Biological Psychology 94 (2013) 319–330

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Heart rate variability and its neural correlates during emotional face processing in social anxiety disorder

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ARTICLE INFO

Article history:
Received 21 February 2013
Accepted 24 June 2013
Available online 3 July 2013

Keywords:
Interoceptive sensitivity
Vagal tone
Social phobia
Functional magnetic resonance imaging (fMRI)
Dorsal striatum

ABSTRACT

The monitoring and regulation of one's own physiological reactions and cardioregulatory abnormalities are central to the aetiology and maintenance of social anxiety disorder (SAD). We therefore explored the neural correspondences of these heart rate alterations.

21 patients with SAD and 21 matched healthy controls (HCs) underwent 3 T-fMRI scanning. Simultaneously, high-frequency heart rate variability (HF-HRV) was acquired during a short-term resting period and an implicit emotional face-matching task.

Compared to HCs, patients with SAD reported increased self-focused attention while being less accurate in estimating their heartbeats. Physiologically, they showed less HF-HRV at rest and during task. Across groups, HF-HRV at rest correlated positively with activation in visual face-processing areas. The right caudate nucleus showed an interaction of group and cardioregulation: Activation in this region was positively correlated in patients with SAD but negatively in HCs. We conclude that cardioregulation is altered in SAD on the subjective, physiological, and brain level.

1. Introduction

1.1. Social anxiety disorder

Patients with social anxiety disorder (SAD) are extremely afraid of the possible scrutiny by others, of doing or saying something embarrassing, and of showing symptoms of their anxiety. This fear results in the avoidance of social situations or, if unavoidable, their endurance with distress. Consequently, SAD affects the daily functioning in all aspects of professional and private life. SAD is classified as a phobic disorder in both DSM-IV (300.23) and ICD-10 (F40.1). It has a mean age of onset in late childhood/early adolescence and a lifetime prevalence of approximately 5–12%, with higher rates among female individuals (Kessler & Chiu, 2005).

A competence- and performance-oriented model of SAD describes the interaction of cognitive and physiological processes in social situations that, on the backdrop of biological vulnerability factors, personal life history, and social learning/competence, leads to avoidance or safety behaviours (Fydrich, 2002).

Physiological reactions such as blushing, sweating, or trembling play a central role in anxiety disorders in general, albeit mostly secondarily, that is, as an *effect* of the fear. In SAD, bodily symptoms of anxiety during interpersonal interactions and especially their visibility additionally become a central *object* of the fear (Gerlach, Mourlane, & Rist, 2004) and SAD patients exhibit heightened self-focused attention, which in turn is considered central in maintaining the disorder (Clark & Wells, 1995; Spurr & Stopa, 2002). Factual or imagined physiological reactions, their monitoring through processes of interoception, and their regulation are thus fundamental in SAD (A. Wells & Papageorgiou, 2001; Anderson & Hope, 2009).

1.2. Heart rate variability

One important non-invasive parameter assessing the capacity to regulate psychophysiological arousal is heart rate variability (HRV). HRV reflects the subject's ability to adjust physiological arousal on a momentary basis and its measures are derived from the temporal variations between consecutive heartbeats (Thayer, Hansen, Saus-Rose, & Johnsen, 2009). The most prominent frequency domain indices for short-term recordings (Berntson, 1997;

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http://dx.doi.org/10.1016/j.biopsycho.2013.06.009

Task Force, 1996) are spectral power in the high-frequency band between 0.15 and 0.40 Hz (HF-HRV) and in the low-frequency range between 0.04 and 0.15 Hz (LF-HRV).

The heart is dually innervated by the autonomic nervous system with activity of the sympathetic nervous system (SNS) accelerating the heart rate (HR) and increased activity of the parasympathetic nervous system (PSNS) lowering it. While the influences of the SNS are slow, rapid modulation of HR is associated with neural influence of the PSNS, particularly via the vagal nerve (e.g., Eckberg, 2003; Grossman & Taylor, 2007).

The differential time scale of the influences by the SNS (seconds) and the PSNS (milliseconds) enables their respective discrimination after power spectral analysis: while PSNS influences span the whole frequency range of the HR power spectrum, SNS influences only affect frequencies up to 0.15 Hz (Saul, 1990). The low-frequency band between 0.04 and 0.15 Hz is therefore assumed to contain both SNS and PSNS information, while the high-frequency band between 0.15 and 0.4 Hz is thought to represent PSNS and mainly vagal influences. Although mechanical respiratory processes also influence HRV (e.g., Grossman & Taylor, 2007; Song & Lehrer, 2003), HF-HRV is generally taken as an index of vagal tone and of the ability to inhibit SNS-mediated arousal, which, in turn, can be approximated through the ratio between power in the low- and high-frequency bands (LF/HF), indicating sympatho-vagal balance (Task Force, 1996). HF-HRV can be measured both as an individual trait marker when acquired in the absence of experimental stimulation (i.e., at rest) or as a response variable in task settings indexing behavioural flexibility or attentional engagement with the environment (Porges, 2007; Thayer & Lane, 2000, 2009).

HF-HRV as an individual trait marker has recently been shown to also influence task performance as individuals with higher HF-HRV at rest perform better on a test of social cognition and emotion recognition (Quintana, Guastella, Outhred, Hickie, & Kemp, 2012) and inhibit unnecessary processing of affective information more efficiently (Park, Van Bavel, Vasey, & Thayer, 2012). Furthermore, anxiety-reducing breathing exercises significantly increase HF-HRV in highly anxious subjects, while simultaneously reducing LF/HF (Wells, Outhred, Heathers, Quintana, & Kemp, 2012). Taken together, these results suggest a connection between HF-HRV and SAD.

1.3. SAD and HRV

Because heart and brain show complex bidirectional interactions, mental health and autonomic control of cardiovascular processes are inherently intertwined. This is evidenced by the increased risk for and heightened mortality following cardiovascular diseases in patients with affective and anxiety disorders (e.g., Goodwin, Davidson, & Keyes, 2009; Gorman & Sloan, 2000).

Convergently, diminished HRV at rest or during anxiety stressors has been found in subsyndromal anxiety (e.g., Kawachi, Sparrow, Vokonas, & Weiss, 1995; Miu, Heilman, & Miclea, 2009) as well as in a range of anxiety disorders (cf. Cohen & Benjamin, 2006; Friedman, 2007, for reviews). In the case of SAD, mixed results have previously been reported: While studies investigating task-related HRV found no (Gerlach, Wilhelm, & Roth, 2003) or only gender-specific (Grossman, Wilhelm, Kawachi, & Sparrow, 2001) differences, studies that acquired HRV at rest reported diminished HF-HRV in patients with SAD (Licht, De Geus, Van Dyck, & Penninx, 2009; Pittig, Arch, Lam, & Craske, 2012). While Licht et al. (2009) attributed decreased HF-HRV in anxiety disorders solely to the effects of antidepressant medication, a meta-analysis of studies on patients with major depressive disorder (MDD) related the reduction in HRV specifically to the class of tricyclic antidepressants (Kemp et al., 2010). However, a more recent study reported reduced HF-HRV in unmedicated MDD patients with or without comorbid anxiety (Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012) suggesting that the true extent of the mediating effect of antidepressants in earlier studies is currently not quantifiable.

1.4. Neural structures associated with SAD and HRV

The empirical literature on disorder-specific alterations in brain activation elicited by affective paradigms in SAD yielded divergent results. While most studies reported increased activation in emotion processing areas such as amygdala and insula (Etkin & Wager, 2007; Freitas-ferrari et al., 2010; Miskovic & Schmidt, 2012), several studies did not find evidence for altered activation of these structures in SAD patients (e.g., Quadflieg, Mohr, Mentzel, Miltner, & Straube, 2008; Sripada et al., 2009; Ziv, Goldin, Jazaieri, Hahn, & Gross, 2013). Hyperactivation of emotion processing areas in SAD thus appears to depend on experimental details such as stimulus type and modality (Quadflieg et al., 2008) or task complexity (e.g., Sripada et al., 2009).

Broader frameworks such as the "Polyvagal Theory" (e.g., Porges, 2007) and the "Neurovisceral Integration Model" (Thayer & Lane, 2000, 2009) relate autonomic, and in particular parasympathetic functioning indexed by HF-HRV, also to regulatory brain regions such as prefrontal and cingulate areas as well as complex feedback circuits involving the hypothalamus and brainstem nuclei. A recent meta-analysis of eight neuroimaging studies on neural correlates of task-related HRV identified several areas, including the ventro-medial prefrontal/anterior cingulate cortex and the extended amygdala/ventral striatum (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). In the only previous neuroimaging study in SAD that combined HRV and measures of regional cerebral blood flow (rCBF), 28 patients with SAD executed a stressful, symptom-evoking public speaking task in a PET scanner. In line with the results of the meta-analysis, task-related HRV showed positive correlations with rCBF in several medial and lateral frontal regions, particularly the anterior cingulate cortex and the caudate nucleus (Ahs, Sollers, Furmark, Fredrikson, & Thayer, 2009).

Hypotheses. The aim of our study was to investigate parasympathetic cardioregulatory processes as well as their conscious accessibility and neural underpinnings in patients with SAD. We measured HRV both as a trait marker in a short-term recording at rest and as a response variable upon emotion induction through a widely-used emotional face-matching task (e.g., Hariri, Bookheimer, & Mazziotta, 2000).

Based on previous findings and theoretical models of the disorder, we expected decreased autonomic control of the heart in patients with SAD at rest, manifesting as decreased HF-HRV and an increased LF/HF ratio. Inconsistent results on group differences in task-related HRV in prior studies did not allow us to make directed hypothesis with respect to HF-HRV during emotional processing.

As increased self-focused attention and physiological monitoring are central to the aetiology and maintenance of SAD, the conscious accessibility of cardioregulatory processes carries behavioural relevance. We tested awareness of HR and the accuracy of its perception through an established heartbeat detection task assessing interoceptive sensitivity (Schandry, 1981). To our knowledge, only one clinical study employed the same task and found no differences between patients with SAD and HCs (Antony, Brown, & Craske, 1995), while studies in healthy subjects report positive correlations between interoceptive sensitivity scores and traits of general (Pollatos, Traut-Mattausch, & Schandry, 2009) and social anxiety (Stevens et al., 2011). Although we assumed interoceptive accuracy important for SAD symptomatology, the paucity of prior clinical studies did not allow us to formulate a directed hypothesis concerning group differences.