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RELIABILITY OF CIRCADIAN HEART PATTERN ANALYSIS IN PSYCHIATRY

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The assessment of circadian heart patterns represents a new methodology for documenting physiological dysregulation associated with psychiatric illness. Previous research has demonstrated abnormal heart rate patterns, especially during the bedtime interval, that are associated with depression, generalized anxiety disorder, panic disorder, and schizophrenia. These patterns are derived from heart rate data obtained while wearing an unobtrusive, two-lead heart rate monitor over a 24-hour period. To establish basic reliability, the second author blindly rated heart-monitored data from 50 subjects on two occasions, separated by an average of 6.6 weeks (range = 2.9–15.7 weeks). Subjects were classified as "definitely psychiatric," "probably psychiatric," "borderline," "broadly normal," and "signature normal." The exact category agreement rate was 78%. If a one-category difference is permitted (e.g., "definitely psychiatric" and "probably psychiatric" counted as an agreement), the agreement rate was 92%. Circadian heart pattern analysis is a promising new technology in psychiatric research and warrants further investigation.

KEY WORDS: circadian; heart pattern; reliability.

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INTRODUCTION

Laboratory testing for a reliable and valid biological marker for depression and anxiety disorders has eluded the profession of psychiatry. There is no doubt that laboratory testing is widely and successfully used to aid in the diagnosis of general medical conditions that can cause or contribute to the manifestation and maintenance of psychiatric illness. Some obvious examples include testing for thyroid function, electroencephalography for seizure disorders, and CT or MRI for structural brain abnormalities (e.g., tumors, strokes, etc.). However, routine and accurate laboratory testing for the most common primary psychiatric conditions, such as depression and anxiety disorders, is unavailable.

It is well known that many forms of psychiatric illness are associated with measurable physiological changes. Vegetative symptoms of depression, for example, usually reflect dysregulation in the autonomic and neuroendocrine systems. These symptoms, to a large degree, are controlled by the hypothalamus. Some specific examples of physiological changes are as follows: (1) sleep disturbance; often characterized by loss of stage IV sleep and difficulty staying asleep; (2) body temperature dysregulation (high versus low in the morning, often causing "morning sweats") (3) disrupted menstrual cycles (e.g., amenorrhea); (4) reduced sex drive (i.e., libido); (5) appetite changes (i.e., increased or decreased); (6) weight changes; (7) gastrointestinal changes (e.g., decreased secretions and/or decreased motility); (8) increased resting heart rate; (9) changes in 24-hour cortisol levels (i.e., usually elevations); (10) cortisol peak (shifting) is usually 1–2 hours after awakening, but in depression it can shift to the middle of the night (e.g., 1–2 AM); in 50–60% of patients, cortisol may fail to suppress with dexamethasone challenge; (11) growth hormone response to amphetamine may be diminished; (12) thyroid response to thyroid stimulating hormone (TSH) can be reduced; and (13) the hypothalamic pituitary axis may be overactive (1).

Recent research has demonstrated that circadian heart rate patterns are affected by psychiatric illness. Stampfer (2) illustrated that nighttime (i.e., sleeping) heart rate patterns in persons with various psychiatric disorders are distinctly different than the "signature normal" pattern found in some individuals who are free of psychiatric illness. Reasonably distinct heart rate patterns were presented for several diagnoses, including depression, generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), and schizophrenia.

As with any newly developed clinical procedure, the reliability and validity of the technique must be established before it can be used on a regular basis. At present, the physiological data derived from heart pattern monitoring are interpreted manually, through systematic examination of both quantitative and qualitative features. The purpose of this study was to examine the most basic aspect of this manual interpretation; namely, blind intra-rater reliability.

METHOD

Subjects and Procedures

Fifty subjects, referred by their physicians into a large-scale blind clinical trial, were selected for this study. Ten family physicians referred most of these outpatients. Some patients clearly had mental health problems and others had minor general medical problems. Participants were referred by their physician into the trial if they met the following criteria: were between the ages of 19 and 65 years of age, were in good general heath and were not pregnant, and were able to provide written informed consent. The average age of these subjects was 35.9 years (SD = 11.2). The sample was 78% female and 22% male. The breakdown of education in this samples was as follows: (a) grade 7 to 12 (without graduating high school) = 12%; (b) graduated high school or high school equivalent = 24%; (c) part college = 30%; (d) graduated 2 year college = 18%; (e) graduated 4 year college = 6%; (f) part graduate/professional school = 4%; and (g) completed graduate/professional school = 6%. The marital status of these subjects was as follows: (a) married or living with someone = 40%, (b) divorced = 6%, (c) separated = 12%, and (d) single (never married) = 42%.

Circadian heart rate and movement data were recorded using a "HeartLink Monitor" (Vancouver, B.C., Canada). The device consisted of two electrocardiogram (ECG) leads, and hardware capable of recording 24-hour continuous beats per minute and minute-averaged movement data. The two ECG electrodes were placed on the skin, one mid-sternum, and one on the mid-left lateral extent of the ribcage. Subjects were required to wear the monitor for a complete 24-hour period. Minute-averaged heart rate and movement data were calculated on-line and were downloaded following completion of the full recording interval. The movement data consisted of detecting horizontal movement, such as walking. Horizontal movement was scaled between zero and 15 for each minute of recording (zero representing no movement, and 15 representing continual movement). The heart rate and movement data consisted of 1,440 data points within the 24-hour period (1,440 = 1 data point per minute over a 24-hour period).

To evaluate the reliability of a single expert rater, the second author blindly rated heart-monitored data from 50 subjects on two occasions. The first rating occurred as part of the blind clinical trial; subjects were rated as they completed the trial. For the second rating, the subjects were given new identification numbers, and all were rated over a two-day interval. The average interval between ratings was 6.6 weeks (Range = 2.9–15.7 weeks). It is important to note that the purpose of this study is to examine the reliability of the broad, physiological classification ratings, not the validity of these ratings. The validity of these ratings is the subject of ongoing, large-scale research in which heart pattern data is being compared to data derived from physician ratings, psychiatric interviews, SCID interviews, and psychometric self-report questionnaires. This study was designed to determine if a human rater would sort the heart pattern data into similar categories, blindly, over a several week interval.

RESULTS AND DISCUSSION

Subjects were classified as "definitely psychiatric," "probably psychiatric," "borderline," "broadly normal," and "signature normal" on the basis of their physiological data. The breakdown of first and second ratings was as follows: (a) Signature normal = 0% and 0%, (b) Broadly normal = 12% and 6%, (c) Borderline = 14% and 4%, (d) Probably psychiatric = 12% and 20%, (e) Definitely psychiatric = 62% and 70%. There was a clear trend toward increased severity ratings during the second rating. The exact category agreement rate was 78%. If a one-category difference is permitted (e.g., "definitely psychiatric" and "probably psychiatric" counted as an agreement), the agreement rate was 92% (14% were classified in a more abnormal category during the second rating).

Figure 1 is an example of a 24-hour circadian heart rate pattern (24-CHP) designated as "signature normal." This pattern was characterized by Stampfer (2) as exhibiting the following characteristics: (a) a sleep interval usually between midnight and 8 AM, (b) a rapid decline in heart rate at the onset of sleep, (c) a flat nighttime interval (defined as the time the individual "goes to bed" to the time that they "get up") with a lower heart rate than observed during waking, and (d) a rapid

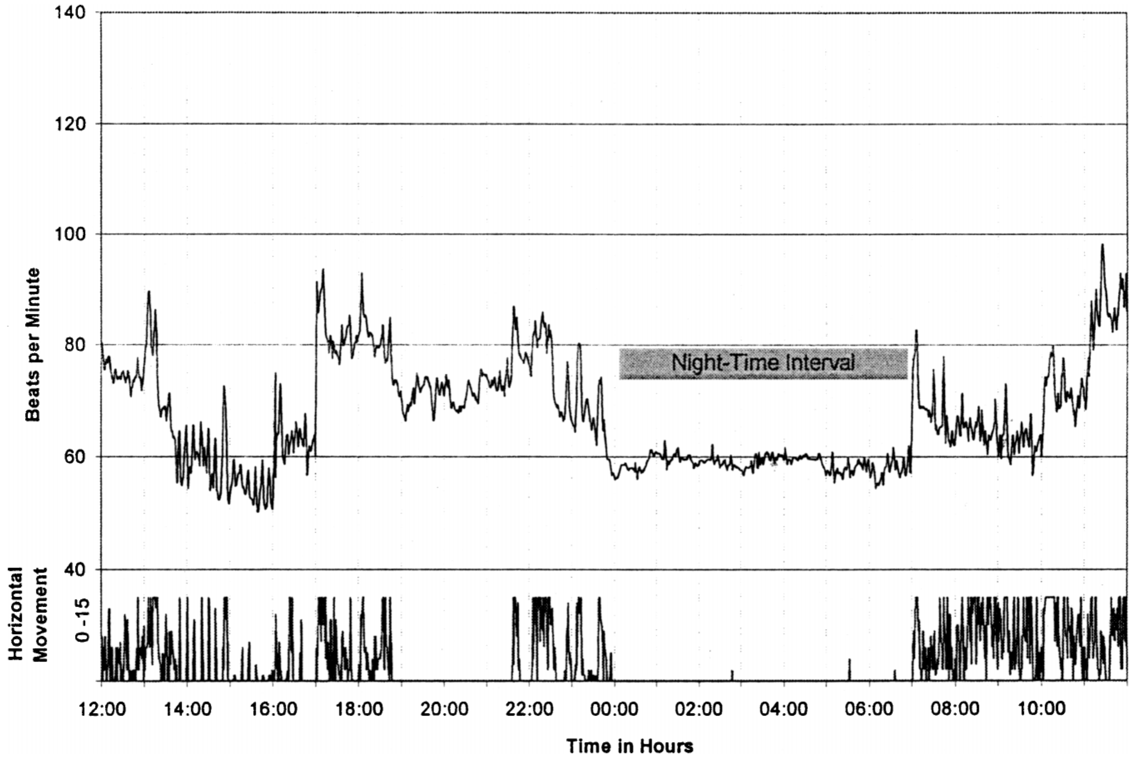

FIGURE 1. "Signature normal" circadian heart pattern.

rise to pre-sleep rates on waking. The movement associated with this pattern during the nighttime interval is typically low or nonexistent. There were no subjects in this study that were classified as signature normal.

Figure 2 is an example of a participant's 24-CHP twice classified as "broadly normal." For the purposes of this study, broadly normal was defined as circadian patterns that while not "signature normal," were generally normal in appearance and did not possess obvious characteristics of patterns believed to reflect psychiatric illness. This individual was a 35-year old female nurse. She had been rated by her physician as "clearly not depressed." Her Structured Clinical Interview for DSM-IV (SCID) indicated no Axis I diagnosis, and her Beck Depression–Inventory II (BDI-II) score was 0.

Figure 3 is a recording from an individual categorized twice as "probably psychiatric." Inclusion in this group required that the 24-CHP had some clear characteristics consistent with a psychiatric pattern. With this pattern, the onset of sleep is not well defined and there is a progressive decline in the mean trend until the end of the nighttime interval. This is followed by a prominent elevation on waking. The SCID diagnoses for this individual were anxiety disorder NOS, mixed

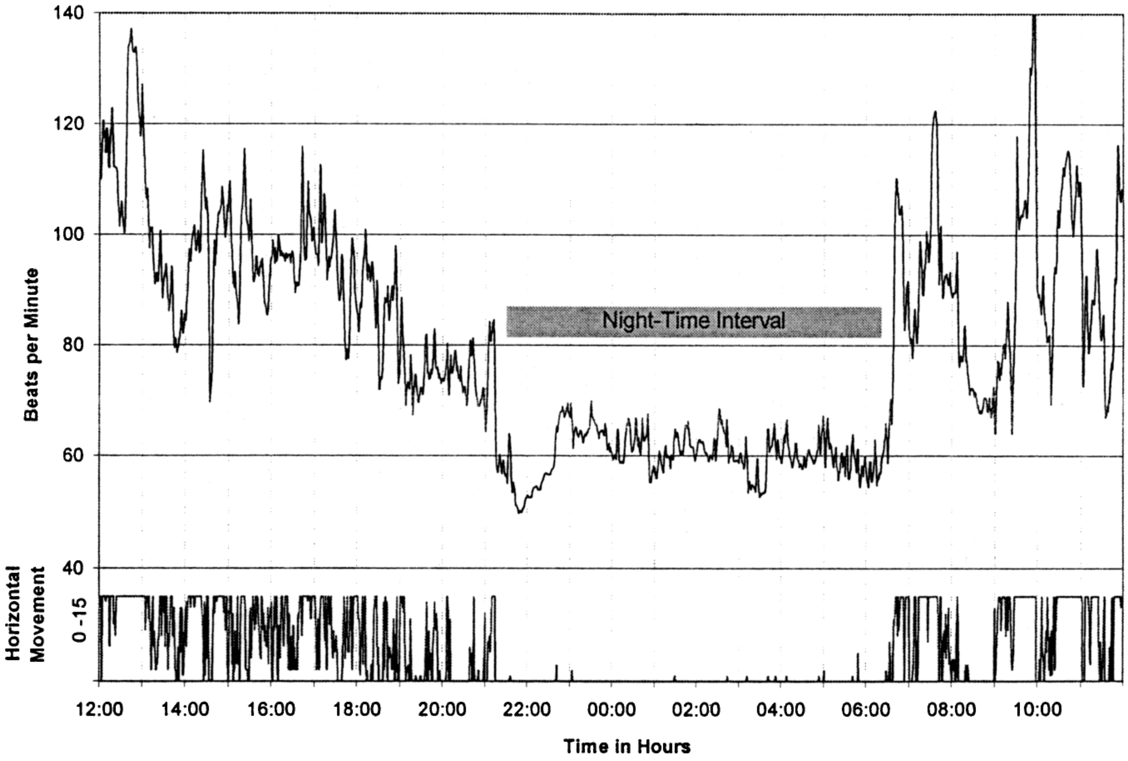

FIGURE 2. "Broadly normal" circadian heart pattern.

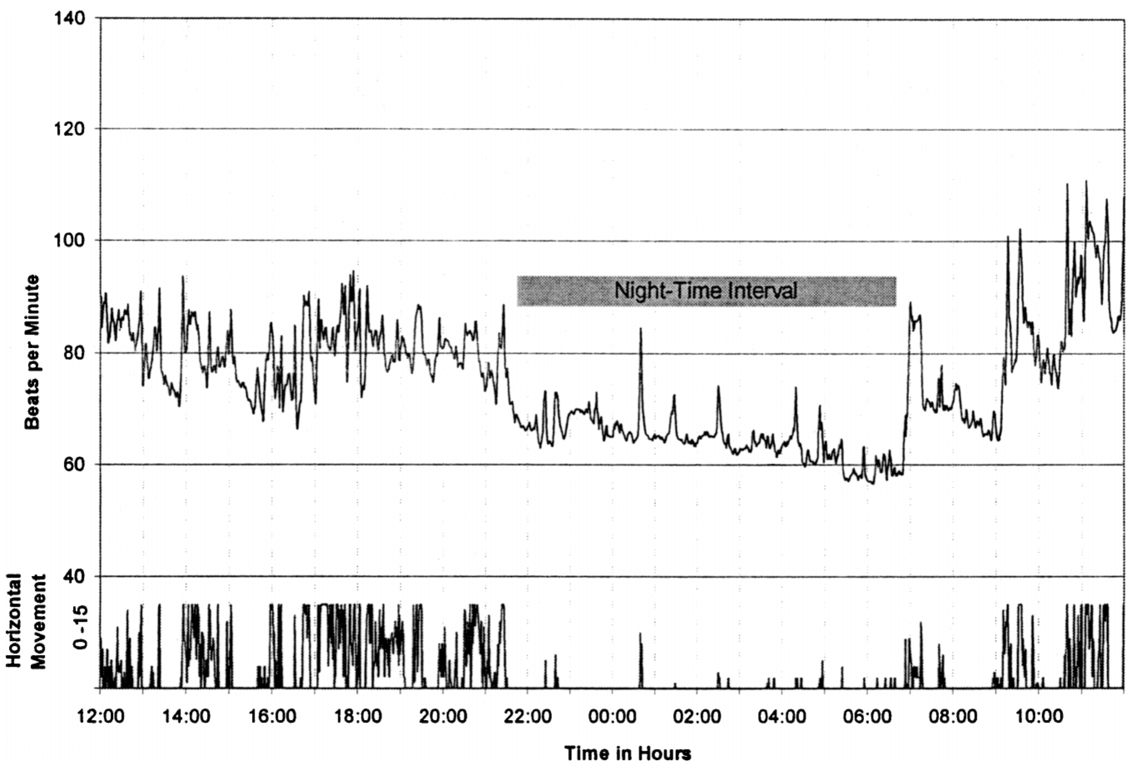

FIGURE 3. "Probably psychiatric" circadian heart pattern.

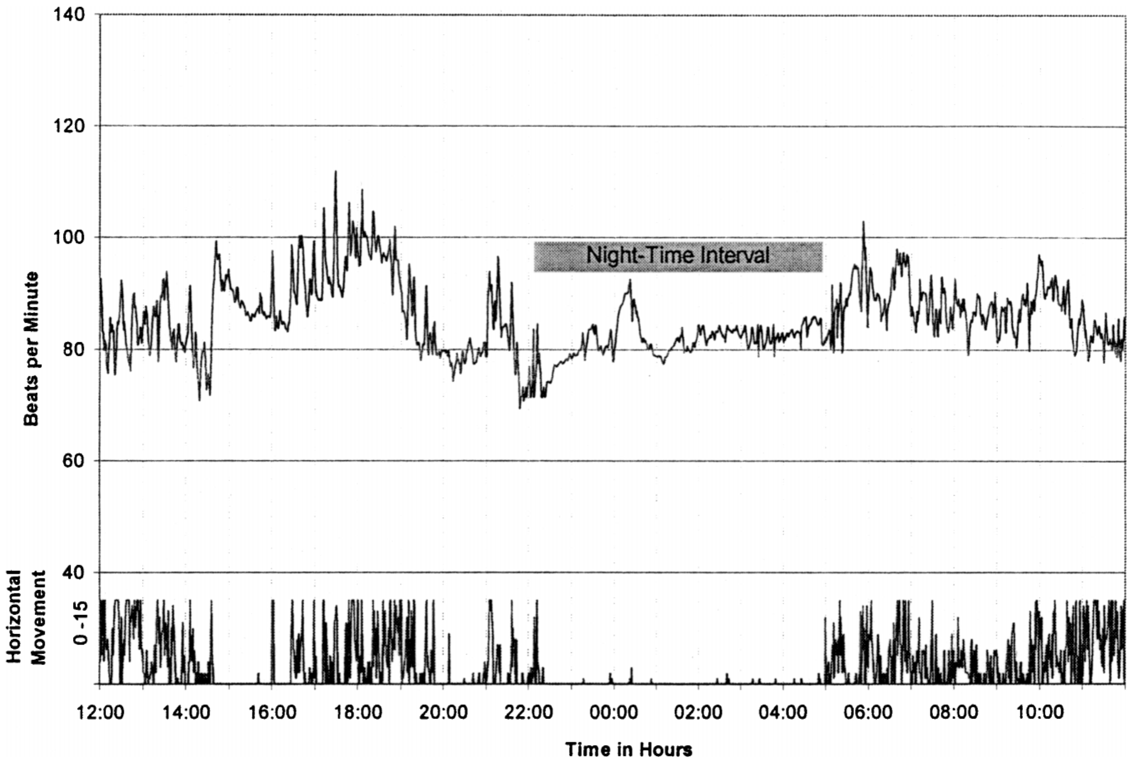

FIGURE 4. "Definitely psychiatric"circadian heart pattern.

anxiety depressive disorder, and some panic symptoms (but did not meet criteria). This individual had a BDI-II score of 6, and scored at the 84th percentile on the trait portion of the State Trait Anxiety Inventory.

Figure 4 is an example of a 24-CHP twice classified as definitely psychiatric. There is a sharp drop in heart rate, followed by a progressive increase to waking levels with no clearly defined sleep-wake transition. Based on a SCID interview, this individual was diagnosed with current major depressive disorder, melancholic type, moderate severity; social phobia, specific phobia, and panic disorder (all sub-threshold); OCD; and GAD (moderately severe). This individual had a BDI-II score of 51, and scored above the 99th percentile on the trait portion of the State Trait Anxiety Inventory.

There is a growing body of literature suggesting that understanding human circadian variation is an important aspect of psychiatry that will improve diagnosis and treatment of mental illness (see 3). Unfortunately, many of the procedures used to assess circadian rhythmicity are "awkward, distressing and expensive" (3, p. 106). In psychiatry, finding a laboratory test for a reliable and valid biological marker for depression and anxiety disorders has been elusive. The use of 24-CHP coupled with movement information is an example of a procedure that uses circadian information to assist in the identification of psychiatric disorders such as depression, anxiety, and panic disorder. While it is not a direct measure of brain structure or function, this technology may serve as a non-invasive, inexpensive, minute-by-minute index of autonomic nervous system dysfunction. For example, sustained hyperactivity of the sympathetic nervous system has been associated with hypercortisolism in depressed subjects (4–6). Vagally-mediated heart rate variability, important for adaptive response to environmental stressors, is lower in patients with GAD (7–9). In addition, autonomic dysfunction related to cardiac physiology has also been implicated in panic disorder (10) and daily mental stress (11).

An important step in the development of a new medical technology is the demonstration that the technique is reliable and valid. Since 24-CHP data is manually interpreted, it was necessary to determine whether a single blind expert rater could provide similar ratings of these patterns at two different times with a high rate of accuracy. The results of these ratings were interpreted as consistent with the position that there are aspects of the data that can be reliably classified into normal, sub-clinical, and clinical groups. Therefore, these results appear to be an encouraging first step towards providing the necessary assessment of reliability and validity for this novel procedure.

Efforts are currently being made to refine the manual interpretation and to evaluate the validity of the interpretations against standard assessment procedures in psychiatry (e.g., psychiatric interviews, SCID interviews, and self-report questionnaires). In addition, we are moving from manual to automated interpretation using currently available pattern recognition techniques. It is anticipated that non-linear algorithms, such as neural network classifiers, will improve the accuracy of classification of 24-CHP. Automated interpretation should also improve the reliability of classification over that of a human rater.

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