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Preliminary communication

Polysomnographic sleep patterns of non-depressed, non-medicated children with generalized anxiety disorder

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ABSTRACT

Background: Polysomnographic (PSG) studies of children with psychiatric illness have primarily focused on depressed samples. Children with generalized anxiety disorder (GAD) report high rates of sleep problems yet investigation of objective sleep patterns in non-depressed children with GAD are unavailable. Identification of unique clinical features linking early GAD with sleep disturbance, including possible HPA activation during the pre-sleep period, is needed to inform effective treatments.

Method: Thirty non-medicated, pre-pubescent children (ages 7–11 years) were assessed including 15 children with GAD and 15 matched healthy controls. Anxious children had GAD as their primary diagnosis and did not meet criteria for secondary mood disorders. All participants underwent structured diagnostic assessment and laboratory-based polysomnography (PSG). State anxiety and salivary cortisol were assessed prior to light out on the PSG night.

Results: Children with GAD showed significantly increased sleep onset latency and reduced latency to rapid eye movement (REM) sleep compared to controls. Marginal differences in the form of reduced sleep efficiency and increased total REM sleep also were found in the GAD group. Pre-sleep anxiety and cortisol levels did not differ between the two groups.

Limitations: A small sample size, time-limited assessment of cortisol, and possible first night effects should be considered.

Conclusions: Results of this study provide initial evidence of PSG-based differences in children with GAD compared to controls. Follow-up studies are needed to explore the course of sleep alterations and whether targeting sleep problems early in the course of GAD might improve clinical outcomes.

1. Introduction

Generalized anxiety disorder (GAD), characterized by pervasive, uncontrollable worry, somatic complaints, and negative affectivity, is one of the most commonly occurring affective disorders in all age groups (Costello et al., 2004; Wittchen et al., 1994). GAD is a chronic disorder associated with increased service utilization, disability and health care costs, as well as reduced quality of life (Barrera and Norton, 2009; Kessler et al., 1999; Roy-Byrne, 1996). Relapse rates, even among successfully treated patients, are among the highest of any anxiety disorder (Bruce et al., 2005; Yonkers et al., 2003). A substantial proportion of patients also meet diagnostic criteria for major depressive disorder (MDD) with evidence for concurrent and sequential comorbidity between childhood anxiety and later depression (Moffitt et al., 2007a; Pine et al., 2001; Pine et al., 1998). The extensive comorbid, genetic and clinical overlap between GAD and depression (Kendler, 1996; Weissman et al., 2005; Beesdo et al., 2010; Moffitt et al., 2007b) has fueled interest in identifying early biologic markers and risk factors that might signal more precise pathways toward these individual disorders.

Insomnia is also a prominent feature of GAD and is included as a symptom criterion in DSM-IV (APA, 2000). Up to 70% of adults with GAD report problems falling and/or staying asleep (Monti and Monti, 2000) which result in functional impairments beyond the effects of anxiety alone (Ramsawh et al., 2009). Polysomnographic (PSG) findings in this population confirm the presence of sleep initiation/maintenance difficulties including reduced total sleep time (TST), prolonged sleep onset latency (SOL), increased wake minutes after sleep onset (WASO), and reduced sleep efficiency (SE; Arriaga and Paiva, 1991; Papadimitriou et al., 1988; Rosa et al., 1983; Saletu et al., 1994). The transition from wake to sleep would

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appear particularly vulnerable for individuals with GAD since chronic worry, rumination, muscle tension, and feelings of hyperarousal are characteristic of the disorder, while diminishing control of cognitive activity and physiologic arousal are essential for sleep onset (Ogilvie, 2001). Although research examining specific clinical symptoms and precise mechanisms linking GAD and insomnia is limited, such findings might inform choice and/or development of effective intervention strategies for this population.

Similar to their adult counterparts, nearly 90% of children with GAD experience difficulty sleeping based on parent and self-reports (Alfano et al., 2006; Alfano et al., 2007; Alfano et al., 2010). Objective sleep patterns in this population have received limited attention however and the extent to which subjective complaints correspond with actual sleep patterns is relatively unknown. It also cannot be assumed that children share the same sleep patterns as adult GAD patients. Example comes from the trait-like sleep abnormalities found in adults with MDD (Reynolds and Kupfer, 1987), including reduced latency to rapid eye movement (REM) sleep, increased REM sleep, and decreased slow wave sleep (SWS) that have not been consistently found in depressed children (see Lofthouse et al., 2009). The precise nature of these developmental differences is unclear but could relate to a more powerful homeostatic sleep drive during childhood that overrides sleep disruption (Carskadon, 2002; Dahl, 1996).

One published study examined the sleep of youth with different DSM-IV anxiety disorders including GAD [as well as panic disorder, separation anxiety disorder (SAD), and social anxiety disorder (SOC)] during two consecutive nights of PSG (Forbes et al., 2008). Anxious children and adolescents exhibited a significantly greater number of awakenings than depressed youth and decreased slow wave sleep compared to both depressed and healthy children. As compared to the first PSG night, the anxious group exhibited prolonged SOL on the second night, whereas latency to REM sleep decreased in the depressed and control groups. Together with a greater percentage of missing data in the anxious group on night two, results suggest that anxious children may have more difficulty adapting to the sleep lab setting. Also, because anxious youth with comorbid MDD were included in the sample, the extent to which findings generalize to purely anxious children remains to be examined.

Based on the disorder's clinical presentation, hypothalamic-pituitary-adrenal (HPA) axis activity may hold relevance for understanding the mechanisms and development of sleep disturbance in GAD. Increased levels of cortisol which index HPA functioning are linked with an anxious temperament and have been shown to predict later internalizing problems (Goldsmith and Lemery, 2000). HPA activity and sleep also follow a circadian pattern and are reciprocally related whereby disruption in one system may create vulnerability in the other (Buckley and Schatzberg, 2005; Van Cauter and Speigel, 1999). Two studies have reported atypical patterns of cortisol secretion among anxiety-disordered youth in the hours prior to and during sleep (Feder et al., 2004; Forbes et al., 2006). In one study, pre-sleep cortisol was significantly elevated in anxious children as compared to adolescents, reflecting possible adaptation of the HPA axis to chronic anxiety (Forbes et al., 2006). However, in both studies, children with a variety of anxiety disorders were examined.

The aim of the current study was to examine the PSG sleep characteristics of children with a primary diagnosis of GAD in comparison to a matched control group of healthy children. Based on the established sleep alterations of depressed patients and the fact that GAD and MDD commonly co-occur, anxious children with secondary mood disorders were excluded. In the absence of available findings, we hypothesized that PSG sleep patterns would mirror those found in adult patients (including reduced TST, increased SOL, increased WASO, and reduced SE). We also examined self-reported state anxiety and salivary cortisol prior to sleep on the PSG night, hypothesizing increased levels of anxiety and neurophysiologic arousal (HPA activity) in GAD participants compared to controls.

2. Methods and materials

2.1. Participants

The sample included 30 children (7 to 11 years) including 15 with primary GAD and 15 controls. Children were recruited through an anxiety specialty clinic at a pediatric hospital using community flyers and print advertisements for a research study about "behavior and emotion" without mention of sleep. A total of 32 children were evaluated in order to attain a sample of 15 children with GAD. Seven children were deemed ineligible at the initial assessment due to the presence of depression or other primary disorders ($n=4$), suspected sleep-disordered breathing ($n=3$), or IQ <80 ($n=1$). Of the remaining 25 eligible children, 8 families decided not to complete the PSG study due to child anxiety or scheduling problems and 2 studies were lost due to computer problems. The 10 eligible GAD children without PSG data were compared to the final GAD sample ($n=15$) in terms of demographic variables (see Table 1) as well as severity of GAD (ADIS-C/P Clinical Severity Scores and the PSWQ-C; see below). No significant differences were detected.

Control children were recruited as part of the same project and were chosen for inclusion in the current study based on similarity of demographic characteristics to the GAD group as shown in Table 1. Control children underwent the same assessment procedures as anxious youth including diagnostic interviews and sleep assessments. Control children were free of psychiatric or sleep disorders as well as any clinically-significant emotional/behavioral problems.

All participants were required to reside with a parent/primary caretaker and be enrolled in a regular classroom setting. Exclusion

Table 1
Demographic characteristics of children with GAD and controls.

	GAD ($n=15$)	Control ($n=15$)	t/X^2 statistic	p value
Age in years (M/SD)	8.5(1.5)	8.9(1.3)	.77	.45
Female (n/%)	9(60)	9(60)	1.0	.65
Race/ethnicity (n/%)			4.8	.44
Caucasian	10(66.7)	10(66.7)		
African Amer	1(6.7)	4(26.6)		
Asian Amer	1(6.7)	0(0)		
Hispanic/Latino	1(6.7)	0(0)		
Other/mixed race	2(13.2)	1(6.7)		
Household income (n/%)			4.97	.42
≤ $59 K	3(21.4)	3(20)		
$60–99 K	1(7.2)	2(13.3)		
> $100 K	10(71.4)	10(66.7)		
Marital Status (n/%)			3.69	.29
Married	10(71.4)	13(86.7)		
Maternal Education (n/%)			.409	.34
< College degree	5(35)	3(20)		
College degree or >	9(65)	12(80)		
Paternal Education (n/%)			1.05	.59
< College degree	4(29)	4(27)		
College degree or >	10(71)	11(73)		
BMI (M/SD)	15.9(1.3)	17.3(2.5)	1.7	.10
PDS (M/SD)	1.4(.41)	1.4(.53)	.36	.73

Note: GAD=Generalized Anxiety Disorder; BMI=Body Mass Index; PDS=Pubertal Development Scale; some demographic data were missing for one GAD participant.