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Clinical Correlates of Sleep Onset REM Periods in Depression

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Introduction

A shortened rapid eye movement (REM) latency (RL; interval between sleep onset and the first REM sleep episode) is considered to represent a biological marker of primary depression (Kupfer 1976). The distribution of RL in primary depression has been studied, but contradictory results have been reported (Schulz et al. 1979; Coble et al. 1981; Ansseau et al. 1984; Kupfer et al. 1986). A markedly shortened RL, or sleep-onset REM period (SOREM), is usually defined as the appearance of REM sleep within 10–15 min of sleep onset (Carskadon 1976; Schulz and Lund 1985). Reports on the clinical characteristics of depressed patients with SOREM are inconsistent (Coble et al. 1981; Ansseau et al. 1984; Kupfer et al. 1986). Because of these disagreements on SOREM and RL distribution in depression, we undertook a study of the distribution of RL in a sample of inpatient depressives and of the clinical characteristics of subjects with SOREM.

Methods

Our patient sample for this study consisted of 62 subjects diagnosed using the Schedule for Affective Disorders and Schizophrenia/Research Diagnostic Criteria (SADS/RDC) (Spitzer and Endicott 1977; Spitzer et al. 1978) as having major depressive disorder–definite, with a Hamilton Rating Scale of Depression (HRSD, 17-item scale) score of 15 or greater. All of our subjects were inpatients on the Clinical Studies Unit for Affective Disorders (CSU) at the University of Michigan, Ann Arbor, MI. Subjects went through the standard CSU protocol comprising: (1) a 2-week drug-free period, (2) complete blood count (CBC), differential, thyroid

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function tests, electrolytes, B_{12}, folate, and VDRL, (3) chest and skull x-rays, and (4) comprehensive medical and neurological exam.

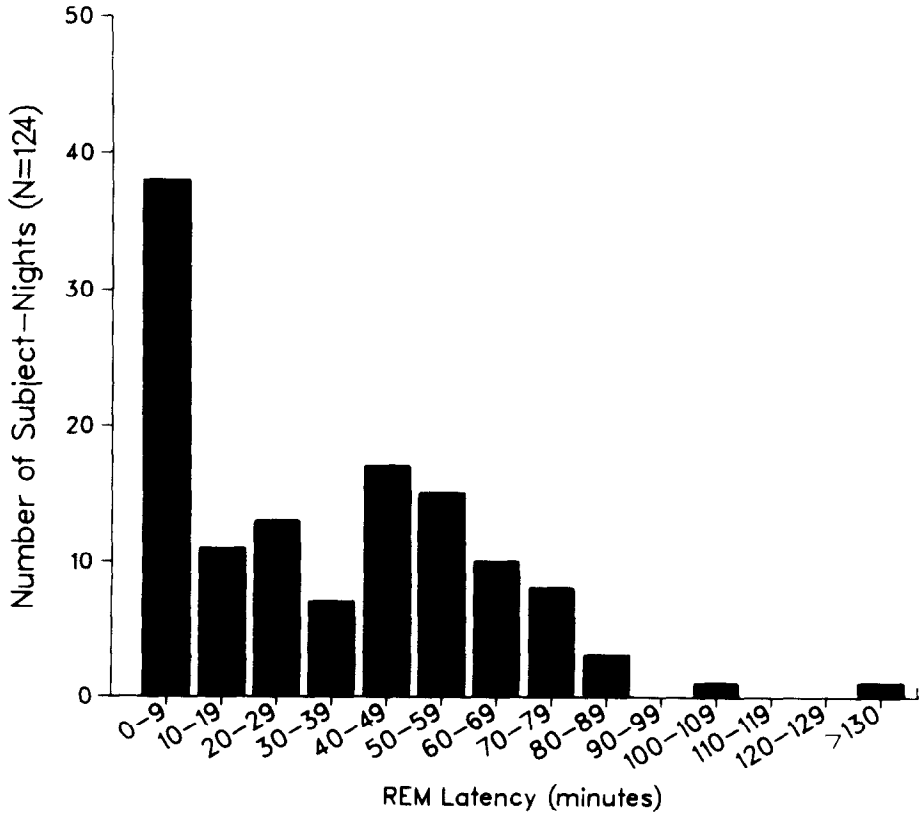
Two consecutive nights of electroencephalogram-recorded (EEG) sleep were completed after a minimum 2-week drug-free period with subjects sleeping in their own hospital beds. Placement of electrodes and scoring was done according to the method of Rechtschaffen and Kales (1968). Sleep onset was defined by the first minute of Stage 2 sleep, followed by at least 10 min of Stage 2 sleep, interrupted by no more than 2 min of awake or Stage 1. RL was defined as the time between sleep onset and the first REM period (minimum duration: 3 min) minus any intervening awake time. Subjects received a weekly rating on the HRSD and a clinical questionnaire (Current Status Questionnaire), which the treating physician completed every week. Patients completed the Carroll self-rating scale of depression weekly (Feinberg et al. 1981). Clinical response was stratified according to the Pittsburgh criteria (cf., Shipley et al. 1985), i.e., subjects were considered to be responders if their HRSD score at discharge was <10 and at least 40% reduced from their admission score, were considered nonresponders if their discharge HRSD score was $\geqq 10$ and showed a reduction of $\leqq 50\%$ of admission HRSD score, and were indeterminate if they fulfilled neither criteria.

Results

RL Distribution

When the data for RLs from nights 1 and 2 were pooled (n = 124 nights), a bimodal distribution was obtained with peaks occurring between 0–

Figure 1. The distribution of REM latency for 124 subject-nights of EEG sleep recording. The distribution of REM latency is bimodal, with peaks occurring between 0 and 10 min and between 40 and 60 min.



10 and 40–60 min, respectively (Figure 1). Thirty percent of the recordings fell between 0 and 10 minutes and 25.6% between 40 and 60 minutes. When the lower of the two recorded RLs was considered for each subject, we found that 42% of our subjects had at least one SOREM-10.

Clinical Correlates of SOREM

As we obtained 2 nights of EEG sleep recording on our subjects, the lower of the two RLs was used to divide our patient sample into three groups, as originally described by Ansseau et al. (1984), to examine clinical correlates of SOREM: (Group 1) patients exhibiting at least 1 night of RL < 10 min, or SOREM-10 yielding an n = 26; (Group 2) patients exhibiting no SOREM-10, but having at least one RL between 10 and 19 min (SOREM-20), yielding an n = 6; and (Group 3) those with both RLs ≧ 20 min, yielding an n = 30. RDC diagnostic categories, demographic features, and clinical response of the RL groups were analyzed using the chi-square statistic. One-way Analysis of Variance (ANOVA) was used to compare parametric information (age, HRSD scores, age at first onset, etc.).

Subjects with SOREM-10 differed demographically from the other groups in that they were older at the time of study and also at the onset of the first depressive episode (Table 1, $p < 0.03$). Attempted analysis of covariance on RL for the three RL groups using age as a covariate demonstrated that age was not a significant covariate ($p = 0.39$) in this sample. The three groups did not differ significantly in any of the RDC diagnostic categories or in terms of treatment response at discharge or family history of mania or depression. Subjects with SOREM-10 had a longer hospital stay and more frequently had a family history of suicide than those without SOREM-10 ($p < 0.03$). In the entire sample of 62 subjects, 7 subjects received electroconvulsive therapy (ECT). Six of the seven were in the SOREM-10 group, and the other belonged to the SOREM-20 category (Table 1,

Table 1. Clinical and Demographic Features of the Three REM Latency Groups

Clinical and demographic characteristics	SOREM-10 n = 26 (mean ± SD)	SOREM-20 n = 6 (mean ± SD)	Non-SOREM n = 30 (mean ± SD)	F or χ^2	$p <$
Age	55.0 ± 11.4	42.5 ± 12.4	40.3 ± 11.9	8.02	0.001
Age of first episode	39.8 ± 11.6	32.6 ± 13.7	29.5 ± 16.0	3.00	0.06[a]
Number of prior episodes	3.7 ± 2.8	2.5 ± 3.0	3.0 ± 3.0	0.64	NS
Length of hospital stay in days	80.7 ± 40.5	55.5 ± 21.5	59.4 ± 22.2	3.71	0.03
HRSD scores	23.8 ± 6.1	21.9 ± 2.7	21.8 ± 4.8	1.08	NS
Carroll scores	33.5 ± 8.0	33.3 ± 6.5	28.2 ± 9.2	2.67	0.08[a]
Sex					
Male	9	1	9		
Female	17	5	21	0.75	NS
Positive family history of suicide	8/26	2/6	2/26	4.87	0.03[b]
Number receiving ECT	6/26	1/6	0/30	7.60	0.03
Bipolarity					
UP	17	6	19		
BP	9	0	11	3.19	NS
BP-1	6	0	3		
BP-2	3	0	8	3.10	NS
Treatment response					
Good	17	4	18	1.08	NS
Poor	6	2	9		
Indeterminate	3	0	3		

[a]SOREM-10 > non-SOREM by follow-up comparison, $p < 0.03$.
[b]For 2 × 2 comparison of SOREM-10 with non-SOREM group.

$p < 0.03$). The SOREM-10 group was not more severely depressed by HRSD than the other RL categories. When Carroll self-rating scores of depression were considered, however, the SOREM-10 group had higher scores than the non-SOREM group (Table 1, $p < 0.03$).

Discussion

Our data show a clear bimodal distribution of RL, with peaks occurring between 0–10 and 40–60 min. Earlier reports on RL distribution in depressives ranged from bimodal (Schulz et al. 1979; Coble et al. 1981) to unimodal (Ansseau et al. 1984). Forty-two percent of our patients exhibited at least 1 night of SOREM-10, and thus, our results confirm earlier reports that SOREM-10 occurs in a significant proportion of inpatient depressives (Schulz et al. 1979; Coble et al. 1981).

Samples with a high mean age show a single RL peak and a high prevalence of SOREM. For example, Reynolds et al. (1985), whose sample had a mean age of 69.9 years, found 42% of all nights with SOREM-10, whereas 30% was found in our more middle-aged sample. A sample with a younger mean age (36.4 years) than our sample had only 8% of nights with SOREM-10 (Ansseau et al. 1984). In accord with this, our patients exhibiting SOREM-10 were older both at the time of study and during the first episode of depression than those without SOREM. This is consistent with reports of an age-related decrease in RL in normals, and even more markedly in depressives (Ulrich et al. 1980; Reynolds et al. 1985). Thus, age appears to at least partially account for the distribution of RL in depression. Other factors appearing to favor the presence of SOREM include inpatient status (Rush et al. 1982; Kupfer et al. 1986) and psychoticism, agitation, or retardation (Kupfer et al. 1986; Thase et al. 1986).

An inverse correlation between RL and severity of depression has been suggested (Spiker et al. 1978), but our subjects with SOREM-10 did not differ from non-SOREM patients in either their HRSD scores or in any of the RDC diagnostic categories. However, they had higher Carroll self-rating scores for depression than those without SOREM-10. Concerning associations of other clinical features with SOREM, with clinicians blind to sleep study results, six of the seven subjects who later received ECT had SOREM-10. The RL of the seventh subject was also less than 20 min. Thus, no non-SOREM patients received ECT. Subjects with SOREM-10 required hospitalization for 3 weeks longer than those without SOREM. In sum, SOREM appears to be associated with a more severe illness.

Our findings should encourage continued study of SOREM. It would be of interest to examine the relationship of RL and SOREM to other psychobiological measures, such as hypothalamic–pituitary–adrenal axis function (Rush et al. 1982).

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Taste and Smell Perception in Depression

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Introduction

In addition to the disorders of appetite, weight maintenance, or hyperphagia encountered in depressive illness (Hopkinson 1981), some depressed patients may also complain specifically of a diminished ability to taste and to enjoy food, and some report a craving for sweets (Steiner et al. 1969; Harris et al. 1984). Steiner et al. (1969) long ago reported that sucrose taste recognition thresholds were significantly elevated in depressives. We undertook to repeat these observations, and because complaints of taste alteration sometimes arise from olfactory deficiency (cf., Doty and Kimmelman 1986), we also studied smell perception.

Experiment 1: Sucrose Taste Perception

Methods

Subjects. Taste intensity and pleasantness ratings were obtained from 36 depressed patients [17 men with a mean age (± SD) of 47 ± 14

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