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Full Length Research Paper

Polysomnographic differences between severe depression and schizophrenia

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Certain subtypes of major depression, particularly if associated with severe psychomotor retardation or psychotic features, may be difficult to differentiate from schizophrenia due to overlapping symptoms. The aim of this study was to assess the potential role of polysomnography as a tool for differentiating between severe depression with or without psychotic features and schizophrenia. Forty patients aged 18 to 50 years were recruited, comprising 20 with severe depression and 20 with schizophrenia who had defaulted from follow-up visits and had been off their medications for over a week. Two successive overnight polysomnographic recordings were done for all patients. Rapid eye movement latency was 26 ± 6.9 minutes and 43.9 ± 16.9 min in patients with depression and schizophrenia, respectively, with a statistically significant difference between the groups (*P* < 0.006). Rapid eye movementintensity was 34 ± 14% in depressed patients and 21.4 ± 4.5% in patients with schizophrenia, again with a statistically significant difference between the groups (*P*<0.015). On the other hand, stage IV intensity was significantly (*P* < 0.03) lower in patients with schizophrenia (9 ± 7.9%) than in depressed patients (17.8 ± 9.2%). Polysomnographic parameters are different in schizophrenia and severe depression. Further research to assess cutoff scores for different polysomnographic parameters are needed to enable the utilization of polysomnography as a potential electrophysiologic tool for differentiating between these diagnoses.

Key words: Depression, schizophrenia, polysomnography, sleep, encephalography.

INTRODUCTION

Polysomnography helps in identifying encephalographic (EEG) sleep architecture in different mental disorders. Patients with schizophrenia tend to have shortened deep sleep and rapid eye movement (REM) latency (Cohrs, 2008; Benca et al., 1992; Yang and Winkelman, 2006). Whether sleep EEG is a trait or a marker of schizophrenia is unfortunately less clear. Some authors found consistent improvement in sleep continuity during neuroleptic treatment, with REM latency that increases with antipsychotics or, in other words, tends to normalize, while slow-wave deep sleep is more or less unchanged, questioning the later as a trait rather than a marker for schizophrenia (Goder et al., 2008; Maixner et al., 1997; Keshavan et al., 1996, 1995). On the other hand, major depression has been the subject of clinical research assessing polysomnographic analysis, and REM sleep as well as, non-REM sleep has been evoked by researchers. Shortened REM latency and ncreased REM intensity (percentage total sleep duration), as well as, shortened slow-wave sleep, have been reported by several authors, which are changes that may be in part attributable to endocrine rhythm disturbance (Germain et al., 2004; Armitage et al. 1999; Dew et al., 1996). Whether these polysomnographic changes represent

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Abbreviation: CGI-S, Clinical Global Impression of Severity; REM, rapid eye movement.

trait ora biological marker of depression has been questioned. The literature suggests correction with antidepressants, indicating a trait rather than a disease marker (Monteleone and Maj, 2008; Dew et al., 1996).

Severe major depression may present with symptoms overlapping with schizophrenia, for example, severe psychomotor retardation versus negative symptoms of schizophrenia. Both diagnoses may share psychotic features, whether they are delusions, hallucinations, or both. Our work focuses on polysomnography as a potential electrophysiological testing tool that may help in differentiating between schizophrenia and severe major depression.

MATERIALS AND METHODS

Twenty severely depressed patients and 20 patients with schizophrenia aged 18 to 50 years were randomly recruited from the outpatient service at Alexandria University Hospital from February to October, 2010. Only outpatients who had defaulted from follow-up visits and had been off their medications for over a week were included. All patients signed a consent form. The study was approved by the ethics committee at Alexandria Faculty of Medicine. Diagnosis was done by a structured clinical interview using DSM IV-TR (Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision) diagnostic criteria (APA, 2004). Only patients scoring ≥ 4 on the Clinical Global Impression Scale for Severity (CGI-S) (Guy, 1976) and whose condition was stable enough to do polysomnography were recruited. Patients with mental retardation, as assessed by previous IQ testing available in records, or debilitating chronic physical illness were excluded. All participants were screened for drug abuse and alcohol before recruitment. Drug screening was done by urine strips for detecting opiates, THC, MDMA, Amphetamines, Benzodiazepines and Barbiturates. Those turning positive for any drug of abuse were excluded due to probable interference with hypnogram.

Sleep architecture study

Polysomnography consisted of simultaneous recording of multiple physiological parameters related to sleep and wakefulness. The software used for data acquisition was the Cadwell version 1.7. We monitored the following neurophysiologic channels:

1. Four EEG channels (central and occipital with an ear reference providing the best amplitude) to monitor sleep stage
2.Two electro-oculogram channels to monitor both horizontal and vertical eye movements (electrodes placed at the right and left outer canthi, one above and one below the horizontal eye axis)
3. One electromyography channel (usually chin or mentalis and/or submentalis) to record atonia during REM sleep.

Procedure

All patients underwent two successive overnight polysomnography recordings. Because the patients were in unfamiliar surroundings and we need them to sleep more naturally, the first recording session was necessary to make the patients familiar with their surroundings, to avoid the" first night effect". Sleep study was scored manually. Patients were off medication on both nights when polysomnography was performed. The scorer was blinded to the diagnosis of the patients. Sleep staging was done according to the Rechtschaffen and Kales staging system approved by the American Sleep Association. The patients also underwent overnight video-monitoring on both occasions.

Statistical methods

The data obtained were analyzed using the Statistical Package for Social Sciences version 13 (SPSS Inc, Chicago, IL). $P < 0.05$ was used as the cutoff value for statistical significance. Due to the small samples in each group (n = 20), we utilized the parametric Student's *t* - test for independent groups. For *t* - testing applied to sleep stage intensity; equal variance was assessed and confirmed before comparing frequencies.

RESULTS

The study included 20 patients with schizophrenia and 20 severely depressed patients all scoring ≥ 4 on the CGI-S. All had not been taking their medication for over one week before undergoing polysomnography. In the schizophrenia group, the mean duration off medication was 3 ± 0.2 weeks compared with 2 ± 0.4 weeks in the depression group.

Medications prescribed for the patients before they stopped taking them due to noncompliance, were as follows. In the schizophrenic group, four (20%) patients had been on haloperidol, 12 (60%) on risperidone, one (5%) on aripiprazole, and three (15%) on quetiapine.In the depression group, 13 (65%) were on sertraline, three (15%) were on amitriptyline, and four (20%) were on sertraline and haloperidol.

Duration of illness was not significantly different between the two groups (4.8 ± 2.01 years and 5.1 ± 2.83 years in the schizophrenic and depressed patients, respectively). Both groups were balanced in terms of age, gender distribution, and disease severity as assessed by the CGI-S scale (Table 1)**.** Polysomnographic recordings show shorter REM latency and greater REM intensity in the depressed patients than in those with schizophrenia (Table 2). Intensity of the different non-REM phases in both groups shows decreased intensity of stage 4 in schizophrenic patients compared with depressed patients (Table 3). A sample hypnogram of a patient with schizophrenia is shown in (Figure 1a) and a depressed patient (Figure 1b).

DISCUSSION

Our study showed that severely depressed patients had increased REM sleep intensity and shorter REM latency than did patients with schizophrenia. On the other hand,

Table 1. Age, gender distribution, and duration and severity of illness.

Variable	Schizophrenic patients (n=20)	Depressed patients (n=20)	Statistical test
Gender	**{N(%)}**	**{N(%)}**	
Male	12 (60)	10 (50)	$X^2 = 0.52$
Female	8 (40)	10 (50)	
Age (years)	35.2 ± 8.01	36.9 ± 7.98	T = 0.67
Duration of illness (years)	4.8 ± 2.01	5.1 ± 2.83	T =1.6
CGI-S score	5.1 ± 0.55	4.6 ± 0.5	T = 0.89

*P < 0.05.

Table 2. REM latency and intensity in schizophrenic and depressed groups.

Variable	Schizophrenic patients (n=20)	Depressed patients (n=20)	*T* - test
REM latency (min)	43.9 ± 16.9	26 ± 6	3.11 (*P* < 0.006)*
REM intensity (%)	21.4 ± 4.5	34 ± 14	2.7 (*P* < 0.015)*

*P < 0.05.

Table 3. Intensity of non-rapid eye movement phases in both groups.

Variable	Schizophrenic patients (n=20)	Depressed patients (n=20)	*T* - test
Phase 1	1.8 ± 1.7	3.8 ± 1.2	-3.03 (*P* < 0.007)*
Phase 2	38.8 ± 8.1	45 ± 7.4	-1.79
Phase 3	16.4 ± 5	12 ± 3.8	2.22 (*P* < 0.04)*
Phase 4	9 ± 7.9	17.8 ± 9.2	-2.29 (*P* < 0.03)*

*P < 0.05.

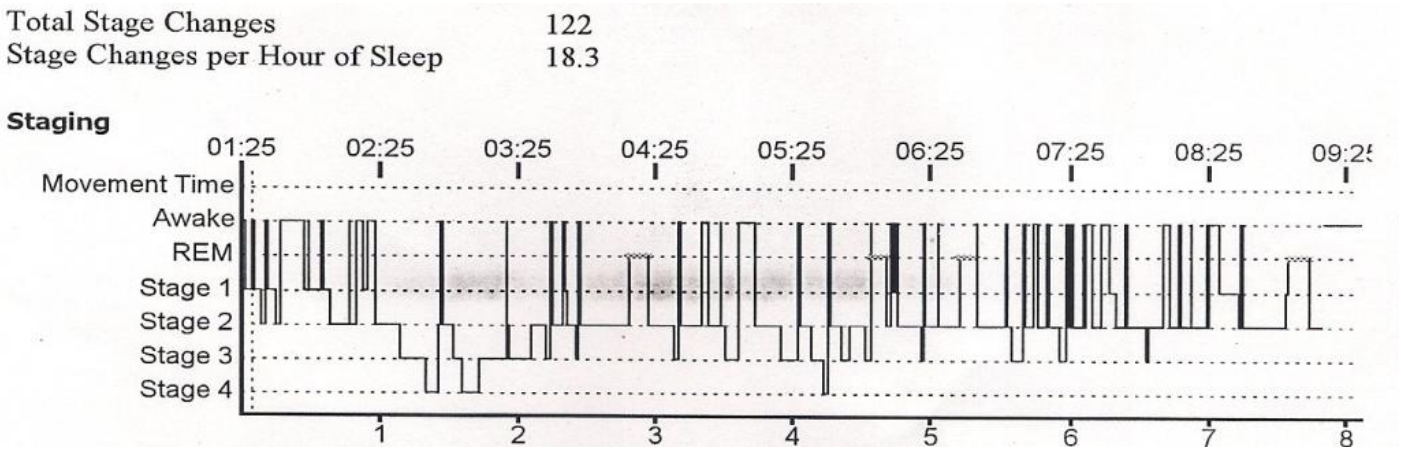

Figure 1a. Hypnogram from a schizophrenic patient.

patients with schizophrenia showed decreased intensity of phase 4 non-REM deep sleep than did depressed patients. Other authors have reported that changes in subjective sleep complaints are paralleled by EEG

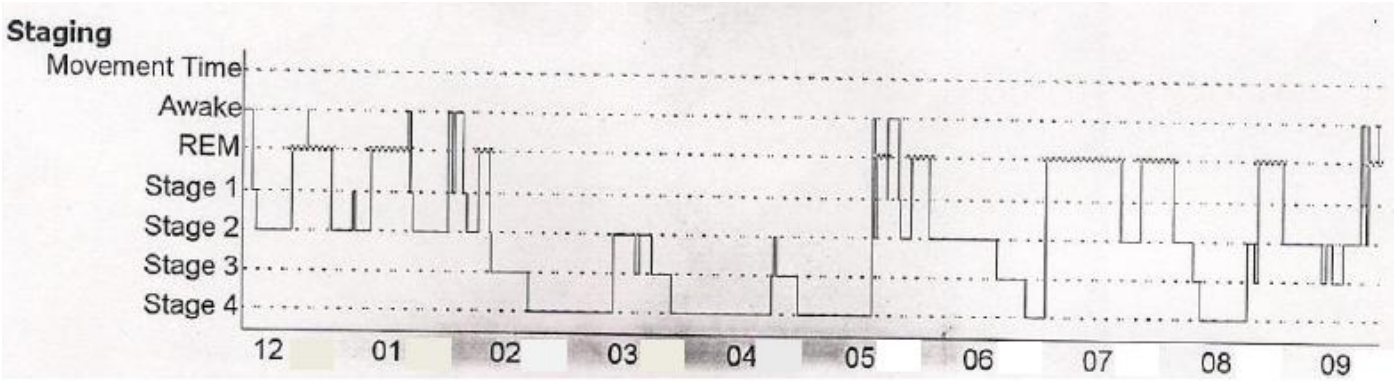

Figure 1b. Hypnogram from a depressed patient.

measures of sleep in patients with depression. These include increased sleep latency and decreased sleep continuity (Nofzinger et al., 1993; Monteleone and Maj, 2008). In terms of EEG sleep stages (that is, sleep architecture), depressed patients often show reduced stage 3 and 4 non-REM sleep, also known as slow-wave sleep because of the presence of slow delta activity on EEG during these stages. Several changes in REM sleep have also been noted. These include an increase in the amount of REM sleep, shortening of the time to onset of the first REM period of the night, shortened REM latency, and increased frequency of eye movements within an REM period (Nofzinger et al., 1993; Ivaneko et al., 2005).

Stressful life events also interact with EEG sleep. For instance, individuals who have severe stressful events preceding the onset of depression are less likely to have reduced REM latency than patients without such a stressor. Among older depressed patients, poor sleep is associated with a shorter episode duration, older age, greater medical burden, the presence of life stressors, and a lower level of perceived social support (Dew et al., 1996).

EEG sleep recordings aid our understanding of the neurobiology, longitudinal course, and treatment outcome in depression. Although, severely reduced REM latencies, phasic REM measures, and sleep continuity disturbances generally move towards control values after remission of depression, most sleep measures show a high correlation across the course of an episode (Monteleone and Maj, 2008; Rush et al., 1989).

Studies examining treatment-naïve patients with schizophrenia have shown no increases in REM sleep, so the increases in REM sleep observed in previously treated subjects may reflect the effects of medication withdrawal and/or changes related to the acute psychotic state. It is unlikely that the observed decreases in REM latency in some schizophrenia patients result from primary abnormalities in REM sleep (Benson, 2006; Keshavan et al., 1998).

Slow-wave sleep is of particular interest in schizophrenia because of the implications of the prefrontal cortex in this disorder and in generation of slow-wave sleep. Several studies have shown a reduction of slow-wave sleep in schizophrenic patients. Moreover, slow-wave sleep deficits have been seen in acute, chronic, and remitted states, as well as, in never-medicated, neuroleptic-treated, and unmedicated patients. However, not all studies show these deficits. Studies that have failed to find differences in slow-wave sleep have generally used conventional visual scoring (Keshavan et al., 1995; Benson, 1993).In fact, automated scoring of sleep stages may show different results based on the spectral analysis of EEG waves.

The polysomnographic patterns in schizophrenia and severe depression have been investigated by many authors, and our work is an attempt to replicate these and translate our findings to clinical application in terms of the potential differentiating diagnostic role of polysomnography when it comes to psychiatric disorders where clear diagnosis is problematic. Major depression, particularly when accompanied by severe psychomotor retardation or psychotic features overlapping with symptoms of schizophrenia, is a good example of a diagnostic dilemma.

Our study was limited by its small sample size. We recommend replication of our research in a larger population to allow more definitive conclusions. Another limitation of this research is the fact that the patients were not drug-naïve. Intake and withdrawal of different psychotropic agents may alter polysomnographic parameters. For example, antidepressants (except for mirtazapine) suppress REM sleep, and their withdrawal may lead to rebound REM. We recommend further polysomnographic studies in drug-naïve patients with

schizophrenia and depression.

Conclusion

Depressed patients tend to show shortened REM latency and increased REM intensity, while patients with schizophrenia tend to have decreased intensity of phase 4 non-REM deep sleep. Further research to determine cutoff scores for different polysomnographic parameters is needed to enable the useof polysomnography as a potential electrophysiologic tool for differentiating between these two diagnoses.

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