

# Older schizophrenia patients have more disrupted sleep and circadian rhythms than age-matched comparison subjects

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## Abstract

Patient reports and laboratory studies suggest schizophrenia patients have disrupted sleep across age groups. Studies have not compared overall sleep/wake patterns or circadian (24-h) activity rhythms of older community dwelling schizophrenia patients to matched comparison subjects. This study examined whether older schizophrenia patients had more disrupted sleep/wake patterns and circadian activity rhythms than age- and gender-matched normal comparison subjects (NCS). Twenty-eight older schizophrenia patients and 28 age- and gender-matched NCS were studied with three days of continuous wrist actigraphy. Nighttime and daytime actigraphically estimated sleep and wake, circadian activity rhythms and light exposure patterns were compared with and without years of education as a covariate. Patients spent longer in bed, had more disrupted nighttime sleep, slept more during the day, and had less robust circadian rhythms of activity and light exposure compared to NCS. Differences persisted in education-adjusted analyses. Within patients, working was associated with improved sleep and circadian rhythms. Findings suggest the sleep and circadian rhythm disruption of older schizophrenia patients was more extensive than that of matched NCS suggesting patients' sleep disruption was above and beyond what is attributable to advanced age alone. A need exists to develop multicomponent interventions to address sleep difficulties specific to older schizophrenia patients.

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## 1. Introduction

Individuals with schizophrenia commonly complain of disturbed nighttime sleep both in inpatient (Morgan and Drew, 1970; Rotenberg et al., 2000) and outpatient settings (Haffmans et al., 1994; Sweetwood et al., 1976). Laboratory polysomnographic studies confirm that nighttime sleep of patients with schizophrenia is highly fragmented (Tandon et al., 1992; Tandon et al., 1988; Nofzinger et al., 1993; Neylan et al., 1992; Goldman et al., 1996; Lauer et al., 1997; Keshavan and Tandon,

1993). In addition, REM and non-REM sleep abnormalities have been described in both medicated and unmedicated patients (Lauer et al., 1997; Jus et al., 1973; Ganguli et al., 1987; Hudson et al., 1993; Kempnaers et al., 1988; Stern et al., 1969). Studies suggest that these differences in nighttime sleep architecture are related to important clinical outcomes, medications, and specific psychiatric symptoms (Benson and Zarcone, 1994; Zarcone, 1979; Keshavan et al., 1994; Tandon et al., 1988; Goldman et al., 1996; Kajimura et al., 1996; Hoffmann et al., 2000).

In addition to subjective and objective nighttime sleep disruption, some studies suggest circadian rhythms of hormones and activity patterns are also disrupted in schizophrenia patients (Rao et al., 1994; Wirz-Justice

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et al., 2001; Wirz-Justice et al., 1997). Based upon analysis with the traditional cosine fitting method, a descriptive study from our laboratory showed that older patients with schizophrenia have disturbed circadian activity rhythms, disrupted nighttime sleep and excessive daytime sleep (Martin et al., 2001). Like other studies in the field, this original descriptive study was limited by the absence of sleep and circadian rhythm data from comparison subjects and by the method used to analyze circadian activity rhythms. Previous studies have not compared sleep/wake recordings or circadian rhythms of older community dwelling schizophrenia patients to matched comparison subjects, so it has not been possible to determine if the disruption in sleep/wake patterns was a result of the psychiatric disorder or a result of aging independent of the psychiatric disorder. Since the publication of our original report, we studied a group of age- and gender-matched normal comparison subjects (NCS) to address this limitation. We also employed a newly developed sophisticated method for circadian rhythm modeling, which enabled examination of additional circadian rhythm characteristics (Martin et al., 2000; Marler et al., 2004).

The current study examined differences between the older patients with schizophrenia we originally studied (Martin et al., 2001) and a group of matched NCS in daytime and nighttime actigraphically estimated sleep/wake and circadian rhythms of activity. We hypothesized that: (a) patients would sleep more at night, but would have poorer nighttime sleep quality than NCS; (b) during the day, patients would be sleepier than NCS; (c) patients would have less robust circadian activity rhythms than NCS; and (d) worse nighttime sleep quality and less robust circadian rhythms would be associated with lower levels of light exposure during the daytime hours. Secondary analyses were undertaken to examine the impact of education, working and living situation on sleep within the schizophrenia patients as well.

## 2. Methods and materials

### 2.1. Participants

Twenty-eight previously studied older patients with schizophrenia (14 men, 14 women, mean age = 58.3 years) were included. Schizophrenia patients were screened using the Structured Clinical Interview for DSM-III-R/DSM-IV (SCID; Spitzer and Williams, 1986), which was administered by geriatric psychiatry or psychology fellows. Patients met diagnostic criteria (DSM-III-R or DSM-IV) for schizophrenia (American Psychiatric Association, 1987, 1994). Diagnosis was confirmed at research staff meetings with two or more Board-certified psychiatrists present. These diagnostic procedures have previously been described in detail (Jeste et al., 1995).

For comparison, a group of age- and gender-matched healthy adults without psychiatric disorders (14 men, 14 women, mean age = 57.3 years) was recruited from a convenience sample of University employees and acquaintances of the research team. These NCS were not diagnosed with or receiving treatment for any psychiatric disorder (either with medication or psychotherapy), were not diagnosed with or exhibiting signs or symptoms of dementia, and had no family history of schizophrenia. All aspects of the study were carried out in accordance with the Declaration of Helsinki. The UCSD Human Subjects Committee reviewed and approved the study. Trained research staff reviewed consent forms with each participant, and all participants signed the consent forms.

### 2.2. Apparatus

The Actillum wrist actigraph (Ambulatory Monitoring, Inc., Ardsley, New York) was used to record minute-by-minute activity and illumination exposure using a linear accelerometer, a light transducer and a microprocessor. The actigraph's microprocessor has sufficient memory to record activity and illumination data for about one week. Since this wrist actigraph is light (3 oz), small ( $1 \times 3 \times 6$  cm) and is worn unobtrusively on the wrist, it is a well-tolerated non-invasive method for sleep/wake estimation.

Sleep/wake variables were estimated from average and maximum per-minute activity using the default automated sleep/wake-scoring algorithm (Cole–Kripke algorithm) in the ACTION3 software package (Ambulatory Monitoring, Inc., Ardsley, New York; Webster et al., 1982). The reliability of the algorithm has been validated for nighttime sleep/wake parameter estimation in several populations including elderly individuals (Cole et al., 1992; Webster et al., 1982; Ancoli-Israel et al., 1997). Actigraphy has been recommended for use in patient groups who might otherwise be difficult to study with traditional sleep recording methods (Ancoli-Israel et al., 2002a).

### 2.3. Procedures

Patients with schizophrenia completed comprehensive assessments every six months at the UCSD Advanced Center for Interventions and Services Research. During these visits, patients completed a battery of clinical measures including a sleep interview questionnaire. This questionnaire asked about sleep over the previous week and has been used in previous studies in our laboratory (Ancoli-Israel et al., 1991). NCS completed the sleep questionnaire prior to wearing the actigraphs.

Participants in both groups wore wrist actigraphs for 72 consecutive hours. Recorders were placed on their

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