

Circadian Disruption and Psychiatric Disorders: The Importance of Entrainment

Anna Wirz-Justice, PhD*, Vivien Bromundt, MSc,
Christian Cajochen, PhD

KEYWORDS

- Circadian rhythms • Sleep regulation • Actigraphy
- Major depression • Dementia • Psychiatric illness

There is a need for more knowledge of sleep medicine to be integrated into psychiatric training and practice. Although many psychiatrists are aware that most patients have some sort of a sleep problem, these mainly are addressed separately from the primary diagnosis, with appropriate choice of sleep-promoting psychopharmacologic agents or additional treatment with benzodiazepines or newer hypnotics. Consideration of circadian rhythms and their impact on sleep-wake behavior in psychiatric disorders is still rare in psychiatric practice.

This is somewhat surprising, because observations linking rhythmic behavior and psychopathology have a long tradition in clinical psychiatric research, particularly in major depression. These observations have been reviewed comprehensively,^{1–3} albeit with rather ambiguous conclusions. The precise nature of the links remains elusive, and it may be too simplistic to expect that the enormous variety of psychiatric disorders have common dysfunctions related to the biological clock. It is not only the problem of clearly defining patient groups within and among diagnoses, but also, different treatments make it difficult to define a specific circadian rhythm abnormality. It may be more the symptoms such as anxiety and depressed mood rather than the diagnosis that are related to sleep disorders. In addition, methodological issues cloud most

investigations, because masking effects of behavior and environment on the rhythms measured often have not been controlled for.

Thus, this article will not address evidence for circadian disruption as etiology. Do clock genes play a role in bipolar disorder?⁴ What is the evidence for phase-delayed rhythms in winter depression?^{5,6} Do different dementias have different rhythm abnormalities?⁷ Rather, circadian disruption of rest-activity cycles will be considered as a clinical symptom, which leads to pragmatic use of circadian-based treatments to support re-entrainment.

Hypotheses of biological clock disorder postulate alterations in suprachiasmatic nuclei (SCN) function that may result in a low amplitude or abnormal phase of the observed circadian rhythm. Alterations in SCN function may be caused not only by malfunction of the clock per se, but by means of changes in factors that set the clock. Importantly, the SCN—and all the peripheral clocks in the brain and the rest of the body—require zeitgebers (synchronizing agents) to ensure circadian entrainment (coupling of an endogenous rhythm to an environmental oscillator with the result that both oscillations have the same frequency), internally among themselves and externally with respect to the light-dark cycle. With insufficient zeitgebers, even correctly functioning biological clocks can become

Centre for Chronobiology, Psychiatric Hospital of the University of Basel, Wilhelm Klein Strasse 27, CH-4025 Basel, Switzerland

* Corresponding author.

E-mail address: anna.wirz-justice@unibas.ch (A. Wirz-Justice).

Sleep Med Clin 4 (2009) 273–284

doi:10.1016/j.jsmc.2009.01.008

1556-407X/09/\$ – see front matter © 2009 Elsevier Inc. All rights reserved.

desynchronized. This points to the important role for the major zeitgeber light, and the usefulness of melatonin, which feeds back on the SCN. Non-photic zeitgebers such as physical exercise, sleep, or food also contribute to entrainment of peripheral clocks. Social zeitgebers (eg, personal relationships, jobs, social demands) act indirectly on the SCN, because they determine the timing of meals, sleep, physical activity, and out- and indoor light exposure. In addition, the zeitgebers must impact on correct functioning receptors to be effective (eg, retinal photoreceptors for light perception).

A major tenet of chronobiology is that appropriate entrainment or synchronization to the 24-hour day–night/light–dark cycle is important for health. This may be particularly relevant to psychiatric illness.⁸ Circadian malentrainment does not necessarily cause the individual psychopathology, but may perpetuate or exacerbate the clinical symptoms. In general, entrainment is not only a prerequisite for good nighttime sleep and daytime alertness, but also for adequate mood state, cognition, and neurobehavioral function.

The chronobiological strategy of attending to entrainment of patients, independent of psychiatric diagnosis, is not entirely new, because it merely reformulates the classical clinical strategy of establishing stable daily structures to support the process of clinical improvement. The primary postulate is that integrity of the circadian rest–activity cycle promotes healthy functioning in all psychiatric disorders.

Here the focus lies on the importance of well-entrained sleep–wake cycles for mental health, with examples from various diagnostic categories. The accent will be on actigraphy, as a well-established,

relatively easy and noninvasive objective measure of the circadian rest–activity cycle.

ACTIGRAPHY AS A CLINICAL TOOL

Actigraphs are small, lightweight, wrist-worn solid-state recorders that record movement-induced accelerations (Fig. 1). The wrist-worn accelerometer generates activity counts, which are proportional to the intensity, frequency, and duration of motion (the higher the black bars, the more active). The activity counts are summed over a given time interval (eg, 2-minutes) and depicted either as single plots (24-hours) or double plots (48-hours represent day 1 and day 2 next to one another); time of day (x axis) begins at midnight. The subsequent days (y axis) are plotted beneath each another.

In general, two sets of parameters can be derived—one representing sleep measures such as sleep fragmentation and movement time, which correlate reasonably well with electroencephalogram (EEG) data⁹—and one set defining circadian rhythm characteristics, such as interdaily stability (IS), intradaily variability (IV), the timing of the most active and most inactive episodes, and the relative amplitude (RA).¹⁰ IS indicates the degree of resemblance between activity patterns on different days, documenting the consistency across days of the daily circadian signal and the strength of its coupling to stable zeitgebers. A higher value indicates a more stable rhythm. IV indicates the degree of fragmentation of the rhythm (ie, the frequency of transitions between periods of rest and periods of activity during a given day). A lower value indicates a less fragmented rhythm. The sequence of the most active

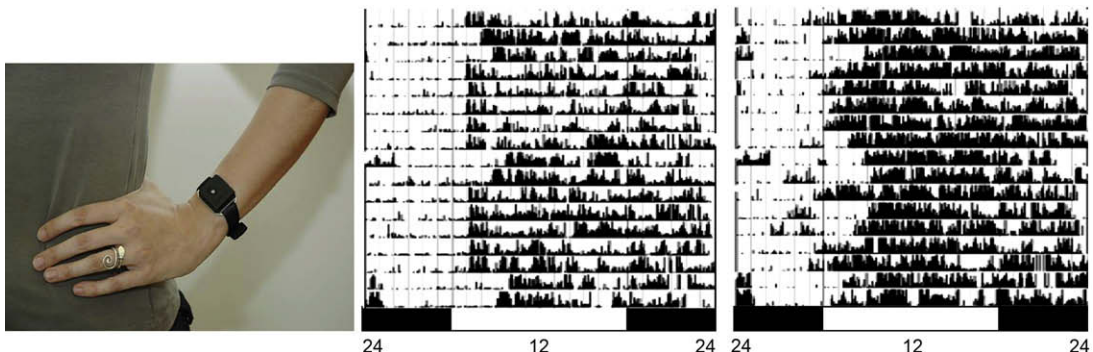


Fig. 1. The circadian rest–activity cycle is documented using an actigraph worn on the wrist of the nondominant hand (inset, Cambridge Neurotechnology Limited, Cambridge, UK, with light meter). Social zeitgebers in a married couple showing weekday work times affecting the onset of daily activity in the employed partner (63-year-old man), *left*, and free choice of wake-up time in the at-home partner (65 year-old woman), *right*. (Data from A. Wirz-Justice, unpublished data, 2009.)

Download English Version:

<https://daneshyari.com/en/article/3837649>

Download Persian Version:

<https://daneshyari.com/article/3837649>

[Daneshyari.com](https://daneshyari.com)