



The role of anxiety sensitivity in sleep disturbance in panic disorder[☆]

E.A. Hoge^{*}, L. Marques, R.S. Wechsler, A.K. Lasky, H.R. Delong, R.J. Jacoby, J.J. Worthington, M.H. Pollack, N.M. Simon

Department of Psychiatry, Massachusetts General Hospital, 1 Bowdoin Square, 6th Floor, Boston, MA 02114-2790, United States

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ABSTRACT

Previous research has demonstrated that individuals with panic disorder (PD) report significant sleep disturbances, although the mechanism of this disturbance is not clear. Patients with PD tend to report abnormally high levels of anxiety sensitivity (AS). Because higher AS involves increases in attention and fearfulness about anxiety and associated physical sensations, which in turn may cause excessive psychological and physiologic arousal, we hypothesized that amongst individuals with PD, higher AS would be associated with sleep disruption, particularly in the form of increased sleep latency. As expected, PD was associated with poorer sleep as measured by the Global Pittsburgh Sleep Quality Index (PSQI) compared to controls and AS was significantly associated with longer sleep latency. Our data suggest that sleep disturbance, and in particular sleep latency, in PD may be partly due to high levels of AS, which can be targeted with cognitive-behavioral therapeutic strategies.

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1. Introduction

Sleep disturbance is a symptom common in several anxiety as well as mood disorders. Sleep disturbance is included in the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) diagnostic criteria for generalized anxiety disorder and post-traumatic stress disorder, though not for panic disorder. Nevertheless, individuals with panic disorder commonly report significant sleep disturbance, including frequent awakenings, even in the absence of concomitant depression (Stein, Chartier, & Walker, 1993).

The etiology of the sleep disturbance, however, is not clear. Though some have suggested that nocturnal panic attacks disrupt sleep (Mellman & Uhde, 1989), subsequent work found that sleep disturbance in panic disorder could not be explained by the existence of nocturnal panic attacks (Overbeek, van Diest, Schruers, Kruizinga, & Griez, 2005). Another proposed cause for disturbed sleep in panic disorder patients is the possibility of increased physiological hyperarousal, as measured by increased baseline levels of the stress hormone, cortisol. Increased cortisol has been implicated in insomnia (Bonnet & Arand, 2010). However, a majority of studies on panic disorder and cortisol found no difference in diurnal, unprovoked levels (Erhardt et al., 2006). Nocturnal levels of cortisol, however, may be more relevant to sleep disturbance; one study

found higher levels of nocturnal urinary cortisol in panic disordered patients than controls (Bandelow et al., 2000), although these levels were not near levels reported for clinically diagnosed insomnia (Vgontzas et al., 1998).

Anxiety sensitivity (AS) is a dispositional variable, defined as excessive fear of anxiety-related sensations based on beliefs that these sensations are harmful (Reiss, Peterson, Gursky, & McNally, 1986). Unlike trait anxiety, which refers to fearful responding to external events and stressors, AS specifically refers to a fearful response to internal sensations and to anxiety symptoms themselves. For example, an individual with high levels of AS may experience abdominal pain as something frightening and worrisome, rather than just a routine stomachache. Additionally, individuals with high levels of AS are more uncomfortable with the emotion of fear, which can create a positive feedback loop to increase fear and anxiety to panic proportions. Thus, as expected, individuals with a diagnosis of panic disorder have been shown to have high levels of AS (McNally, 2002). For example, Taylor, Koch, and McNally (1992) reported that a group of individuals with panic disorder and generalized anxiety disorder had indistinguishable trait anxiety levels, but the group with panic disorder had significantly higher AS.

Because AS involves a higher selective attention to fear of anxiety and physical sensations, individuals with panic disorder may be attending to these sensations or feelings at night while trying to fall asleep. This may increase sleep latency initially and make a return to sleep more difficult. For example, in a study of 53 subjects with chronic insomnia, anxiety sensitivity was associated with greater sleep-related impairment and sleep medication use, although not with sleep disturbance overall. In another study of

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^{*} Corresponding author. Tel.: +1 617 644 0859; fax: +1 617 726 4036.

E-mail address: ehoge@partners.org (E.A. Hoge).

non-anxious individuals who experienced frequent nightmares, AS was correlated with distress from the nightmares although not with nightmare frequency itself (Levin, Lantz, Fireman, & Spendlove, 2009). However, the relationship between AS and sleep, and sleep latency specifically, has not been examined in anxiety disorders. We hypothesized that in panic disorder, AS would be associated with sleep disturbance, and especially sleep latency.

2. Method

2.1. Participants

Subjects were individuals seeking care and/or participating in research studies at the Center for Anxiety and Traumatic Stress Disorders at Massachusetts General Hospital from 2004 to 2007 who completed a battery of questionnaires including those presented in this study. Subjects 18 years old and higher with a primary diagnosis of panic disorder (PD) were recruited. Healthy controls 18 years old and higher were recruited with print advertisements. All subjects received and signed informed consent prior to participation.

Individuals were eligible for study inclusion if they gave informed consent and were willing and able to comply with study procedures. Those with PD had a primary DSM-IV diagnosis of PD assessed by structured interview with the Structured Clinical Interview for DSM-IV (SCID-IV; First, Spitzer, Gibbon, & Williams, 2002) or the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) by a trained study clinician. Patients with concurrent anxiety disorders or depression were eligible if PD was judged to cause the patient the most distress and clinically determined to be the predominant disorder. Healthy controls had no current affective, anxiety, substance dependence or psychotic axis I DSM-IV diagnosis, as determined by psychiatric diagnostic interview completed within the past 6 months.

Exclusion criteria included a history of schizophrenia, psychotic disorders, bipolar disorder, mental disorder due to a medical condition or substance, alcohol or substance abuse or dependence within the past six months. Those with severe unstable medical illness, acute risk of suicide, and those pregnant or lactating were also excluded.

2.2. Assessments

Panic disorder symptom severity was measured with the Panic Disorder-specific Clinical Global Impression of Severity Score, an adapted version of the CGI-S with specific anchor points for number and frequency of panic attacks, intensity of anticipatory anxiety, degree of phobic avoidance and impairment of function (PD-CGI-S; Simon et al., 2009).

All participants completed the 16-item Anxiety Sensitivity Index (ASI; Reiss et al., 1986) scale, which includes items such as “When I notice my heart beating rapidly, I worry that I might have had a heart attack” and “It scares me when I am nervous.” Items are scored on a five-point scale and summed; normative data have indicated mean scores between 17 and 19 for nonclinical samples (Peterson & Reiss, 1992). The Cronbach’s alpha for samples of patients with anxiety disorders ranged from 0.88 to 0.90 (Reiss, Peterson, Gursky, & McNally, 2000).

Participants also completed the 19-item Pittsburgh Sleep Quality Index, a well-validated self-report instrument that comprehensively assesses current sleep impairment in the following seven domains: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction (Buysse, Reynolds, Monk, & Berman, 1989). The component scores are summed to yield a global PSQI score; higher

Table 1

The association of anxiety sensitivity with sleep disturbance in panic disorder.

	Univariate			Multivariate ^a		
	β	SE	<i>p</i>	β	SE	<i>p</i>
Total PSQI	0.149	0.061	0.02	0.116	0.060	0.06
Sleep quality	0.027	0.013	0.04	0.018	0.012	0.14
Sleep latency	0.035	0.014	0.02	0.029	0.014	0.05
Sleep duration	0.018	0.013	0.18	0.014	0.014	0.29
Sleep efficiency	0.016	0.018	0.36	0.012	0.018	0.52
Sleep disturbances	0.009	0.009	0.384	0.006	0.010	0.557
Sleeping medication	0.029	0.017	0.095	0.024	0.017	0.161
Daytime dysfunction	0.014	0.010	0.180	0.011	0.009	0.281

^a Multivariate regression with covariates for age, current depression, and panic disorder symptom severity.

scores reflect more sleep disturbance. A Global PSQI scores >5 is indicative of significant sleep impairment.

2.3. Statistics

After examining normality assumptions, PSQI scores and subscales in participants with panic versus controls were examined with two-sided *t*-tests. The association of PSQI with ASI scores was examined using univariate and multivariate regression analyses. Significance was set at alpha = 0.05, with no adjustment for multiple testing.

3. Results

The sample comprised 43 individuals with panic disorder (PD) and 30 healthy controls. Gender did not differ in panic (46% women) vs. controls (43% women), but panic participants were on average older (40.1 vs. 33.7 years, t (df) = 2.3 (71), p = 0.03). Fourteen (33%) of the individuals with panic disorder had comorbid current major depressive disorder. Patients with panic disorder had a mean (SD) severity score on the PD-CGI-S of 4.81 (0.8) (4 = “Moderately ill” and 5 = “Markedly ill”).

As hypothesized and consistent with prior research, PD was associated with poorer sleep as measured by the Global PSQI compared to controls (t (df) = -3.86 (71), p < 0.0005). The mean (SD) Global PSQI for the panic disorder group was 9.9 (4.8) and 6.0 (3.4) for the controls; scores above 5 represent sleep impairment. In addition, specific subscales on the PSQI were worse in patients than controls: sleep latency (t (df) = -2.9 (71), p = 0.01), sleep quality (t (df) = -2.4 (71), p = 0.02), sleep disturbance (t (df) = -5.1 (71), p < 0.0001), use of sleep medication (t (df) = -2.3 (71), p = 0.02), and daytime dysfunction (t (df) = -5.3 (71), p < 0.0001). To confirm that this finding was not due to the difference in age between the two groups, a multiple regression was performed with age added as a covariate.

Within the PD group, the mean (SD) AS score was 36.7 (11.5), compared to 12.2 (7.1) for the controls. AS was univariately associated with sleep impairment (β (SE) = 0.15 (0.06), p = 0.02), suggesting higher AS was associated with poorer sleep as measured by the PSQI. We then adjusted for other measured factors that could affect sleep, including age, current major depressive disorder, and overall panic symptom severity as measured by the PD-CGI-S. In this analysis, AS continued to be associated with PSQI score, but only at the level of a statistical trend (β (SE) = 0.12 (0.06), p = 0.06). However, we looked specifically on the effect of AS on sleep latency, and found a significant relationship both in univariate analyses and after adjusting for age, major depressive disorder, and overall panic symptom severity (see Table 1) (β (SE) = 0.03 (0.01), p = 0.047). Other PSQI components were not related to AS in multivariate regression models adjusting for these same covariates (see Table 1).

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