

2.4. Spectral analyses

Sleep stages and conventional parameters of sleep macrostructure were scored according to Rechtschaffen and Kales standardized criteria (Rechtschaffen & Kales, 1968) by two experienced sleep researchers who were blind to the group membership of the participants. Overlapping (50%), artifact-free four-second-epochs of all EEG derivations were Hanning-tapered and Fourier transformed by using the FFT (Fast Fourier Transformation) algorithm in order to calculate the average power spectral densities ($\mu V^2/0.25$ Hz) for whole night NREM (stages 2–4) and REM sleep periods. Since the absolute power values may be biased due to differences in the thickness – and thus the conductivity – of the skull, leading to disproportionate discrepancies between males and females (Carrier, Land, Buysse, Kupfer, & Monk, 2001), we applied the relative spectral power values. Relative spectral power values were obtained for each frequency bin (width: 0.25 Hz) by dividing the absolute power of the given frequency bin with the total spectral power (the sum of the absolute power of the whole range of analysis between 0.75 Hz and 48.25 Hz). The relative power values reflect the relative contribution of a given frequency range to the total spectrum. Relative spectral power values were log-transformed by using a 10 base logarithm in order to normalize their distribution before performing statistical analyses.

2.5. Statistical analyses

Statistical analyses were carried out with the Statistical Package for the Social Sciences version 19.0 (SPSS, IBM) and MATLAB (version 7.10.0.499, R2010a, The MathWorks, Inc., Natick, MA). Group differences of mean scores regarding the