Sleep Onset REM Periods in Schizophrenic Patients

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Sleep EEG studies in depression have consistently shown shortened rapid-eye-movement (REM) latency in many patients (Kupfer et al 1986), with a smaller subset experiencing sleep-onset REM (SOREM), defined as the onset of REM within 10–20 min of the onset of sleep. In depression, SOREMs have been associated with greater illness severity (Reynolds et al 1985; Coble et al 1981), psychotic symptoms (Coble et al 1981; Kupfer et al 1986; Thase et al 1986), and older age (Schultz et al 1979; Ansseau et al 1984; Reynolds et al 1985; Kupfer et al 1986; Kumar et al 1987). Research to date cannot yet determine whether SOREMs represent an extension of the same process or processes that cause shortening of REM latency or result from a different process. Kupfer and Ehlers (1989) have suggested that SOREMs may indicate shortening of REM latency because of increased REM "pressure," as opposed to deficient slow-wave sleep, which could also shorten REM latency. Examination of this process in schizophrenic patients may be useful, because some schizophrenic patients, like depressed patients, exhibit shortened REM latencies, including SOREM (Zarcone et al 1987; Kempenaers et al 1988). We undertook the following retrospective analysis of our schizophrenia–sleep data base, comparing patients who experienced SOREM periods with those who did not to see whether the groups showed differences in clinical presentation, sleep variables, or prognosis.

Methods

The sample consisted of 36 schizophrenic inpatients (mean age = 28.6 ± 7.7, range 19–47) diagnosed by SADS/RDC and DSM-IIIR criteria who gave informed consent to participate in the study. After a minimum of 2 weeks free of medication, they underwent two consecutive nights of sleep EEG studies in their own hospital beds, with the first night for adaptation and to rule out any primary sleep disturbance, such as sleep apnea. Data from the second night only were used in the analysis. Patients were clinically screened to exclude those with signs of narcolepsy, and staff prevented patients from napping on the days when sleep studies were performed. Placement of electrodes and scoring were in accord with the methods described by Rechtschaffen and Kales (1968). Sleep onset was defined as the first minute of stage 2 sleep followed by at least 10 min of stage 2 sleep not interrupted by more than 2 min awake or in stage 1. REM latency was defined as the time between sleep onset and the occurrence of the first REM period of at least 3 min duration, minus intervening time awake (RLMA).

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Once during the medication-free period and once after 4 weeks of treatment with 8–30 mg haloperidol equivalents, patients were assessed by the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptoms (SANS), and the Hamilton Rating Scale for Depression (HRSD, 17 item). One-year follow-up was done on 27 patients and scored according to the Strauss–Carpenter Outcome Scale (Strauss and Carpenter 1972).

Results

Of the 36 patients, 6 (16.7%) experienced REM latency less than 10 min and 1 experienced a REM latency between 10 and 20 min. As seen in Figure 1, the distribution of REM latencies suggests a bimodal distribution. Using the strict definition of SOREM as REM onset < 10 min, we have compared these 6 patients with SOREM with the remaining 30 patients with RLMA ≥ 10 min.

The SOREM and the non-SOREM group did not differ significantly in age at the time of the study or at the onset of illness, duration of illness, number of hospitalizations, education, sex distribution, or subtype distribution (Table 1). Only 1 patient in the SOREM group had never been on medication, and of those who had been, 2 of 5 had been medication-free for more than 4 weeks, compared with 9 of 15 in the non-SOREM group.

Analysis of sleep variables was by Mann–Whitney U test. With regard to measures of sleep (Table 2), the SOREM group differed from the non-SOREM group only in having a shorter first REM period and less first period REM activity. The two groups exhibited no significant differences in other measures of REM sleep, measures of sleep continuity, or sleep architecture.

Two-way analysis of variance (ANOVA) of rating scales (Table 1), with pretreatment and posttreatment scales as repeated measures, revealed a strong group effect for SANS scores ($df = 1,34$, $p < 0.005$). Post hoc t-test with degrees of freedom corrected for the disparity in sample sizes (Glantz 1987) showed greater negative symptoms pretreatment and posttreatment in the SOREM group. We found a group effect for BPRS total scores ($df = 1,34$, $p = 0.05$), but these scores did not differ by post hoc t-test. BPRS positive subscales (conceptual disorganization, suspiciousness, hallucinatory behavior, and unusual thought content) and HRSD scores did not differ between the groups. ANOVA also revealed a very strong treatment effect for all scales ($df = 1,34$, $p < 0.0001$), and no treatment by group interaction, indicating that both groups improved equally with treatment. On the Strauss–Carpenter Outcome Scale, the SOREM group had significantly poorer global functioning at 1 year by Student's t-test.

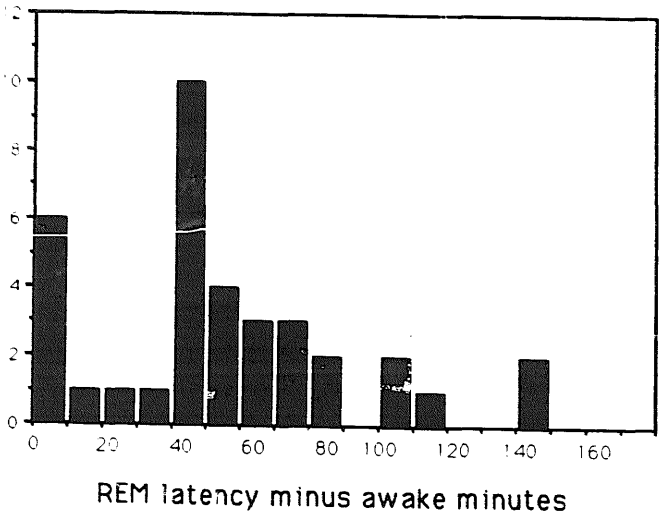

Figure 1. Frequency distributions of REM latencies in schizophrenic patients ($n = 36$ patients).

Table 1. Characteristics of SOREM and Non-SOREM Schizophrenics

Variable	SOREM (n = 6) Mean ± SD	Non-SOREM (n = 30) Mean ± SD	F	t^a or χ^2	$p<$
Age (yr)	32.2 ± 9.75	27.9 ± 7.34		1.24	NS
Sex	3M, 3F	21M, 9F		0.9	NS
Age at onset	27.5 ± 11.1	23.0 ± 7.1		1.29	NS
Education (yr)	12.3 ± 1.4	13.1 ± 2.4		0.76	NS
Duration of illness (mo)	56.8 ± 75.5	48.2 ± 60.3		0.39	NS
Number of hospitalizations	3.3 ± 4.1	1.9 ± 3.0		1.03	NS
Number neuroleptic naive (%)	1 (16.7)	15 (50)		2.26	NS
DSM-IIIR subtypes	Patients (n)				
Paranoid	2	13			
Undifferentiated	4	15			
Disorganized	0	2			
Clinical variables					
BPRS total			4.12		=0.05
Pretreatment	53.8 ± 8.9	46.2 ± 7.6		2.17	NS
Posttreatment	39.7 ± 5.3	35.4 ± 7.1		1.39	NS
BPRS positive symptoms			2.51		NS
Pretreatment	16.5 ± 3.1	14.3 ± 2.7			
Posttreatment	11.2 ± 2.6	9.8 ± 3.0			
SANS			12.23		0.005
Pretreatment	16.0 ± 2.0	11.1 ± 4.2		2.76	0.05
Posttreatment	12.5 ± 3.6	7.6 ± 2.7		3.84	0.01
HRSD			0.065		NS
Pretreatment	14.7 ± 2.2	13.8 ± 4.7			
Posttreatment	8.5 ± 2.7	8.7 ± 4.2			
Outcome: Global function[b]	7.2 ± 3.1[c]	12.0 ± 3.1		3.39	0.01

[a]For t-tests, df corrected according to Glantz (1987).
[b]For the non-SOREM group, n = 21.
[c]Higher score means better outcome.

Discussion

Our percentage of patients with SOREM (16.7%) compares to Zarcone et al (1987), who found 3 of 12 schizophrenic patients (25%) to have a RLMA of less than 15 min. Kempenaers et al (1988) report REM latencies of less than 20 min in 3 of 26 patient-nights. SOREMs can occur in normals when the sleep–wake cycle is altered (Carskadon and Dement 1975) and have been described in amphetamine withdrawal, but neither of these factors appeared to be operative with our patients. One has to consider the possible effects of neuroleptic withdrawal with only a 2-week washout period, although half of our SOREM patients had either never been on psychotropics or had been withdrawn for more than 4 weeks.

SOREM periods in our schizophrenic patients have relatively short durations when compared with SOREMs in depressives, which tend to be long (Ansseau et al 1984), except when

Table 2. Sleep Parameters

REM latency minus awake, min	SOREM (n = 6)	Non-SOREM (n = 30)
	Mean ± SD	Mean ± SD
	3.7 ± 3.3	64.6 ± 31.7
Sleep continuity		
Sleep latency (min)	70.3 ± 60.5	75.7 ± 65.7
Total time asleep (min)	296.3 ± 85.9	307.4 ± 80.2
Arousals	5.2 ± 3.2	4.4 ± 4.0
Early morning awakening (min)	13.5 ± 18.3	5.8 ± 11.8
Sleep efficiency (%)	72.5 ± 20.4	74.6 ± 17.4
Sleep maintenance (%)	90.3 ± 12.7	93.9 ± 8.1
Sleep architecture		
Stage 1 %	13.2 ± 6.7	13.8 ± 6.2
Stage 2 %	52.1 ± 6.5	52.1 ± 10.8
Delta %	8.6 ± 5.9	10.3 ± 11.6
REM %	26.1 ± 5.5	23.8 ± 7.7
REM sleep		
REM periods	3.8 ± 1.3	3.1 ± 1.0
Total REM time (min)	76.2 ± 22.1	72.4 ± 28.8
Total REM activity	88.3 ± 43.7	86.3 ± 52.1
Total REM density	1.13 ± .25	1.16 ± .47
First REM period		
Time (min)	7.2 ± 3.4[a]	20.4 ± 12.4
Activity	8.3 ± 4.6[b]	22.9 ± 17.9
Density	1.2 ± .55	1.1 ± .61

[a] $p < 0.005$ by Mann–Whitney U test.
[b] $p < 0.01$ by Mann–Whitney U test.

psychosis accompanies the depression (Thase et al 1986; Ganguli et al 1987).

Schizophrenic patients with SOREM, compared with those without SOREM, had a shorter first REM period, more negative symptoms both before and after treatment, and poorer global functioning at 1 year. SOREMs may simply indicate greater overall severity (higher pretreatment BPRS and SANS scores and poor outcome), and that would be consistent with the demonstrated association between shortened REM latency (Tandon et al 1989) and the poor outcome associated with negative symptoms in schizophrenia (Andreasen 1982). After neuroleptic treatment, the major differences occur in ratings of negative symptoms, suggesting that additional research examine the links between persistent negative symptomatology and neurotransmitter mechanisms involved in the control of REM sleep onset and duration.

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