SLEEP AND HEART RATE VARIABILITY IN PATIENTS WITH OBSESSIVE-COMPULSIVE DISORDER: PRELIMINARY FINDINGS

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Abstract

Objective: Research on self-reported sleep quality and clinical experience indicate that comorbid sleep disorder is a common problem among patients with obsessive-compulsive disorder (OCD). However, few studies have investigated this issue. Recent research suggested that primary insomnia might be related to inhibition of arousal, which in turn may be linked to altered executive functioning in the prefrontal cortex. Studies on other anxiety disorders such as panic disorder, have found associations between sleep impairment and reduced cognitive and physiological flexibility as indicated by a standard Stroop paradigm and heart rate variability (HRV), respectively. These possible relationships have previously not been investigated in OCD.

Method: The relationship between self-reported sleep quality, high-frequency (HF) HRV and cognitive inhibition was investigated in a sample of 31 OCD patients, recruited from a waiting list.

Results: The OCD patients were characterized by a negative correlation between HRV measured in the upright position and cognitive inhibition. A majority of the sample reported high rates of sleep disturbances, which were significantly associated with symptoms of depression and anxiety but unrelated to HRV and OCD symptoms.

Conclusions: The study is to our knowledge the first to indicate a relationship between cognitive inhibition and HF HRV in a sample of OCD patients.

Key words: obsessive-compulsive disorder, heart rate variability, executive functions

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Introduction

Obsessive compulsive disorder (OCD) is characterized by highly disturbing, intrusive and unwanted thoughts or obsessions which the patient unsuccessfully tries to regulate by engaging in senseless rituals or by avoiding stimuli that triggers obsessions (American Psychiatric Association 2000). The lifetime prevalence of OCD is estimated to 2-3 % (Karno, Golding, Sorenson, & Burnam 1988) and the condition has debilitating consequences if left untreated (Koran, Thienemann, & Davenport 1996). Although sleep disturbances are not among the criteria for a diagnosis of OCD, both clinical experience and research indicate that a significant number of OCD patients suffer from sleep disturbances like late sleep onset and frequent awakenings. To date few studies have investigated this issue and reports about comorbid OCD and sleep disturbances are contradictory (Paterson, Reynolds, Ferguson, & Dawson 2013). For example, one study found no differences in sleep architecture between OCD patients and healthy controls (Hohagen et al. 1994), while another study reported sleep disturbances in near 50 % of an OCD sample (Mukhopadhyay et al. 2008). More severe OCD symptoms have been linked to higher rates of sleep disturbances (Turner et al. 2007), and severity of OCD is known to be related to depression (Regier et al. 1988). Whilst sleep disorders were previously seen as a result of physiological hyper activation (Borbely 1982), Bastien (2011) in a recent review of the neurocognitive explanations of functional sleep disorders suggested that primary insomnia alternatively might be understood as a consequence of impairment in cognitive *inhibition* of arousal. Metaphorically speaking, primary insomnia might not be the consequence of a stuck gas pedal (arousal), but rather a result of impaired brakes (inhibition). This interpretation has generally been advocated for anxiety disorders (Friedman 2007), and it was recently found that sleep impairment was related to both cognitive

and physiological flexibility as measured by cognitive inhibition and HRV, respectively, in patients with panic disorder (Hovland et al. 2013). Anxiety disorders also show high comorbidity with functional sleep disorders (Johnson, Roth, & Breslau 2006). OCD is considered to be driven by anxiety, and the function of the rituals is to temporarily reduce the discomfort evoked by the uncontrollable thoughts. The long term consequence of this dynamic process is a rigid and dysfunctional emotional regulation, and it has been suggested that this emotional rigidity is associated with reduced flexibility in cognitive functions related to the prefrontal cortex.

Hyperactivity in frontal striatal networks is considered to be involved in the OCD pathophysiology (Harrison et al. 2006; Nedeljkovic et al. 2009; Purcell, Maruff, Kyrios, & Pantelis 1998), and a neurocognitive understanding of the disorder focuses both the diminished capacity to inhibit intrusive cognitions, as well as the disability to stop a repetitive activity (executive functions). Especially the ability to flexible combine inhibition of dysfunctional emotional processes with an attention shift to relevant situational aspects are important for adaptive behavior, and impaired inhibitory regulation is seen as a risk for emotional dysregulation and psychopathology (Thayer, Hansen, Saus-Rose, & Johnsen 2009).

Thayer and Lane (2000) have developed a model which suggests that variations in cardiovascular functioning are part of a network which integrates autonomic, attentional and emotional systems. Basically, increased heart rate (HR) can be due to increased activation of the sympathetic part of the autonomic nervous system (ANS) or decreased activation of the parasympathetic part of the ANS, or a combination of the two. Thayer and Lane (2000) have suggested that heart rate variability (HRV) may be seen as an index of a self-regulatory system. HRV thus reflects neural feedback mechanisms of the central nervous system as well as being an index of a functional unit within the central autonomic network (Appelhans & Luecken 2006; Hansen, Kvale, Stubhaug, & Thayer 2013; Thayer & Lane 2000). According to the Thayer and Lane (2000) model, diminished HRV is a sign of lower flexibility and poorer regulatory abilities. A number of studies have demonstrated a relationship between reduced HRV and impaired cognitive inhibition in healthy subjects (Hansen, Johnsen, Sollers, Stenvik, & Thayer 2004), thus lending support to the model. Regarding anxious subjects, Johnsen et al. (2003) investigated how dental phobics showed reduced HRV and decreased attentional abilities measured with the Stroop test. Hovland et al. (2012) recently demonstrated that low HRV in panic patients correlated with measures of cognitive inhibition. In line with these findings it has been hypothesized that impaired cognitive inhibition and reduced HRV may be a characteristic of anxiety disorders in general and that this may be a reason why anxiety disorders are marked by attentional bias towards threat stimuli in addition to a rigid response style with low flexibility in meeting situational demands.

In a recent study on patients with panic disorder, Hovland and colleagues (2013) found that flexibility in executive functions as indexed by HRV as well as by a standard Stroop test, was inversely related to overall sleep disturbances, suggesting a relationship between sleep and cognitive inhibition. These findings may be highly relevant also for OCD patients. Extensive research has previously shown that OCD is characterized by reduced cognitive inhibition (Muller & Roberts 2005) and a recent study by Pittig, Arch, Lam, and Craske (2013) demonstrated the first evidence of lower HRV in OCD patients. Research on OCD, sleep disorders and inhibitory processes are sparse. Thus, in the current paper we want to explore the prevalence of self-reported sleep disturbances in a clinical sample of OCD patients. Further we will investigate if there is a relationship between high frequency (HF) HRV and measures of cognitive inhibition. Based on the reported literature we expect to find that 1) the sample will be characterized by self-reported sleep disturbances, 2) the sample will have reduced HRV, and finally 3) HF HRV will be significantly correlated to measures of cognitive inhibition and sleep disturbances.

Methods

Diagnostics and screening

31 patients (19 female) between 22-54 years old (mean 31.2, SD 8.1), consecutively referred for treatment of obsessive-compulsive disorder (OCD), were asked to participate in the study. The data collection was carried out while the patients were waiting to begin treatment. The OCD diagnosis was established by assessing the patients with the Structured Clinical Interview for DSM-IV axis 1 disorders (SCID-I; First, Spitzer, Gibbon, & Williams 1995). Any use of benzodiazepines was banned prior to inclusion, however, 12 patients were taking a stable dosage of SSRI medication. 16 patients had comorbid disorders, including mild depression (2), moderate depression (3), dysthymia (2), social phobia (2), generalized anxiety disorder (4), panic disorder (3).

Severity of obsessive-compulsive symptoms was measured with the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Goodman et al. 1989). The Y-BOCS has 5 questions assessing obsessions and 5 questions assessing compulsions, each question is rated on a 0-4 scale with higher score indicating more severe symptom level.

Self-reported sleep problems were measured with the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer 1989). This 19-item self-report questionnaire measures sleep disturbances on seven subscales which equals a global score from 0-21, where higher scores indicate more severe sleep disturbances.

Depressive symptoms were measured with the Beck Depression Inventory (BDI; Beck, Steer, & Brown 1996). This self-report scale has 21 questions, each with a 0-3 scale with higher scores indicating higher symptom severity. To assess general anxiety symptoms the Beck Anxiety Inventory (BAI; Beck & Steer 1993) was administered. The BAI has 21 items measuring anxiety symptoms on a 0-3 scale, higher total score indicating more severe symptoms.

Please refer to **table 1** for sample scores on Y-BOCS, PSQI, BDI and BAI.

Psychophysiological data recording and processing

Measures of HRV were obtained in accordance with the procedure outlined in Hovland et al. (2012). HRV measures were obtained using a three lead electrocardiogram (ECG) within the Vrije Universiteit Ambulatory Monitoring System (VU-AMS; de Geus, Willemsen, Klaver, & van Doornen 1995). Data were obtained with Ag/AgCl electrodes (1700 Cleartrace™, Conmed, Utica, NY) at a 1000 Hz sampling rate and electrodes were placed in the following locations: One

Table 1. *Sample baseline scores*

Measure	Mean	SD	Range
Y-BOCS	26.2	4.0	20-34
BDI	19.8	11.0	0-41
BAI	21.6	13.2	0-53
PSQI	8.1	4.3	2-16

Note. Y-BOCS = Yale-Brown Obsessive-Compulsive Scale; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; PSQI = Pittsburgh Sleep Quality Index.

below the right clavicle, 4 cm to the right of the sternum; one on the right side between the two lower ribs; and one under the left breast, 4 cm below the nipple. An investigator was present during the recording in a quiet location. Recordings of ECG were performed both in the sitting and upright position, as (Yeragani et al. 1993) have recommended measurement in standing position, while other studies have recorded with participants sitting (e.g. Slaap, Nielen, Boshuisen, van Roon, & den Boer 2004). 7 minutes were recorded in each condition, for analysis of the data 1 minute was cut away at the beginning and end of the recording to ensure stable and artifact free data. High frequency (HF) HRV was recorded as the main measure of vagally mediated HRV. HRV recordings were visually inspected in VU-AMS for QRS-detection and further analyses were conducted with Kubios HRV (version 2.0; University of Eastern Finland). To derive HF-power (ms2) estimates, an autoregressive (AR) algorithm was used, with a standard model order of 16 and a frequency-band of 0.15-0.40 Hz. Trend components were eliminated by applying the smoothness priors methods (Tarvainen, Ranta-Aho, & Karjalainen, 2002). HF HRV has been shown to be a robust measure of vagal functioning (Lewis, Furman, McCool, & Porges 2012).

Neuropsychological testing

Executive functioning was measured with a computer-based version of a standard color-word Stroop test, which tests the ability to inhibit prepotent responses (Miyake et al. 2000). In this test words are presented and the content of the word will either be presented in congruence with the color of the writing, or incongruently. The time needed to perform the test, as well as the total number of errors, are registered with higher scoring indicating better performance. The scaled scores have a mean of 10 and a standard deviation of 3.

Statistical analysis

Statistical analyses were conducted in SPSS version 19.0. Pearson's *r* correlations for continuous variables were conducted to measure the relationship between HF HRV, cognitive inhibition, sleep disturbances, and symptoms of depression and anxiety. In accordance with the hypothesized direction of the relationship between the variables one-tailed tests were applied (Ferguson & Takane 1989).

Results

Scores on Y-BOCS were significantly and inversely correlated with HF HRV measured in the upright condition (r = -.319, p = .04), the correlation was not significant in the sitting condition (r = -.233, p = .103). Cognitive inhibition measured with the Stroop test correlated significantly with HF HRV in the upright position (r = -.427, p = .017). The relationship between cognitive inhibition and HR HRV measured in the sitting position was non-significant (r = -.066, p = .376). 58 % of the sample had a global PSQI score > 5 points, indicative of insomnia (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin 2006). Please refer to **figure 1** for correlational analyses between PSQI, BDI and Y-BOCS. Scores on PSQI correlated significantly with severity of depressive symptoms as measured with the BDI (r = .475, p = .003) and anxiety symptoms as measured with the BAI (r = .442, p = .006). PSQI and obsessive-compulsive symptoms measured with Y-BOCS correlated positively, but this relationship was non-significant (r = .269, p = .071). Scores on PSQI did not correlate significantly with neither cognitive inhibition nor HF HRV (upright and sitting positions).

Discussion

The results show that HF HRV and cognitive inhibition were significantly correlated, and our study is to our knowledge the first to demonstrate this relationship in patients with OCD. OCD was significantly related to HRV. Reduced HRV has just recently been demonstrated in OCD patients (Pittig et al. 2013), and our study extends these findings as HRV is found to be inversely related to severity of the OCD. The Thayer and Lane (2000) model suggests that HRV, as an index of autonomic flexibility, will be strongly influenced by executive functions in prefrontal areas. The relationship between HRV and cognitive inhibition in our sample supports the anticipated relationship between the role of executive functioning in prefrontal cortex areas and vagally mediated HRV, indicating that this relationship is meaningful also in OCD. Taken in consideration that this relationship previously has been demonstrated in healthy subjects (Hansen et al. 2004), dental phobics (Johnsen et al. 2003) and patients with panic disorder(Hovland et al. 2013), this may suggest that this relationship is a reasonable stable and maybe universal indication of reduced cognitive flexibility, as suggested by Thayer and Lane (2000).

OCD symptoms and HRV correlated significantly only in the condition where patients were standing. The results match those found in a study of panic patients, in which HF HRV also was measured in the upright position (Hovland et al. 2012). However, our results must be treated with some caution as HRV is expected to be lower while a person is standing compared to sitting, due to increased blood pressure in the former condition. The fact that the relationship between OCD

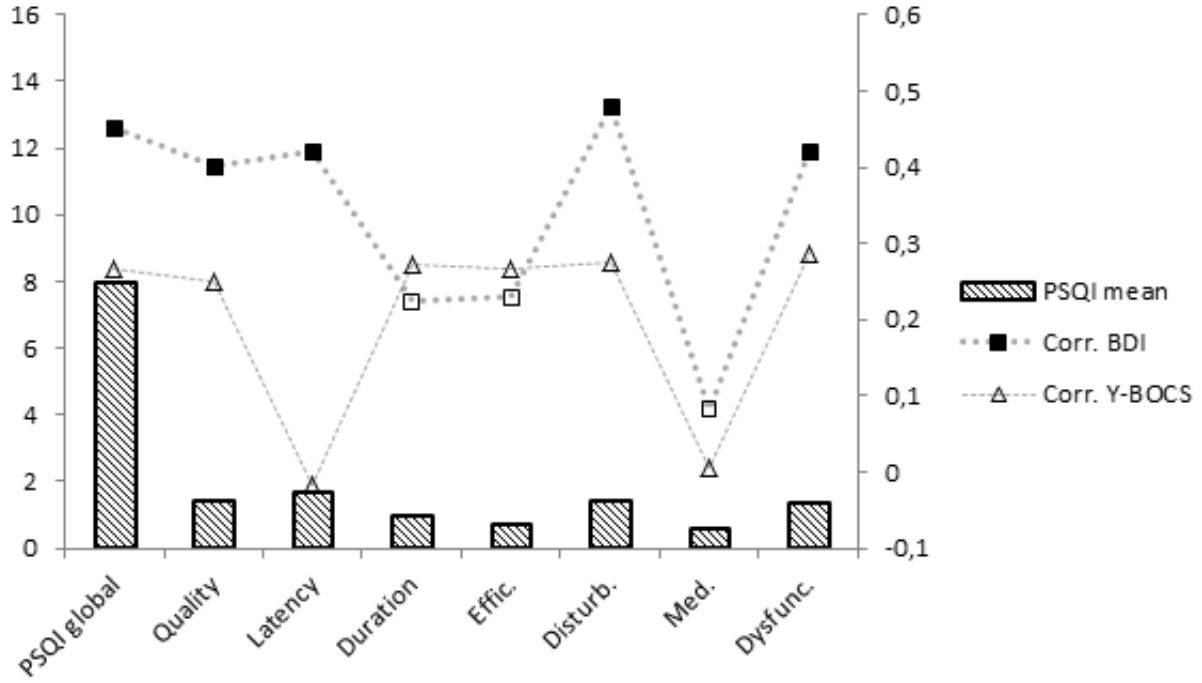

Figure 1. *The bar-chart shows mean PSQI score with all subscales. Line-graphs show the correlation between PSQI, Y-BOCS and BDI. Black filled indicators imply significant correlation, level of significance is denoted by stars. 'PSQI global' = Global PSQI index; 'Quality' = Rated sleep quality; 'Latency' = Sleep latency; 'Duration' = Sleep duration; 'Effic.' = Habitual sleep efficiency; 'Disturb.' = Sleep disturbances; 'Med.' = Use of medication; 'Dysfunct.' = Daytime dysfunction, 'Corr.' = Level of correlation; BDI = Beck Depression Inventory; Y-BOCS = Yale-Brown Obsessive-Compulsive Scale. * = p < .05; ** = p = < .01 (one-tailed)*

and HRV was non-significant in the sitting position may indicate that the results from the standing position must be treated cautiously, still, the correlation between HRV from the sitting condition and obsessive-compulsive symptoms was nevertheless in the hypothesized direction. It is therefore reasonable to conclude that our hypothesis about a relationship between heart rate abnormalities and impaired cognitive inhibition in OCD patients is partly supported by the positive correlation between these variables.

Also, impaired sleep was a reported problem for a majority (58%) of the sample, in line with our expectations. Correlational analyses showed that sleep disturbances were significantly correlated with level of depressive symptoms and anxiety symptoms, but showed a non-significant relationship with obsessive-compulsive symptoms. This suggests that the reported sleep difficulties may be due to depressive and anxiety symptoms, rather than obsessions and compulsions, which are in line with previous studies. Contrary to our expectations, cognitive inhibition was not significantly related to sleep disturbances in the current sample. Furthermore, the results from our sample did not show a significant relationship between HRV and subjective sleep disorders, meaning that our study does not provide further support for the role of inhibitory processes in sleep disorder. In this way the results from the present study do not match the relation between cognitive inhibition and sleep disturbances found in the study on panic patients by Hovland et al. (2013).

The uncontrolled nature of the study is an obvious limitation. Given the first evidence of a link between HRV and cognitive inhibition among OCD patients the study should be replicated with larger sample and include a control group. The sample reported a high degree of sleep disturbances, however, it is a limitation that only self-reported sleep quality is obtained, as subjective quality of sleep may differ from objectively measured sleep disturbances. Further studies should include also include objective measurements of sleep, like actiwatch.

Conclusion

The study is to our knowledge the first to indicate a relationship between cognitive inhibition and HF HRV in a sample of OCD patients. The results are in line with the Thayer and Lane (2000) model which suggests HRV as an index of autonomic flexibility. Sleep disorders have been found to be related to cognitive inhibition, however, our study failed to show this relationship. Still, a majority of the sample reported significant sleep disturbances. Correlational analyses implied that these problems were more strongly related to depressive symptoms than obsessive-compulsive symptoms. The major limitation of the study is its correlational design and its lack of a control group. The results must therefore be considered cautiously and the role of sleep disturbances, cognitive inhibition and HRV in OCD should be further investigated.

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