Actigraphy in patients with treatment-resistant depression undergoing electroconvulsive therapy

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Abstract

Depressive disorder is frequently accompanied by changes in psychomotor activity and disturbances of the sleep–wake cycle. The chronobiological effects of electroconvulsive therapy (ECT) in patients with treatment-resistant depression (TRD) are largely unknown. The objective of the current study was to measure the influence of ECT on patients’ activity and sleep. 15 patients with unipolar TRD were treated with ECT. Activity levels were measured with wrist actigraphy before and after ECT. Remission rate (score on the 17-item Hamilton Depression Rating Scale lower than 8 points) was 40.0%. Remitters had increases of 56.0% on light activity, 49.8% on total activity, and 70.2% on circadian amplitude, while there was no significant change of these variables in subjects who did not experience remission. The circadian acrophase and actigraphic sleep-parameters were not significantly affected by treatment.

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1. Introduction

Depression is frequently accompanied by changes in psychomotor activity and disturbances of the rest-activity cycle. These symptoms represent key features of depression and have diagnostic, pathophysiological and therapeutic significance (Bunney and Potkin, 2008; Schrijvers et al., 2008). Despite a wide range of available antidepressant treatment strategies, treatment resistant depression (TRD) remains an important clinical phenomenon (Souery et al., 2007; Schlaepfer et al., 2012). Approximately 50–60% of patients do not achieve full remission after adequate antidepressant treatment (Fava, 2003; Nemeroff, 2007). Electroconvulsive therapy (ECT) is one of the most effective treatment strategies in TRD (Kellner et al., 2012) and appears to exceed the short-term efficacy of antidepressant medication with faster onset of action, fewer residual symptoms and higher remission rates (Mathew et al., 2005). However, the mechanism of action and the physiological changes occurring during ECT are still not completely understood (Bolwig, 2011; Lanzenberger et al., 2013; Tendolkar et al., 2013). Specifically, as of yet, no study has examined chronobiological changes accompanying the use of ECT.

Actigraphy is a non-invasive technique which uses a small wrist-worn device to create a high resolution time series of motor activity, which can be evaluated to assess subjects’ sleep–wake cycle. In contrast to electrophysiological techniques, wrist actigraphy allows ambulatory measurements for long periods with minimal interference to the subjects’ lifestyle (Ancoli-Israel et al., 2003). The American Sleep Disorders Association has proposed actigraphy as “an effective means of demonstrating multiday human rest-activity patterns” (American Sleep Disorders Association, 1995). Actigraphy has repeatedly been employed in research of different psychiatric disorders (Kripke et al., 1978; Satlin et al., 1991; Kasper et al., 2010; Pjrek et al., 2012), and several studies have shown the ability to derive measures of sleep and circadian rhythms from actigraphic data (Liéberman et al., 1989; Brown et al., 1990).

The aim of the present study was to examine the effect of ECT on the rest-activity cycle in TRD. Based on prior research with different antidepressant strategies (Raoux et al., 1994; Volkers et al., 2003; Winkler et al., 2005; Berle et al., 2010), we hypothesized an increase of motor activity and improvements in blunted circadian rhythms in patients with remission after ECT as compared to patients not remitting after ECT. Furthermore, we wanted to investigate the effects of ECT on sleep in this sample in an explorative way.
2. Method

2.1. Subjects

15 inpatients (10 women, 5 men; age: 47.9 ± 10.4 years, range: 22.1–64.6 years) with an episode of (recurrent) major depressive disorder according to the diagnostic criteria of the DSM-IV-TR (American Psychiatric Association, 2000) and the ICD-10 (World Health Organization, 1991) were recruited at the Department of Psychiatry and Psychotherapy (Medical University of Vienna, Austria). Only treatment-resistant patients, i. e. after a failure of treatment of at least two adequate trials with antidepressants of different pharmacological classes were selected (Bauer et al., 2013). Subjects had to be eligible for electroconvulsive therapy (ECT) after being medically cleared. Patients completed the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002) and had to obtain a total score of 23 or higher on the 17-item Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960) on inclusion. The psychopharmacological medication of the subjects (Table 1), with the exception of occasional doses of benzodiazepines, was kept stable throughout the study starting at least 10 days before inclusion. Patients with a history of substance abuse, schizophrenia, schizoaffective disorder or bipolar disorder as well as incompliant patients, pregnant females, and subjects involuntarily hospitalized according to the Austrian Hospitalization Act (Bundesgesetzblatt für die Republik Österreich, 1990) were not included. Patients with a history of past ECT treatments were also not enrolled. Subjects had to be in good overall physical health without somatic or neurological illnesses, that could have potentially influenced activity levels or circadian rhythms. The study was approved by the local institutional review board, the Ethics Committee of the Medical University of Vienna (project number EK 556/2008); all subjects provided written informed consent before any study procedures were performed.

2.2. Study procedures

ECT was performed using a Thymatron System IV device (Somatics Inc.; Lake Bluff, IL, USA) according to national and international guidelines and consensus statements for ECT (Conca et al., 2004; Lisanby, 2007; Bauer et al., 2013). Treatment was performed three times per week under general anesthesia with methohexital and muscle relaxation with succinylcholine. Seizure duration was measured by simultaneous electroencephalography (EEG) and electromyography (EMG). At each patient’s first treatment, repeated stimuli of increasing intensity were administered until a seizure occurred and the lowest stimulus intensity able to induce an epileptic seizure was defined as the threshold (Frey et al., 2001). In the following treatment, the charge was set at three times the seizure threshold. The intensity was further increased in the absence of seizure activity or in case of inadequate seizures (i. e. <20 sec; Peterchev et al., 2010). In all patients, ECT was started with unilateral stimulation using an electrode placement in the right frontotemporal position (d’Elia and Raotma, 1975). Bilateral stimulation was used after 5 ECT sessions in the case of insufficient clinical response. The number of administered ECT sessions was 9.8 ± 2.4 (range: 4–14).

Study participants were instructed to wear activity monitors (Actiwacth Plus by Cambridge Neurotechnology Ltd., Cambridge, UK) on their non-dominant wrist. Subjects were told to only remove the actigraphs when showering or bathing during the study period. The device contains a piezo-electric accelerometer that records the intensity and duration of all movements over 0.05 g. Recording epoch was adjusted to 60 s. Altogether, we were able to obtain 4.1 ± 4.7 days of actigraphic measurement before ECT and 3.6 ± 2.1 days after ECT. At the end of the study, patients had a second clinical evaluation, and treatment outcome was measured using the HAM-D.

2.3. Data collection and statistical analysis

Data were downloaded to a computer and processed subject-wise with the Actiwacth software (Cambridge Neurotechnology Ltd., 2001). Data were carefully reviewed and checked for missing values and outliers. A nonparametric circadian rhythm analysis (Van Someren et al., 1999) of the data and cosinor analysis (assuming that a sinusoidal curve can be fitted to the 24-h activity rhythm) were performed (Nelson et al., 1979). A sleep analysis (Kushida et al., 2001) was conducted with the sensitivity of the algorithm set to “medium” (an activity score of 40 or more during an epoch will designate that epoch as being awake) to estimate actigraphic sleep parameters. We calculated a percentage change between measurements before and after ECT for our outcome variables to account for intrindividual differences in baseline activity. Resulting data were further analyzed with IBM SPSS Statistics (IBM Corporation, 1989–2010) for differences before and after ECT in remitters (HAM-D ≤ 7) and non-remitters. We preferred to group our data by remission rather than by response to treatment because frequent residual symptoms such as daytime fatigue, lack of drive or sleep disturbances (Zajecka et al., 2013) would inevitably obscure changes in actigraphic variables. Light activity (activity between 08:00 a.m. and 22:00 p.m.) was selected as the primary outcome measure of our analysis. Total activity, amplitude, cosine peak (acrophase of the circadian rhythm), sleep efficiency, sleep latency, and fragmentation index (during sleep) were considered as secondary actigraphic outcome parameters. The use of these parameters has been previously validated (Oakley, 1997; Van Someren et al., 1999; Kushida et al., 2001; Lichstein et al., 2006; Thomas and Burr, 2008). Kolmogorov–Smirnov test was used to check for deviations from normal distribution in our variables. Student’s t test, Wilcoxon signed rank test and Pearson’s correlation coefficient were used for hypothesis testing. Effect sizes (Cohen’s d) were calculated from t-statistics and sample sizes using the following formula: $d = \frac{(\overline{y}_1 - \overline{y}_2)}{\sqrt{\frac{s_1^2 + s_2^2}{n_1 + n_2}}}$. For large samples, where $n_1 = n_2$ and $s_1^2 = s_2^2$, this reduces to a standard deviation $d = \frac{\overline{y}_1 - \overline{y}_2}{s}$. The $p \leq 0.05$ level of significance (two-tailed) was...
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