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Original Article

Sleep stage dynamics in fibromyalgia patients and controls

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Abstract

Objective: To determine whether previously described sleep stage dynamics, reflecting the mean duration of specific sleep stages, may have clinical utility in a sample of patients with fibromyalgia syndrome (FMS) and controls.
Methods: Women with FMS ($n = 15$, screened to exclude other sleep disorders) and age-matched women in good health ($n = 15$) were studied with nocturnal polysomnography, multiple sleep latency tests, 2-week pain diaries, and a measure of current pain intensity.
Results: The FMS subjects, in comparison to controls, did not show differences in several common polysomnographic measures, except for increased numbers of stage shifts (126 ± 27 vs. 107 ± 22, $p = .042$). Mean durations for episodes of total sleep, stage 1 sleep, stage 3/4 sleep, and rapid eye movement sleep failed to distinguish FMS and control subjects (Wilcoxon rank sum tests, $p > .10$ for each), but those for stage 2 sleep were shorter in the FMS subjects ($p = .006$), possibly because transitions to stage 3/4 sleep occurred more quickly ($p = .036$). Shorter stage 2 sleep durations predicted higher pain diary scores (Spearman $rho = -.56$, $p = .0014$) and current pain intensity ($rho = -.71$, $p < 0.0001$).
Conclusions: Sleep stage dynamic, and, more specifically, shorter durations of sleep stage 2 periods, distinguish FMS and control female subjects and may predict pain levels experienced in FMS. Analysis of the lengths of individual sleep stages, in addition to the usual sleep stage amounts and percentages listed in standard polysomnogram reports, may have clinical utility.

Keywords: Polysomnography; Fibromyalgia; Sleep; Sleep stages; Sleep fragmentation; Pain

1. Introduction

Most reports of nocturnal polysomnograms performed for clinical purposes list the amount and percentage of specific sleep stages, but say nothing about the variability or distribution of sleep or stage durations. The distribution of sleep or single-stage periods could conceivably provide new information on sleep fragmentation. Recent data show that the durations of nocturnal sleep and wake periods can be characterized by different statistical distributions in healthy individuals [1]: wake periods are characterized by a power-law distribution, whereas sleep periods are characterized by an exponential law distribution. The durations of wake and sleep periods follow the power-law and exponential distributions, respectively, in both healthy adults and those with sleep apnea [2]. However, the parameters of the distributions differ between these two groups. The durations of individual sleep stages follow an exponential distribution, but again the parameters of the distributions differ between sleep stages [2].

Penzel et al. [2] suggested that the changes in parameters of the exponential distribution could have diagnostic value, but did not elaborate on any specific clinical example. The probability density function of the exponential distribution is expressed as $p(t|\tau) = \exp(-t/\tau)/\tau$, and is characterized by the time scale parameter τ. Changes in the parameter of the distribution, the time

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scale τ, may well assess the amount of sleep fragmentation, and medical conditions associated with sleep fragmentation may be distinguished by changes in the parameters of the observed distributions. One observation not made previously in the literature cited above is that the expected value or mean of an exponentially distributed random variable is the scale parameter [3]. Thus, the measure is equivalent to the variable mean. Assuming sleep periods or specific sleep stage periods follow an exponential distribution; the scale parameter τ equals the mean duration of the sleep periods or specific sleep stage periods in question.

To evaluate the idea that sleep stage dynamics, reflecting the mean duration of sleep stages, might provide useful information beyond the sleep stage information reported from most polysomnograms, we used data that had been collected from 15 patients with fibromyalgia syndrome (FMS) and 15 age and gender-matched control subjects [4]. This dataset was ideal for an initial clinical test of the utility of the new analysis because FMS is well known to be associated with sleep complaints [5]; polysomnography in FMS shows physiologic signs, though variable, of sleep disruption when special approaches and signal analysis are employed [5–8]; and the dataset included both standard polysomnographic variables and outcome measures (pain scores). The main hypotheses that we addressed were (1) that sleep stage dynamics would distinguish FMS and control subjects, and (2) that mean durations of specific sleep stages would correlate with pain measures in these patients.

2. Methods

2.1. Subjects

The subject data were obtained from a recent, Institutional Review Board-approved study of objective measures of disrupted sleep in fibromyalgia patients [4,9]. Patients were recruited from outpatient rheumatology referral clinics or through advertisements. Healthy control subjects were identified by advertisements and matched to within four years of age to each patient. All patients and controls signed informed consent. An investigator board-certified in rheumatology interviewed and examined all subjects to determine that they met (patients) or failed to meet (controls) criteria for FMS as outlined by the American College of Rheumatology [10]. For each patient testing to confirm the diagnosis included, a dolorimeter exam, complete blood count with differential, complete metabolic profiles, creatine phosphokinase, erythrocyte sedimentation rate, thyroid stimulating hormone, urine pregnancy test (if necessary), and urine drug screen. Screens for psychiatric disorders included the validated Mini-International Neuropsychiatric Interview, which identifies DSM-IV and ICD-10 psychiatric disorders [11].

Inclusion criteria were (1) age $\geqslant$18 and $\leqslant$65 years; (2) ability to discontinue psychotropic medications, hypnotics, analgesics, and herbal or over-the-counter supplements at least two weeks prior to the study (exceptions included only acetaminophen and diphenhydramine, which were allowed up to three days prior to the study); (3) American College of Rheumatology 1990 criteria for FMS (for patients); and (4) signed informed consent. Exclusion criteria included (1) presence of an ongoing medical condition (other than FMS) associated with pain or fatigue; (2) caffeine, cigarette, or alcohol use in excess of 500 mg/day, ½ pack/day, or five drinks/week and unwillingness to discontinue this at least three days prior to the study; (3) recreational drug use confirmed on urine drug testing; (4) average time in bed of <4 h or regular bedtime later than 1:00 a.m.; (5) receipt of exogenous corticosteroids in any form for three months prior to study, or regular use of corticosteroids in the last six months; (6) pregnancy; (7) evidence of concurrent psychiatric illness in patients or at any time in the past for controls; (8) known primary sleep disorder; polysomnographic evidence of obstructive sleep apnea (on baseline night, with apnea/hypopnea index >5 events per hour of sleep); or polysomnographic evidence of periodic leg movements (on baseline night, with periodic leg movement index >15).

2.2. Pain measures

Daily diaries were used for two weeks prior to study and included information regarding the time in bed, sleep quality, and pain. The McGill pain questionnaire [12] was used as the measure of clinical pain in the diaries. We also used a numerical rating scale, the Gracely box scale [13,14], to assess present pain intensity. The Gracely box scale consists of 20 sequentially numbered boxes arranged vertically with "0" as the lowest box. Beside the numbered boxes are words that convey degrees of pain intensity. The positions of the words relative to the numbers are consistent with previous cross-modality matching procedures for the word descriptors: subjects received graded standardized evoked pain and provided pain ratings by nominating the number consistent with their sensory experience and word descriptors [15,16]. This method of developing the Gracely box scale has resulted in it being a logarithmic pain scale (as opposed to linear like most) to better reflect the psychophysiologic properties of how pain is actually experienced.

2.3. Nocturnal polysomnograms and multiple sleep latency tests

Polysomnography was performed for three consecutive nights in the University of Michigan General Clinical Research Center. Digital polysomnography (Telefactor DEEG/TWIN, W. Conshohocken, PA)