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Research report

A blunted sympathetic and accentuated parasympathetic response to postural change in subjects with depressive disorders

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ABSTRACT

Background: In recent years, the bi-directional relationship between depression and ANS dysfunction has received considerable attention, but findings remain inconclusive. In this study, we aimed to examine the spectral HRV response to postural change in subjects with depressive disorders and in healthy controls, in order to gain insight into the characteristics of autonomic nervous system (ANS) response to postural change in subjects with depressive disorders.

Methods: We compared HRV response to postural change between subjects with depressive disorders and healthy controls aged 20–37 years. Depression severity was assessed by the self-reported Beck Depression Inventory-II (BDI-II). Spectral HRV was analyzed at two moments: 10 min seated rest and 10 min at standing position, with spontaneous breathing.

Results: No significant differences existed in the resting spectral HRV indices between subjects with depressive disorders and controls, however, following postural change, the increasing level of LF and LF/HF was lower and the decreasing level of HF power was higher, in the individuals with depression than that in healthy subjects. The differences in the LF power, HF power and the LF/HF ratio between seated rest before standing up and after postural change were found negatively correlated with depression severity.

Conclusion: We found a blunted sympathetic and accentuated parasympathetic response to postural change in subjects with depressive disorder, suggesting that the autonomic impairment and early ANS dysfunction may exist among depressed individuals. These findings indicated that spectral analysis of HRV associated with postural change may be a more sensitive method than resting HRV analysis for detecting ANS dysfunction in depressive disorders.

Limitations: Further studies are needed to expand the sample size and to clarify the mechanisms responsible for the autonomic dysfunction observed in individuals with depressive disorders.

1. Introduction

It is increasingly being recognized that depressive disorders are independently associated with an increased risk of cardiovascular disease (including fatal arrhythmias and coronary artery disease) (Carney et al., 2005; Rabins et al., 1985; Tsuang et al., 1980). Autonomic disturbances have been thought to be responsible for the increased cardiovascular risk observed in patients with depression (Dekker et al., 2000; Liao et al., 1997; Tsuji et al., 1994). Specifically, it was thought that depressive disorders might be associated with increased sympathetic activity, which lowers the threshold for cardiovascular disease (Dalack and Roose, 1990; Eaker et al., 2005; Flaa et al., 2008; Glassman, 2008; Penninx et al., 2001; Veith et al., 1994). However, other studies have reported decreased SNS activity in subjects with depressive disorders or no association between psychopathology and SNS activity (Ahrens et al., 2008; Esler, 2004; Roth et al., 2008). Thus, findings about the bi-directional relationship between depression and ANS function remain inconclusive.

Spectral analysis of resting heart rate variability (HRV) is a non-invasive method often used to assess cardiac autonomic nervous activity (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Akselrod et al., 1981). However, baseline autonomic functioning varies with age, sex, weight, emotional state, and environmental or physiological stimuli (Spiegelhalder et al., 2011). Thus, because studies have used different methodological designs, it has been impossible to draw firm conclusions.

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In recent years, the spectral HRV response to postural change has been hypothesized to be a more sensitive measure of cardiac autonomic modulation than resting spectral HRV because cardiac autonomic dysfunction is thought to occur primarily through impairment of sympathetic response to environmental or physiological stimuli (Guzzetti et al., 1988; Lombardi et al., 1996; Carnethon et al., 2002a). Normal HRV activity in response to postural change reflects a shift from parasympathetic predominance at rest to sympathetic control while standing(de Souza et al., 2014). Some studies have reported an attenuated or absent HRV response to postural change in subjects with chronic diseases such as hypertension (Guzzetti et al., 1988) and diabetes (Pagani et al., 1988), suggesting that autonomic impairment and early sympathetic dysfunction may be present in such individuals. However, to our knowledge, HRV response to postural change has not been examined in subjects with depressive disorders.

In this study, we aimed to examine the HRV response to postural change in subjects with depressive disorders and in healthy controls. The primary purpose of this study was to gain insight into the possible bi-directional relationship between depression and ANS dysfunction and hence to discover whether ANS response to postural change could be a marker of autonomic dysfunction and early sympathetic dysfunction in depressive disorders.

2. Methods

2.1. Subjects

The study sample consisted of two groups of adult subjects: subjects with depressive disorders ($n=42$; age, 28.3 ± 7.8 years; range, 20–36 years), and healthy controls ($n=49$; age, 30.1 ± 8.1 years; range, 20–37 years). All the depressive disorder patients were from the inpatients of School of Public Health and Tropical Medicine of Southern Medical University. Informed consent was obtained from all subjects prior to commencement of the study, and the Ethics Committee of School of Public Health and Tropical Medicine in Southern Medical University approved all the procedures.

The psychiatric diagnosis of depressive disorder in each patient was verified by a psychiatrist using criteria based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM IV), and each subject's history of psychiatric illness, medical disease, and medication use was evaluated by an interview and a medical chart review carefully (Robles-Pina, 2011; Vignatelli et al., 2005). Subjects were screened and excluded if they suffered from other serious psychiatric, somatic or sleep disorders, or they had a comorbid substance-related disorder. They consumed no illicit, prescription or OTC (over-the-counter) drugs as confirmed by physical and mental examination and biological analysis. Subjects were also excluded if they had the habits of cigarette smoking or alcohol consumption, that have a documented effect on the autonomic nervous system (Carnethon et al., 2002a, 2002b; Shinozaki, et al. 2008; Quintana, et al., 2013). If subjects suffered from hypertension (presence of systolic blood pressure ≥ 140 mmHg; diastolic blood pressure ≥ 90 mmHg), diabetes (fasting glucose ≥ 126 mg/dL), cardiovascular disease, severe cardiac arrhythmia, a frequent ectopic heartbeat, or an acute medical illness within 3 months of the start of the study, they were then excluded from the study. Any medications that have a documented effect on the autonomic nervous system (e.g. β-blockade and anticholinergic drugs) were stopped at least 14 days prior to the recordings (Zhou et al., 2013).

2.2. Study design

Volunteers were instructed to avoid consuming alcohol, caffeine, smoking and substances that influence the ANS for 24 h before evaluation. All procedures necessary for the data collection were explained to the individuals. Data were collected between 8 and 12 a.m. in our laboratory under controlled temperature (21–25 °C) and humidity (50–60%). Food intake also has effects on autonomic function (van Baak, 2008), so the postural change tests were conducted in a fasting state.

After the initial evaluation the heart monitor belt was then placed over the thorax and aligned with the distal third of the sternum, and the polar heart rate receiver was placed on the wrist. The subject remained seated at rest with spontaneous breathing. After 10 min the volunteers quickly stood up from a seated position in up to three seconds according to verbal command and remained standing for 10 min (de Souza et al., 2014). Heart rate variability (HRV) was analyzed at two moments: 10 min seated rest with spontaneous breathing, and 10 min at standing position. The subjects were instructed to avoid talking and moving during the data collection.

2.3. Measures

2.3.1. Beck Depression Inventory (BDI)

Depression severity was assessed by the self-reported Beck Depression Inventory-II (BDI-II) (Vanheule et al., 2008; Ward, 2006), which is one of the most commonly used self-report instruments for estimating the severity of depression. The total score indicates whether the individual presents a mild, moderate or major depression. The BDI-II consists of 21 items, each of which is scored on a scale from 0 to 3. The maximum score is 63. The recommended cutoff for minimal depression is 13, whereas a score of 14–19 indicates mild, 20–28 moderate and 29–63 serious depression.

2.3.2. Analysis of spectral HRV

The R–R intervals (RRI) were computed from the electrocardiogram (ECG). All the QRS complexes were detected by Matlab (Matlab2007a) program, and the RRI time series were obtained. For maximum precision in measurement of the RRI data, artifacts were automatically detected using the following criteria: RRI <350 ms or RRI $>$ 1500 ms (Barry et al., 1991; Brown et al., 2013). For calculation of the spectral indices we used the HRV Analysis software (Kubios HRV v.1.1 for Windows, Biomedical Signal Analysis Standard). Spectral HRV measures include high-frequency power (HF: 0.15–0.4 Hz), low-frequency power (LF: 0.04–0.15 Hz), and very-low-frequency power (VLF: 0.003–0.04 Hz). LF power is thought to be modulated by both sympathetic and parasympathetic activities, whereas HF power is mainly modulated by parasympathetic activity. The LF/HF ratio was computed as a measure of the sympathovagal balance towards sympathetic activity. The very low frequency (VLF) power is assumed to be due to long-term regulatory mechanisms such as humoral factors, temperature, and other slow components (Otzenberger et al., 1998; Stein and Pu, 2012).

2.4. Statistical analysis

All participants were divided into two groups: depressive disorders and normal controls. Demographic variables were compared with a non-parametric test (Mann–Whitney U test) and Chi-squared tests or student's t test. Analysis of variance (AVONA) and pairwise test comparisons were carried out to compare HRV responses to postural change in subjects with depressive disorders and those without. All variables were presented with standard deviations if there was no specified explanation (mean ± SEM). All data calculations were performed with SPSS 13.0 (Chicago, IL, USA). A two-sided α-level of significance of 0.05 was used for all tests, and a value of $P<0.05$ was considered statistically significant.