ELSEVIER

Journal of Anxiety Disorders 22 (2008) 453–463

Journal of Anxiety Disorders

Sleep-based heart period variability in panic disorder with and without nocturnal panic attacks☆

Deane E. Aikins [a,b], Michelle G. Craske [c,*]

[a] Department of Psychiatry, Yale University, CT, United States
[b] National Center for Posttraumatic Stress Disorder, West Haven, CT, United States
[c] Department of Psychology, University of California, UCLA, 405 Hilgard Avenue, Los Angeles, CA 90095-1563, United States

Received 6 September 2006; received in revised form 14 March 2007; accepted 15 March 2007

Abstract

In this paper, we investigated ambulatory sleep heart period variability in panic disorder participants with nocturnal panic (NP) compared to daytime panic attacks only. A time-derived measure of heart period variability (HPV) during sleep was significantly reduced in the NP group ($n = 32$) relative to the daytime panic ($n = 17$) and nonanxious ($n = 17$) control groups. Consistent with previous work, NP participants also reported greater fear of relaxation and sleep than daytime panic and control groups. Based on a neurovisceral model of attention [Thayer, J. F., & Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders*, *61*, 210–216] that predicts that decreased HPV is related to disregulated behavioral adaptation, we hypothesized that HPV measured during sleep would be most reduced in NP participants. These findings indicate that HPV is related to nocturnal panic disorder insofar as it is measured during sleep.

Keywords: Nocturnal panic disorder; Heart period variability; Sleep studies

Heart period variability, or the amount of change or variance in the time between heart beats, is considered a reflection of the confluence between sympathetic and parasympathetic effects on heart rate (Berntson et al., 1997). Heart period variability (HPV) has been conceptualized an index of central–peripheral neural feedback mechanisms (Thayer & Lane, 2000) that engage physiological resources with appropriate behavioral response selection. In this manner, HPV may reflect the integration between central and autonomic nervous system activity. In support of this model, nonanxious individuals with high baseline HPV perform better on tests of executive functioning and working memory than individuals with low baseline HPV (Hansen, Johnsen, & Thayer, 2003). Additionally, the phasic suppression of HPV (associated with an increase in heart rate, reflective of cardiac parasympathetic withdrawal) is thought to relate to an increased ability to sustain attention (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996) and has been shown to predict improved performance during high stress (Morgan, Aikins, Steffian, Coric, & Southwick, 2007). Theorists suggest that a high capacity for a dynamic range of heart period variability is associated with better cognitive ability and healthy adaptation to environmental demands (Beauchaine, 2001). Thus, an increased degree of

☆ This study was supported by a R01 grant (MH49713) awarded to the second author by the National Institutes of Mental Health.
* Corresponding author. Tel.: +1 310 825 8403; fax: +1 310 825 9048.
E-mail address: craske@psych.ucla.edu (M.G. Craske).

0887-6185/$ – see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.janxdis.2007.03.010

neurovisceral integration should reflect the ability to appropriately engage with environmental demands and disengage when those demands are no longer present (Thayer & Lane, 2000).

Chronic reductions in heart period variability are often associated with groups characterized as having information-processing biases (e.g., anxiety and mood disorders; see Beauchaine, 2001, for review) or behavioral dysregulation (e.g., behaviorally inhibited children; see Kagan, Reznick, & Snidman, 1987). In regard to panic disorder, HPV appears to be consistently restricted across a variety of laboratory conditions (Middleton, Ashby, & Robbins, 1994; Rechlin, Weis, Spitzer, & Kaschka, 1994; Sloan et al., 1999; Yeragani et al., 1990, 1992, 1993, 1995; Yeragani, Srinivasan, Balon, Ramesh, & Berchou, 1994). Despite a consistent profile of reduced HPV in panic disorder patients during daytime assessments, sleep studies have yielded inconsistent results. Whereas decreased HPV in panic disorder patients relative to controls was found in an ambulatory analysis of sleep (McCraty, Atkinson, Tomasino, & Stuppy, 2001), increased HPV in panic disorder relative to nonanxious controls was reported during a sleep laboratory session (Yeragani et al., 1998).

A subset of panic patients has nocturnal panic (NP), which refers to waking from sleep in a state of panic. NP is distinct from panicking after a lapse of waking time, nor does NP refer to night-time arousals induced by nightmares or environmental stimuli (such as unexpected noises). Instead, NP occurs without an obvious trigger. NP is a common clinical phenomenon that occurs with regularity in 18–45% of panic disorder patients (Craske & Barlow, 1989; Mellman & Uhde, 1989; Stein, Chartier, & Walker, 1993; Uhde, 1994). It is distinct from other sleep behaviors (Hauri, Friedman, & Ravaris, 1989; Mellman & Uhde, 1989; Uhde, 1994), including sleep terrors, nightmares, nocturnal seizures, and sleep apnea (for a review, see Craske & Rowe, 1997). Patients with NP report more distress about sleep and relaxation and exhibit more distress during conditions of meditative relaxation (Craske, Lang, Tsao, Mystkowski, & Rowe, 2001) and hypnotic imagery (Tsao & Craske, 2003) relative to patients without NP. Whereas NP has been associated with increased self-reported retrospective estimates of greater difficulty with sleep and sleep onset – which were *not* corroborated by ongoing self-monitoring – greater rates of incidence were not found for other sleep disorders (e.g., sleep walking, nightmares) compared to non-NP panic disorder patients (Craske et al., 2002). Also, measures of severity of panic disorder, comorbidity, anxious and depressive symptoms, and interference with functioning have not differed between NP and non-NP panic disorder patients.

Only one study to date has evaluated heart period variability in relation to NP. Sloan et al. (1999) compared sleep architecture and heart period variability during sleep in panic disorder patients with and without NP with that of healthy controls across laboratory and ambulatory procedures. Overall, differences between the two panic disorder groups were minimal and limited to higher total heart period variability during non-REM sleep for the NP group. However, there were major methodological limitations, including unreliability of the assessment of NP, small sample sizes, medication confounds, absence of an adaptation night, failure to match groups on age and gender, and failure to statistically control for Type I error.

With the present study, we attempted to improve on the previous research methodology in a number of ways. First, we implemented careful recruitment procedures for selecting a NP group, of relatively large size, to be compared to panic disorder patients who never had NP, and healthy controls, matched on age and gender. All subjects were medication free. Second, previous work has established the need for verifying heart period variability differences independent of respiratory disturbances or motor activity (see Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Therefore, we incorporated measures of respiration rate and volume, in addition to gross body motion to rule out potential confounding physiological variables. Third, we conducted our evaluation in the natural environment. Sleep-related disorders of arousal (e.g., nightmares and sleep walking) tend to occur less often in laboratory settings (Broughton, 1968), perhaps due to perceived safety. At the same time, anticipatory anxiety is often elevated by the threat of experimental procedures in laboratories (e.g., Roth et al., 1992). Either way, generalization to the natural environment is compromised. Thus, we elected to use an ambulatory measurement system for recording in the home environment. Finally, we incorporated measures of self-reported sleep behaviors as an additional check on the quality of sleep physiology data recorded. As sleep and sleep-like states are more anxiogenic for NP patients than for those with panic disorder who have never experienced nocturnal panic attacks (henceforth referred to as DP patients), we hypothesized that heart period variability would be lowest in patients with NP relative to DP patients and nonanxious controls. A similar profile was hypothesized for heart rate, with the shortest cardiac