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24-h activity rhythm and sleep in depressed outpatients

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ABSTRACT

Disturbances in sleep and circadian rest-activity rhythms are key features of depression. Actigraphy, a non-invasive method for monitoring motor activity, can be used to objectively assess circadian rest-activity rhythms and sleep patterns. While recent studies have measured sleep and daytime activity of depressed patients using wrist-worn actigraphy, the actigraphic 24-h rest-activity rhythm in depression has not been well documented. We aimed to examine actigraphically measured sleep and circadian rest-activity rhythms in depressed outpatients. Twenty patients with DSM-IV major depressive episode and 20 age- and sex-matched healthy controls participated in this study. Participants completed 7 consecutive days of all-day actigraphic activity monitoring while engaging in usual activities. For sleep parameters, total sleep time, wake after sleep onset, and sleep fragmentation index were determined. Circadian rhythms were estimated by fitting individual actigraphy data to a cosine curve of a 24-h activity rhythm using the cosinor method, which generated three circadian activity rhythm parameters, i.e., MESOR (rhythm-adjusted mean), amplitude, and acrophase. Subjective sleep was also assessed using a sleep diary and the Pittsburgh Sleep Quality Index. Patients showed significantly lower MESOR and more dampened amplitude along with significant sleep disturbances. Logistic regression analysis revealed that lower MESOR and more fragmented sleep emerged as the significant predictors of depression. Correlations between subjectively and actigraphically measured parameters demonstrated the validity of actigraphic measurements. These results indicate marked disturbances in sleep and circadian rest-activity rhythms of depression. By simultaneously measuring sleep and rest-activity rhythm parameters, actigraphy might serve as an objective diagnostic aid for depression.

1. Introduction

Alterations in sleep patterns and psychomotor activities are among the characteristic features of depression. These symptoms are very frequently present in depressed patients and as such are included in the diagnostic criteria for major depressive disorder (MDD) (e.g., Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5); American Psychiatric Association, 2013).

Besides the sleep disturbances and reduced daytime activity, alterations in the circadian sleep-wake cycle are considered to be a key aspect of depression (Germain and Kupfer, 2008; McClung, 2013; Monteleone et al., 2011). Circadian rhythms refer to wide-ranging cyclic physiological processes across a period of around 24 h, among which the sleep-wake cycle is probably the most obvious one in our everyday lives. The involvement of circadian rest-activity rhythm in the pathophysiology of depression has been supported by the efficacy of bright light therapy in the treatment of depression (Oldham and Ciraulo, 2014). Circadian rhythms of other biological systems, such as core body temperature, melatonin and cortisol, have also been shown to be disrupted in depression (Germain and Kupfer, 2008). Indeed, depressive symptoms themselves often exhibit diurnal fluctuation, typically with more severe symptoms in the morning (Gordijn et al., 1994). However, the relative role of sleep and the circadian rhythm in depression is less clear, while these two factors are presumed to be interrelated (Borbély, 1982).

Actigraphy, a non-invasive method for monitoring a high-

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resolution time series of motor activity, can be used to objectively assess circadian rest-activity rhythms and sleep patterns with minimum interference to subjects' daily lives. With the recent advancement of actigraph devices and analysis methods, this technology has been increasingly applied to various clinical settings (Martin and Hakim, 2011). During the past several years, sleep and daytime activity in depression have been quantified using actigraphy (Burton et al., 2013; Martin and Hakim, 2011). In most of these studies, however, activity data were obtained during either daytime or nighttime (reviewed in Burton et al., 2013), thus not allowing circadian rhythms to be determined. In addition, while previous actigraphy studies of depression have tended to be conducted in hospitalized settings, these settings are considered unsuited for studying rest-activity rhythms since inpatients are displaced from their usual environments and required to adhere to daily routines of a hospital ward (Burton et al., 2013). Recently, a few actigraphy studies have investigated sleep and circadian activity rhythms in relation to depression (Luik et al., 2015b; Robillard et al., 2015). Luik et al. (2015b) identified depressive symptoms by screening community-dwelling middle-aged and older persons (mean age of 62.2 years) and found that depression was associated with fragmented 24-h activity rhythms. Robillard et al. (2015) targeted help-seeking young people with various emerging mental disorders (mean age of 20.0 years for those with primary depression) and observed that 24-h activity rhythms were altered in those with depression. While the targeted populations in these two studies were of importance in terms of public health, studies examining circadian rest-activity rhythms in depression that is more directly relevant to usual clinical settings are lacking.

At present, there are no objective measures available to aid in the diagnosis or prognosis of depression. Biomarkers that can serve as a complementary diagnostic tool for depression have therefore been enthusiastically studied, and actigraphic rest-activity parameters are considered as promising candidates. It should be noted, however, that several studies have reported greater discrepancies between subjectively and objectively measured sleep parameters in depressed patients than in healthy controls (Armitage et al., 1997; Rotenberg et al., 2000). While such an inconsistency may be attributable to sleep misinterpretation in these patients, there is growing evidence that subjective sleep quality can have a significant influence on mental health outcomes (Bernert et al., 2014; Maglione et al., 2014). These findings point to the importance of comparing subjectively and objectively measured sleep parameters in depression.

The present study aimed to examine actigraphically measured sleep and circadian rest-activity rhythms in depressed outpatients compared to healthy controls. Our hypotheses were: (1) that depressed patients would show disturbances in both 24-h rest-activity rhythm and sleep and (2) that compared to sleep parameters, 24-h rhythm parameters would be more strongly associated with depression. We also assessed subjective sleep measures and examined their relationships with the actigraphic parameters.

2. Materials and methods

2.1. Participants

Twenty patients with DSM-IV major depressive episode (age range: 16–62 years; 10 women) were recruited from our specialized depression outpatient clinic of the National Center of Neurology and Psychiatry (NCNP) Hospital, Tokyo, Japan. Many of these patients had suffered from prolonged depression despite previous treatment attempts and were therefore referred to our clinic in order to seek intensive diagnosis and treatment for their refractory depressive illness. Clinical diagnosis was made by an experienced psychiatrist based on interviews, observations and case notes. This clinical diagnosis was confirmed using the Structured Clinical Interview for DSM-IV Axis-I disorders (First et al., 1997) by a trained research psychiatrist. Of the 20 patients, 14 were diagnosed as having MDD and 6 as having bipolar disorder (all currently in a depressive episode). Patients who were in remission, as defined by the total score on the GRID-Hamilton Depression Rating Scale 21-item version (HAMD-21) (Hamilton, 1967) of less than 8, were excluded from the study. For the patients with bipolar disorder, manic symptoms were in remission as defined by the total score on the Young Mania Rating Scale (Young et al., 1978) of 12 or less (range: 0–8; median: 2) (Tohen et al., 2002). Patients with a history of past electroconvulsive therapy were not enrolled. The Global Assessment of Functioning scale (Endicott et al., 1976) was used to assess patients' current functioning. Detailed information on medication prescribed at the time of study participation is presented in Table 1.

Twenty healthy control participants (age range 22–63 years; 11 women) were recruited from the same geographical area via a free local magazine and our website announcement. They were interviewed using the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) by a trained research psychiatrist, and only those without current Axis-I psychiatric disorders were enrolled. A non-structured interview was also performed by an experienced psychiatrist to exclude individuals who demonstrated one or more of the following conditions: having past or current regular contact to psychiatric services, having a history of regular use of psychotropics, and presenting other obvious self-reported signs of past primary psychotic and mood disorders.

Additional common exclusion criteria for patients and controls were having a regular night shift work and presenting a history of independent sleep disorders, central nervous system diseases, severe head injury, or current substance abuse/dependence. The present study was approved by the ethics committee of the NCNP, Tokyo, Japan, and was conducted in accordance with the Declaration of Helsinki. After description of the study, written informed consent was obtained from every participant (or his/her parent when the participant was minor).

2.2. Actigraphy

Participants completed 7 consecutive days of all-day actigraphic activity monitoring while engaging in usual activities. They wore a Micromini-Motionlogger Actiwatch (Ambulatory Monitoring Inc., NY, USA) on the non-dominant wrist, and activity data were recorded over 1-min epochs. Participants were asked to remove the actigraphy only when showering or bathing. Actigraph records were processed using AW2 software (Ambulatory Monitoring Inc., NY, USA) to determine sleep and awake intervals and to extract sleep parameters. Data collected over the 7-day period were averaged into a single 24-h profile for analyses. Activity data were used to derive the following sleep and 24-h rhythm parameters:

For sleep parameters, total sleep time (TST; total amount of time scored as “sleep” during the down interval), wake after sleep onset (WASO; total amount of time scored as “wake” during the down interval) and sleep fragmentation index (SFI; total number of awakenings divided by total sleep time) were determined. We did not include actigraphically measured sleep onset latency (SOL; bed time to sleep onset time) because this parameter is not completely objective, in that in order to derive it we need to rely on diary information about the time he/she went to bed; this may be related to less consistent findings on actigraphic SOL compared to TST and WASO (Martin and Hakim, 2011).

Circadian rhythms were estimated by fitting individual actigraphy data to a cosine curve of a 24-h activity rhythm, which was