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Frequency Analysis of the Sleep EEG in Depression

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Abstract. Eight patients with major depressive disorder (seven bipolar and one unipolar) and matched controls had sleep studies, on which frequency analysis of the electroencephalogram (EEG) was performed. Total sleep and sleep efficiency were decreased in the patients, but there was no significant difference in rapid eye movement (REM) latency between the two groups. Frequency analysis revealed no group differences in power in the delta band (0.23-2.5 Hz) or the whole EEG spectrum (0.23-25 Hz). These findings suggest that mean REM latencies are not always shorter in major depression. The results are discussed in light of a previous report of decreased delta energy in the sleep EEG of unipolar patients.

Key Words. Sleep, frequency analysis, electroencephalogram.

Most depressed patients complain of disturbed sleep, and this is reflected in polysomnographic studies that tend to show decreased total and delta sleep, and increased sleep latency and awakenings (e.g., Mendelson et al., 1977; Gillin et al., 1984). It has also been suggested that some aspects of sleep, notably a short REM (rapid eye movement) latency, may serve as biological markers of major depression (Kupfer, 1976). More recently, a frequency analysis study of the sleep electroencephalogram (EEG) has shown that in unipolar depression there is less power in the whole EEG spectrum, due primarily to a decrease in the delta band (Borbély et al., 1984). This observation has been the basis of a new hypothesis about the pathogenesis of depression (Borbély and Wirz-Justice, 1982). To explore this hypothesis, we have completed a series of recordings in a primarily bipolar depressed population and matched controls.

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Methods

Subjects were eight inpatients (seven females and one male) meeting Research Diagnostic Criteria (Spitzer et al., 1978) for affective disorder (four bipolar I, three bipolar II, and one unipolar) and with a mean age of 43.9 (SD 11.7) years. Patients were actively ill at the time of study, with mean Hamilton rating scores of 25.4 (SD 4.1). The mean duration of the current episode was 5.6 (SD 1.0) weeks, and there was a history of 16.2 (SD 7.0) previous episodes. All had been medication free for at least 2 weeks. Controls were eight age- and sex-matched normal volunteers who were interviewed by a psychiatrist and found to have no psychiatric or medical disorder, no family history of affective disorder, no sleep/wake complaints, and no current employment or travel causing frequent changes in hours of sleep. All were drug and alcohol free for 2 weeks. Both groups had a physical examination and blood chemistry testing to assure good physical health.

After an adjustment night in the laboratory, all subjects had a sleep study recorded on a Grass polygraph with a paper speed of 10 mm/sec and calibrated to 50 μV/7.5 mm. The low frequency linear filter was set at 1 Hz to match the study of Borbély et al. (1984); the high frequency filter was at 35 Hz, the closest possible setting on the polygraph that was used (Grass Model 6). Analog recordings were also made on an Ampex PR2230 tape recorder with a tape speed of 15/16 inches/sec. Calibration was performed with an 8 Hz, 100 μV (peak-to-peak) sine wave signal, with settings such that the output of the tape recorder was 2 volts peak-to-peak. The paper records were interpreted in 30-second epochs according to the criteria of Rechtschaffen and Kales (1968) by a single investigator who was unaware of diagnosis. Statistical significance of differences in sleep parameters between patients and controls was determined by t tests for independent groups.

The tape recordings of the EEG ($C_3/A_1 + A_2$) underwent frequency analysis by a Bruel and Kjaer High Resolution Signal Analyzer (Type 2033) with a sampling rate of 80/sec and which averaged data gathered in 12.5-sec epochs. Sections of the tape that included movement artifact or waking of longer than 3 minutes' duration as determined visually were eliminated from the analysis. Data were presented in units of power (μV^2/ Hz) for both the delta (0.23-2.5 Hz) and whole EEG (0.23-25 Hz) bands, the closest settings available on the equipment to those used by Borbély et al. (1984). These values were determined for each non-REM (NREM) period, and expressed graphically at the end point of each NREM-REM cycle in the manner described by Borbély et al. (1984). The presentation of power divided by Hz was used to be comparable to the data of Borbély et al. Technically speaking, both studies are dealing with "power density," which is often presented in engineering textbooks in units of watts/ Hz (e.g., Schwartz, 1959). With resistance constant, this is the same as energy^2/ Hz. Among other reasons, we divided by the number of Hz in the bandwidth because the historically defined bands (alpha, delta, etc.) have different widths; after dividing by the number of Hz, we present data as power per Hz, which facilitates comparisons across bands. Statistical analysis was performed by a two-way analysis of variance (ANOVA) for repeated measures in independent groups (Winer, 1962).

Results

Sleep Stage Data. As seen in Table 1, the depressed patients had significantly less total sleep ($p < 0.02$), due to a decrease in NREM sleep ($p < 0.02$). Their sleep was less efficient ($p < 0.03$), and there was a trend toward increased sleep latency. There was also a trend toward reduced delta sleep ($p < 0.07$). There were no significant differences in measures of REM sleep, including REM density, length of first REM period, or REM latency.

Frequency Analysis Data. Two-factor ANOVAs were run on data for both delta and total power. The F tests on groups (depressives vs. controls) were not significant

Table 1. Sleep in affective disorder patients and matched controls

	Depressives ($n = 8$)		Controls ($n = 8$)		Significance (t test)
	Mean	SD	Mean	SD	
Total recording[1]	450.88	26.00	454.50	15.22	
Sleep latency[2]	30.44	24.24	17.75	8.26	
REM latency[3]	86.50	63.60	63.30	28.30	
Intermittent awake time	26.31	37.26	21.31	25.83	
Total sleep time	360.69	42.60	405.75	26.03	$p < 0.02$
NREM time	264.19	37.42	310.06	45.06	$p < 0.02$
REM index	131.88	62.77	135.60	30.30	
REM density	1.38	0.51	1.61	0.72	
Length of first REM period	16.80	5.67	16.19	8.03	
Stage 1 time	20.06	19.73	34.44	44.45	
Stage 2 time	215.31	26.99	227.94	70.52	
Stage 3 time	18.94	14.84	24.75	13.50	
Stage 4 time	9.88	16.92	22.84	15.84	
Slow-wave sleep time	28.81	25.08	47.69	22.94	
REM time	97.56	34.17	95.63	34.00	
Stage 1%	5.81	5.68	8.54	11.10	
Stage 2%	59.93	7.46	55.95	16.20	
Stage 3%	5.10	3.81	6.10	3.31	
Stage 4%	2.45	3.85	5.71	3.95	
Slow-wave sleep %	7.54	5.91	11.78	5.75	
REM %	26.74	7.89	23.69	8.57	
Sleep efficiency	80.41	10.29	89.33	6.29	$p < 0.03$
Early morning awakening	28.13	49.03	3.00	5.12	
Movement time	5.31	3.51	6.69	4.04	

Note. All values except percentages are mean ± SD minutes. REM = rapid eye movement. NREM = non-REM.

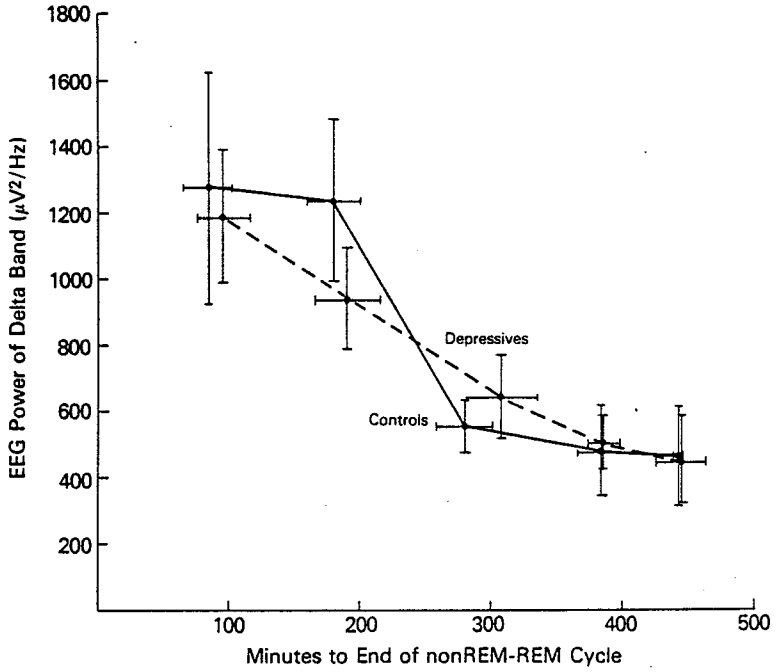
1. Total recording is equal to the sum of total sleep, sleep latency, early morning awakening, intermittent awake time, and movement time.
2. Time from "lights out" until sleep onset. Sleep onset equals first 10-minute period beginning with Stage 2 and followed by at least 8 minutes of sleep.
3. Time from sleep onset until the first full minute of REM sleep.

in either case (total power: $F = 0.00$, $df = 1/14$, $p = 0.96$; delta power: $F = 0.15$, $df = 1/14$, $p = 0.70$). The tests on interaction were also not significant (total power: $F = 0.71$, $df = 4/47$, $p = 0.96$; delta power: $F = 0.15$, $df = 4/47$, $p = 0.58$). The F tests on NREM-REM period were statistically significant (Figs. 1 and 2), indicating that the profiles were not flat, but by inspection showed a downward trend across the night (total power: $F = 26.8$, conservative $df = 1/12$, $p < 0.01$; delta power: $F = 21.9$, conservative $df = 1/12$, $p < 0.01$).

Discussion

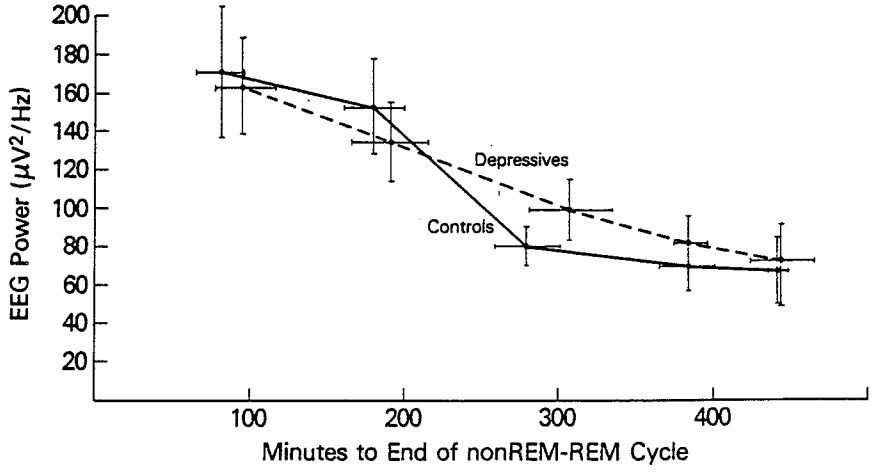
In summary, the patients' sleep was consistent with the previous literature insofar as it was shorter and less efficient, with a trend toward decreased delta sleep (Gillin et al., 1984). It is notable that the mean REM latency of 86.5 minutes is not unusually short, although a shortened REM latency has been thought to be characteristic of

Fig. 1. Power in delta band (0.23-2.5 Hz) across sequential NREM periods in depressed patients and controls



NREM (non-rapid-eye-movement) periods are defined as in Borbély et al. (1984).

Fig. 2. Power in EEG band (0.23-2.5 Hz) across sequential NREM periods in depressed patients and controls



EEG = electroencephalogram. NREM = non-rapid eye movement.

depression (Kupfer, 1976). This study, then, adds to previous work suggesting that normal REM latencies may be found in groups of unipolar (Hauri et al., 1974; Taub et al., 1978; Taub, 1982) or bipolar (Jovanovic, 1977; Jernajczyk, 1986; Thase et al., 1986) patients. Similarly, in the present study the mean length of the first REM period and REM index did not differ between patients and controls.

The frequency analysis data are similar to a previous report (Borbély et al., 1984) insofar as delta power was found to be high during the first NREM period, declining across the rest of the night. The present study, however, did not find any group difference between depressed patients and controls in this measure. A possible explanation for this discrepancy between the two studies is that the current work involved a primarily bipolar population, while Borbély et al. (1984) studied unipolar patients. The current patients had a mean age of 43, 12 years older than those in the earlier study. It is possible that the diagnosis or age difference might be responsible for the differing results in the two studies.

It should also be mentioned that definitions of the delta band may differ, and ranges of up to 5 Hz are sometimes used. The upper limit used here (2.5 Hz) was selected to match the study of Borbély et al. (1984). Most importantly, both patients and controls were studied using the same criterion for delta, with no difference detected. The use of delta power analysis is also somewhat different from visual examination of delta sleep. In the latter approach, only waves with amplitudes > 75 μV peak-to-peak are counted, and the final parameter is a measure of *time* (the number of epochs during which delta waves of at least that amplitude occupy at least 20% [stage 3] or 50% [stage 4] of the recording). The frequency analysis method employed here presents the *power* of all waves meeting a certain frequency criterion. This distinction explains why it is possible for depressed patients to have less slow-wave sleep time, but not significantly different delta power, than controls. Other possible methods include use of a baseline crossing detector to present *number* of delta waves meeting certain amplitude criteria (Kupfer et al., 1984).

Analysis of the sleep staging revealed that the mean REM latency for the normal controls was somewhat lower than expected, although it did not differ significantly from that of the patients. The relatively short REM latency did not appear to be due to old age (control mean age was 45) or to delayed bedtime (10:39-11:40 p.m.), which are thought to be associated with this phenomenon. It is interesting that the mean control REM latency of 63 minutes reported here is in the general range seen in some other recent studies. Jernajczyk (1986), for instance, found the mean REM latency in normal controls to be 67.1 minutes, while Hiatt et al. (1985) had a value of 70.4. Kupfer et al. (1986) found the most common category of REM latencies among 52 younger and 23 older controls to be 53-71 minutes. This study emphasizes, then, the variability of REM latency in the normal population, and the importance of carefully matched controls in investigations of depression.

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