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Clinical utility of heart rate variability during Head-up tilt test in subjects with chronic posttraumatic stress disorder

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ABSTRACT

Posttraumatic stress disorder (PTSD) is characterized by psychophysiological abnormalities, such as an altered baseline heart rate and hyperarousal, implying dysfunctional arousal regulation. Heart rate variabilities (HRVs) is known to reflect autonomic nervous system activity. We examined the changes of HRVs in PTSD patients with head-up tilt position to closely investigate disease-specific changes in autonomic function in PTSD patients. Sixty-seven patients with PTSD and 72 patients without PTSD were assessed using the PTSD Checklist for DSM-5 (PCL-5) and psychiatric interview. Heart rate data including standard deviation of the NN intervals, the square root of the mean squared differences of successive NN intervals, log low-frequency and log high-frequency were collected for 10 min before and after tilting. Considering interactions between groups and head-up tilting, the head-up tilting induced reduction of the high-frequency component of HRVs was significantly greater in the PTSD group [F (1, 272) = 4.718, p = 0.031]. The change of HRVs in PTSD patients suggested the presence of autonomic dysfunction in despite of the posture.

1. Introduction

Posttraumatic stress disorder (PTSD) is characterized by more than 1 month of re-experiencing, avoidance, negative alteration of mood and cognition and hyperarousal symptoms (American Psychiatric Association, 2013). PTSD is a common psychiatric condition triggered by exposure to an intensely distressing traumatic event. The estimated lifetime prevalence of PTSD among adult Americans is 6.8%, representing a small proportion of those who have experienced a trauma in their lives (Kessler et al., 2005). However, veterans have a higher prevalence of PTSD, with 30.9% of men and 26.9% of women reported to have PTSD in the National Vietnam Veterans Readjustment Study and 23.0% of veterans reported to have PTSD in a Korean Vietnam Veterans Study (Chung et al., 2002). Alterations in both the hypothalamic-pituitary-adrenal axis and the sympatho-adrenal medullary axis were related to the stress response mediating anxiety and fear in PTSD. Some clinical symptoms of PTSD such as intrusive thought and hyperarousal, were also reported to involve the autonomic nervous system. In particular, the parasympathetic nervous system is suppressed and the sympathetic nerve system is activated in a sustained manner, which leads to the secretion of epinephrine and norepinephrine into blood vessels (Draghici and Taylor, 2016; Sgoifo et al., 2015). As a result, blood vessels constrict, leading to elevated blood pressure and muscle stiffness, which cause changes in heart rate and heart rate variabilities (HRVs).

HRV is a simple and non-invasive index, which demonstrates periodical changes in heart rate during normal autonomic function. Traditional HRV analysis methods involve long-term electrocardiogram (ECG) recording (12–24 h) or short-term ECG recording (2–5min) (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996a). Time-domain analysis has been shown to be better than frequency-domain analysis for the evaluation of HRV using long-term recordings due to the low stability of heart rate modulations during long-term recording.

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For short-term recording, the frequency-domain methods are usually able to provide results that are more easily interpretable in terms of physiological regulation (Draghici and Taylor, 2016). Many studies have reported significant relationships between HRV and physiological and psychological activities such as mental stress and anxiety disorders. Meta-analysis study for PTSD reported high frequency HRV was reduced with small effect size, but Low frequency HRV did not differ between subjects with PTSD and controls (Chalmers et al., 2014). The reason for the inconsistency in *t* results across studies is unclear. utSmall sample size and common confounds including psychiatric and medical comorbidity, as well as medication use might be possible confounding factors reason to be explained.

In addition, traditional HRV analysis methods have the limitation that they cannot adequately assess the transient changes in heart rate that are associated with rapid changes in physiological status in the short term (Draghici and Taylor, 2016; Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996b). Thus some investigations tried to measure response to stimulus such as showing traumatic scene, listening traumatic events or emotional stress in the PTSD patients (Hauschildt et al., 2011; Nachar et al., 2014; Norte et al., 2013). However, it still remains unclear that PTSD might be directly related to reduced parasympathetic function, dysfunction of sympathetic tone or other mechanism. Recently head-up tilt test can be used to completely work up the susceptibility to the heart rate variation (Kenny et al., 1986). In contrast to the supine position, the head-up position induces a hemodynamic stress on the cardio-vascular system. Tilt position progressively increases average muscle sympathetic nerve activity and systolic and diastolic pressures, and their spectral powers at low and respiratory frequencies. Meanwhile tilting decreases vagal baroreflex gain and vagal cardiac nerve activity progressively. Therefore, we performed a head-up tilt test using a tilt table and compared the changes after tilting in indices of HRVs between PTSD patients who had no current major depressive disorder and anxiety disorders that might influence autonomic function and non-PTSD subjects, to evaluate disease-specific changes in autonomic function in chronic PTSD patients under physical stress.

2. Methods

2.1. Subjects

All participants were recruited in the Department of Psychiatry at Veteran Health Service Medical Center in Seoul from October 2014 to June 2015 through advertisements. Participants with other mental health problems, including organic mental disorder, psychotic disorders, bipolar disorder, current substance use disorder, current major depressive disorder and current anxiety disorders were excluded. Subjects taking medications for hypertension and hyperlipidemia, diabetes mellitus, or cerebrovascular disease were classified as medication positive. Candidates with uncontrolled hypertension, hyperlipidemia, diabetes mellitus, or cardiovascular problems, such as ischemic heart disease, arrhythmia, or heart failure, were excluded. Of the 211 participants, 52 were excluded because of medical problems (n = 47; uncontrolled hypertension = 4, uncontrolled hyperlipidemia = 1, uncontrolled diabetes mellitus = 12, ischemic heart disease = 8, arrhythmia = 10, angina = 4, myocardial infarction = 5, and mild cognitive impairment = 3) and 5 because of the use of beta or calcium-channel blockers. All participants provided written informed consent. The study protocol was approved by the Institutional Review Board at the Veterans Health Service Medical Center in Seoul, Korea.

2.2. Procedure

One hundred fifty-nine individuals underwent a clinical examination, a psychiatric evaluation, and HRV measurements. PTSD was diagnosed using the Diagnostic and Statistical Manual of Mental Disorders-5 (American Psychiatric Association., 2013) by a psychiatrist. All participants were investigated about past history of depression and anxiety disorders. Current psychiatric medications such as antidepressants (four SSRIs = 32, three SNRIs = 11, one tricyclic antidepressant = 1) and sleep medications (zolpidem = 46, benzodiazepine = 23) also were examined. In addition, the PTSD Checklist for DSM-5 (PCL-5) was used to evaluate symptoms severity of PTSD, the Beck Depression Inventory (BDI) was used to estimate depressive symptoms, the Beck Anxiety Inventory (BAI) was used to examine anxiety symptoms, and the Pittsburgh Sleep Quality Index (PSQI) was used to assess subjective sleep complaints. Participants were asked to complete questionnaires at interview room of hospital, without the help of anybody else. And then their heart rates were measured after 7 days.

Finally, the 141 subjects were divided into two groups except 18 subjects with artifact in HRVs measurements: normal (n = 73) and PTSD (n = 68). Within PTSD group, 44 participants were developed PTSD symptoms by entering Vietnam war, and 23 subjects was considered to be PTSD group by other trauma exposure except combat (natural disaster = 4, vehicle accidents = 4, sexual assault = 1. life threating injury = 8, sudden death of loved one = 4, other very stressful event = 6) recruited at the outpatient clinic. The 73 individuals in the non-PTSD group were recruited via advertisements or from established subject pools. Of these, 43 participants who had experienced the Vietnam War did not meet the criteria for PTSD, and 30 subjects, who had no experience of combat, were deemed to be non-veterans and were placed in the non-PTSD group

2.3. Measure

2.3.1. Clinical variables

Clinical variables were collected using a standardized protocol. Body mass index (BMI) was defined as body weight (kg) divided by the square of the body height (m^2). Hypertension was defined as systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg, or current use of antihypertensive medication. Hyperlipidemia was defined as low-density lipoprotein cholesterol level $\geq$160 mg/dl. Diabetes mellitus was defined as fasting blood glucose level $\geq$126 mg/dl or the current use of antidiabetic medications. Information regarding cerebrovascular disease, including history of ischemic brain stroke and brain hemorrhage was also obtained. Smoking was classified into current smoker. Wine (148 ml), beer (355 ml), liquor (44 ml) were checked with one more drink in 2 ~ 4 times /month. Coffee and tea consumption were measured in drinks/day.

2.3.2. HRVs

The central phenomenon underlying HRV is the oscillation between successive heartbeats and that between successive instantaneous heart rates (the reciprocal of the RR interval). The terms describing the variation in the RR interval and instantaneous heart rate include cycle length variability, heart period variability, RR variability, and RR interval tachogram; however, the term HRV is widely accepted. The simplest method of analyzing heart rate variability is time domain analysis. Time domain analysis measures the time interval between normal QRS complexes or instantaneous heart rate at a specific time; i.e., a normal-to-normal interval or instantaneous heart rate is calculated between consecutive normal QRS complexes, which are caused only by the depolarization of the sinus node in the continuously recorded electrocardiogram (ECG). Time series measurements are easy to compute, although they do not clarify which branch of the autonomic nervous system affects the distribution of transient power and do not provide a way to quantify the autonomic nervous system balance. The main advantage of a power spectrum analysis over that of a time series analysis is that the former provides information on the power distribution as a function of frequency and also provides a means to quantify the balance of the autonomic nervous system. In addition, graphs of low and high frequencies, which reflect the sympathetic

nervous system and parasympathetic nerve branches of the autonomic nervous system, can be quantified and analyzed.

A measuring HRVs was conducted by a physician after the procedure was explained. Participants were examined in a quiet, dimly lit room at a comfortable temperature (22–24 °C). The RR interval was measured using three electrodes (right arm, left arm, and left leg) and the bipolar leads (I, II, and III). were monitored To obtain the best results with the convenience of measurement in mind, the electrodes were placed on the chest wall equidistant from the heart rather than on specific limbs. After the three electrodes were attached, the participants were provided with at least 10 min to adjust to the environment to minimize any effects from short-term activity. After this period, the medical worker checked the limb-lead conduction and confirmed that the graph was clear and had no interfering wavelengths. HRV was measured in a resting supine position for 5 min using an AFT-800 (Medicore; Seoul, Korea). Overall HRV results were assessed based on the widely used time-domain and frequency-domain analyses. The preprocessing value of the RR interval and ECG data were collected. Then we rotated the table, which had an electric motor, to a head-up tilting that was maintained for 10 min. The inclination of the table was set at an angle of 70°. After measuring HRV in head up tilt test, the subjects were moved again to a horizontal position for 10 min. The total procedure took approximately 60 min, and none of the subjects experienced syncope or pre-syncopal symptoms during the recordings.

HRV results were assessed based on the widely used time- and frequency-domain analyses. To remove noise from ECG data, a fast Fourier transform filter was applied. Following the guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, data were collected over a 5 min period, and statistical analysis of the time domain was performed. The artifacts were removed at the third 30-Hz ECG signal that was received from the analog-digital (A/D) converter, which converts the output signal from the abovementioned signal detection system into a digital signal (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996b). Subsequently, the inflection point was distinguished from the differentiation wave. The time interval from the second R point, which is the interval from the time of the second peak to that of the first peak (the RR point to the first R Point), was obtained by deducting the time of the first peak from that of the second peak. The abovementioned RR interval, i.e., the interval from the normal R point to the next normal R point, is called the NN interval. The RR interval can be considered as one cycle of ECG, i.e., the RR interval indicates the time required for one heartbeat. The beat rate per minute data were calculated by multiplying the A/D converter sampling frequency by 60, and the heart rate per minute was calculated by dividing this number by the RR interval. Finally, the mean of the 5 min standard deviation of NN intervals (SDNN) and the square root of the mean squared differences of successive NN intervals (RMSSD) were estimated for short-term HRV. Frequency-domain analysis can be divided into three period components through power-spectrum analysis. The high-frequency component (HF) is an index of parasympathetic system function in the range of 0.15–0.4 Hz. The low-frequency component (LF), between 0.05 Hz and 0.15 Hz, is affected by both sympathetic nerve system and parasympathetic nerve system, but mainly reflects the activity of sympathetic nerve system. The very-low-frequency component (0.003–0.05 Hz) was not analyzed due to poor accuracy in its measurement on account of the 5 minute measurement period (Heathers, 2014). Raw power was log-converted before analysis to normalize the relevant distributions.

2.3.3. Psychological variables

PTSD symptoms were evaluated using PCL-5 (Blevins et al., 2015), which is a self-report rating scale. The PCL-5 consists of four components: “intrusion” with 5 items, “avoidance” with 2 items, “negative alteration in cognition and mood” with 7 items, and “hyperarousal” with 6 items. The subjects rated their symptoms during the past month individually using a 5-point Likert scale, from “1 = not at all” to “5 = absolutely yes” . The total scores ranged from 0 to 80 and a cut-off score was set at 33 (Weathers et al., 2013). Depression was measured using the Korean version of the BDI. This measurement is a self-report questionnaire that evaluates the existence and level of depression and includes questions regarding cognitive, emotional, motivational, and physiological symptoms. Responses on the BDI use a four-point scale, from 0 (mild) to 3 (severe) to describe the levels of symptoms reported for each question (Beck et al., 1996). Anxiety was also estimated using the Korean version of the BAI, which describes 21 anxiety symptoms. Respondents were asked to rate how much each of these symptoms had disturbed them in the past week, on a scale ranging from 0 (not at all) to 3 (severely, I could barely stand it). The total score has a minimum of 0 and a maximum of 63 (Yook and Kim, 1997). Sleep quality was assessed using the seven components of the PSQI, which assesses subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction over the preceding month (Buysse et al., 1989). The global PSQI score ranges from 0 to 21, and a global PSQI score >5 is known to provide a sensitive and specific measure of poor sleep quality.

2.4. Data analyses

Kolmogorov-Smirnov tests were performed to assess the normality of the collected data. Intergroup differences between two groups were assessed using chi-square tests and independent *t*-tests. Next, multivariate analysis of covariance (MANCOVA) was performed to assess the effects of PTSD, head-up tiling, and both of them on HRV variables. Gender, history of cerebrovascular disease, taking antidepressant, and using sleep medication were considered to be adjustment factors based on results of comparison. Moreover, the score of BDI and BAI, which revealed the severity of depression and anxiety disorders, were added to covariates. The statistical significance criterion was defined to be $p < 0.05$ for each two-tailed test. IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

3. Results

The mean age was 64.8 years in the PTSD group and 62.7 years in the non-PTSD group. Of the 139 subjects, 88 individuals were veterans. There was no significant difference in the prevalence of diabetes and hypertension, although cerebrovascular disease was found to be significantly more common in the PTSD group. Of 68 individuals in the PTSD group, forty-five veteran PTSD patients reported their symptoms after discharging army. They could not describe exact date of developing PTSD, but only demonstrated time of experience painful trauma events. Based on their reports, the mean time since the target traumatic event was 13.9 years (SD = 6.4). Furthermore, 23 subjects who were not veterans reported having PTSD for 6.4 years(SD = 3.6). More subjects in PTSD group have history of depression and anxiety disorders. Antidepressants were also more used in PTSD group currently. Additionally, subjects with PTSD showed more taking sleep medications then those without PTSD (Table 1).

In the comparison of the changes of HRVs according during position change, seventy-two non-PTSD subjects and 67 PTSD subjects were examined before and after head-up tilting. Lower values of SDNN [F (1, 272) = 7.882 $p = 0.005$], RMSSD (F (1, 272) = 6.659, $p = 0.010$), and LNHF (F (1, 272) = 21.035, $p < 0.001$) were observed in the PTSD group than in the non-PTSD group. In the comparison of HRV indices as postural changes within groups, the PTSD group had higher HR [F (1, 272) = 39.538, $p < 0.001$)] and lower HF [F (1, 272) = 33.963, $p < 0.001$] than the non-PTSD group. Regarding interactions between the presence or absence of PTSD and head-up tilting, the head-up tilting-induced reduction of the HF component of HRV [F (1, 272) = 4.718, $p = 0.031$] was significantly greater in the PTSD group

Table 1
Demographic and clinical characteristics.

	Non-PTSD (n = 73)	PTSD (n = 68)	t/χ^2	p
Age (years)	62.7(11.0)	64.4(11.3)	−0.884	0.378
Female (N, %)	9(12.3)	2(2.9)	4.313	0.038*,†
Veterans (N, %)	43(58.9)	45(66.2)	0.794	0.373
Time since target trauma (years)		13.9(6.4)		
BMI (kg/m^2)	25.1(3.6)	24.1(3.2)	1.727	0.086
Smoking (N, %)	35(47.9)	24(35.3)	2.315	0.172
Alcohol (N, %)	36(49.3)	24(35.3)	2.831	0.125
Coffee (cup/day)	2.1(1.3)	1.9(1.4)	1.457	0.452
Education (years)	12.3(3.6)	11.9(3.5)	0.679	0.498
DM med, N (%)	13(17.8)	19(27.9)	2.060	0.151
HD med, N (%)	32(43.8)	32(47.1)	0.148	0.701
CV med, N (%)	3(4.1)	11(16.2)	5.732	0.017*,†
Depression, N (%)§	14(9.6)	48(35.3)	27.125	<0.001**
Anxiety disorders, N (%)¶	8(5.5)	42(30.9)	31.149	<0.001**
Antidepressant use, N (%)	4(2.7)	40(29.4)	30.039	<0.001**
Sleep medication use, N (%)	22(30.1)	47(69.1)	21.408	<0.001**

* $p < 0.05$,
** $p < 0.001$ Data are presented as mean (standard deviation) for continuous variables and number (%) for categorical variables.
† Chi-square test and Fisher's exact test were performed for statistical analysis. PTSD, posttraumatic stress disorder; BMI, body mass index; PCL, posttraumatic stress disorder checklist for DSM-5; DM, diabetes mellitus; HD, heart disease; CV, cerebrovascular disease
§ Life time history of depression
¶ Life time history of anxiety disorders

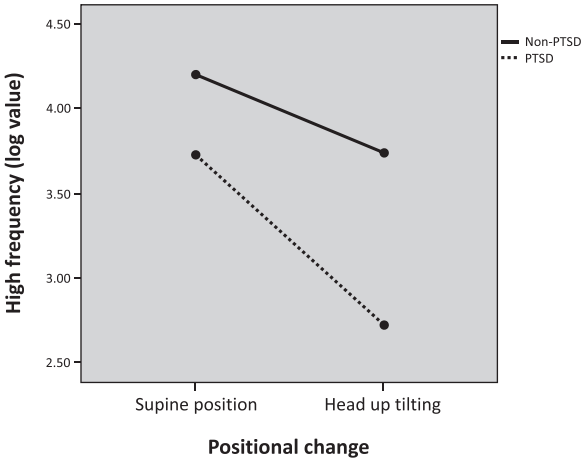

Fig. 1. Mean for HRV component of high frequency (LF log) during head-up tilt position changing between Non-PTSD and PTSD group. PTSD, post-traumatic stress disorder The high frequency of HRV indices was significant difference between two groups after adjusting gender, history of cerebrovascular medication, BDI score, BAI score, taking antidepressant and taking sleep medication considering interaction effect with groups and position changes.

than in the non-PTSD group (Table 2, Fig. 1).

4. Discussion

This study assessed the changes in sympathovagal balance before and after head-up tilt in the PTSD patients and controls by HRVs measurements. In the supine position PTSD groups had significantly lower values in the SDNN and RMSSD of time-domain analysis and in the LNHF of frequency-domain analysis, partially supporting previous studies (Cohen et al., 2000b; Dennis et al., 2014; Hauschildt et al., 2011; Lakusic et al., 2007; Shaikh al arab et al., 2012). The SDNN value is reported to reflect the overall degree of activity of autonomic nerve system (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996a). Higher or more irregular HRV indices were associated with increased SDNN values, . SDNN may reflect physiological resilience in relation to stress (Sgoifo et al., 2015). Some study reported lower SDNN value in patients with PTSD, which suggested to reflect a reduced flexibility of entire autonomic function, indicating a lowered ability to cope with stress (Cohen et al., 2000a; Dennis et al., 2014; Lee and Theus, 2012). The RMSSD is also used to evaluate short-period variations in HR. This is an index of the degree of parasympathetic nerve system activity (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996a). A significantly lower RMSSD in the PTSD patients might result from the decline of parasympathetic activity due to various traumatic experiences, similar to findings in the previous literatures (Hauschildt et al., 2011; Lakusic et al., 2007; Shaikh al arab et al., 2012). In the frequency-domain analyses HF component was significantly lower in the PTSD group than in the non-PTSD group, which is consistent with previous studies (Cohen et al., 2000a; Hauschildt et al., 2011; Lakusic et al., 2007; Shah et al., 2013). Although various physiological interpretations for the HF component have been documented, HF in HRV refers to rapid changes in HR, which are assumed to reflect respiratory sinus arrhythmia (Green et al., 2016; Sgoifo et al., 2015). HF component also has a correlation with the RMSSD index in time-domain analysis (Berntson et al., 2005). Thus emotional states of constant stress, anxiety and fear seemed to influence parasympathetic stimulus, which lead to decrease the HF index (Chalmers et al., 2014; Sgoifo et al., 2015). Interpretations of the LF index are controversial in HRVs studies.

Table 2
The changes of autonomic function after head-up tilting.

	Non-PTSD (n = 73)		PTSD (n = 68)		Main effect†		
	Supine	Stand	Supine	Stand	PTSD	Tilt	PTSD•Tilt
HR	66.1 (1.4)	74.9 (1.4)	69.6 (1.4)	77.2 (1.4)	2.285	38.111*	0.203
SDNN	28.5 (1.4)	24.7 (1.4)	22.2 (1.4)	21.6 (1.4)	9.022*	2.591	1.315
RMSSD	23.0 (1.7)	18.9 (1.7)	15.6 (1.8)	15.8 (1.8)	6.767*	1.447	1.766
LF§	4.3 (0.1)	4.1 (0.1)	4.2 (0.1)	3.9 (0.1)	1.433	2.761	0.326
HF§	4.2 (0.1)	3.7 (0.1)	3.7 (0.1)	2.7 (0.1)	22.512**	32.972**	4.580*

* $p < 0.05$,
** $p < 0.001$ Data are presented as mean (standard error)
† The main effects are shown as F-values
§ Logarithmic transformation was employed before analysis and values were given as log-transformed data. Multivariate Analysis of Covariance (MANCOVA) was performed with gender, history of cerebrovascular medication, BDI score, BAI score, taking antidepressant and taking sleep medication as covariates. HUT, head-up tilt; HRV, heart rate variability; PTSD, posttraumatic stress disorder; HR, heart rate; SDNN, standard deviation of the NN interval; RMSSD, the square root of the mean squared differences of successive NN intervals; LF, low frequency; HF, high frequency

Although many studies reported that LF is involved in the activities of both the sympathetic nerve system and the parasympathetic nerve system (Draghici and Taylor, 2016; Goldstein et al., 2011), It was more dominant that LF is a marker of sympathetic modulation (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996b). In the PTSD researches meaning of LF component also has debated. Some research reported higher LF power in PTSD patients relative to controls but the other studies were not found significance (Cohen et al., 2000a; Cohen et al., 2000b; Lakusic et al., 2007). Present study showed PTSD group had lower LF power without significant difference between the two groups similar to previous investigations (Hauschildt et al., 2011; Keary et al., 2009).

In the analysis of HRVs based on position changes within group, a significantly increasing HR and reduced HF component in HRV were found. In addition, the change in patterns of the HF component of HRV after head-up tilting were different between PTSD and non-PTSD subjects. The head-up position creates acute stress and a hemodynamic load on the cardio-vascular system. When a normal individual stands, excessive blood congestion in the lower extremities causes reduced venous return, reduced cardiac output, and arterial blood pressure (Fortrat and Gharib, 2016). This reduced blood pressure activates arterial baroreceptors, which lead to a subsequent reflexive increase in sympathetic outflow and parasympathetic inhibition, in turn causing peripheral vasoconstriction, increases in heart rate, and increases in cardiac contractility. In healthy adolescents or adults, standing up or passive tilt is invariably accompanied by a relative increase in the LF component and a decrease in the HF component of RR variability (Malliani, 2005). There is a reciprocal relationship between the LF and HF components, which corresponds to the sympathovagal balance.

Higher HRV implicates parasympathetic dominance favoring energy conservation, while lower HRV suggests enhanced sympathetic cardiac modulation or attenuated cardiac parasympathetic modulation. Thus, present findings suggested that activation of the sympathetic nerve system might be weak, meanwhile the parasympathetic nerve system was strongly inhibited in PTSD patients. Diminished parasympathetic activity altering HR dynamics suggested central autonomic dysregulation that could represent a possible link to increased cardiovascular disease in PTSD. In addition, there was a negative correlation of HF-HRV and basal HR, implying a parasympathetic contribution independent of the sympathetic nervous system which supports the notion that poor vagal tone might play a significant role in PTSD (van der Kolk, 2006). Sympathetic and parasympathetic changes might be able to occur in parallel to one another, not in a reciprocal manner (Minassian et al., 2014).

Underlying mechanism might be assumed to be changes in the activation of the amygdala and the ventral portion of medial prefrontal cortex, which underlie fear and threat responses in PTSD (Etkin and Wager, 2007). These structures, which comprise the prelimbic and infralimbic cortices are connected with the anterior cingulate and the insula, which have in turn been implicated in controlling attention and vigilance (Resstel et al., 2004). Diminished amplitudes of HF and LF were documented in association with altered connectivity between both of these brain structures (Blevins et al., 2015; Minassian et al., 2014; Thayer et al., 2012). In conclusion PTSD should damage to brain function as well as baroreflex dysfunction, which might develop psychiatric symptoms such as nightmare, avoidance or hyperarousal.

This study has several limitations. The present sample were older persons and predominantly men, limiting the generalizability of our findings to the general population. Particularly elderly is often accompanied by depression or anxiety, which should effect on HRV results. To overcome these problems, BDI an BAI score, history of taking antidepressant, and using sleep medications were included as covariates in the analysis. Secondly, despite efforts to educate the participants to abstain from activities affecting results of HRVs and tilt test, such as smoking, the consumption of caffeine and other medication, and alcohol drinking, these remain limitations. This study used PCL-5, which is a self-report scale, to evaluate the severity of symptoms, instead of an interview-based measurement such as the Clinician-Administered PTSD Scale for DSM-5. However, a psychiatrist interviewed all participants for diagnosis based on DSM-5. To generalize the results of this study, the findings should be verified using objective assessment scales, as well as the subjective evaluation of patients. Nevertheless, we assessed the changes of HRVs in the PTSD patients and controls to evaluate sympathovagal response under physical stress with head up tilt position. Present study provided no significant sympathetic reaction was noted in both the supine and tilting in the PTSD patients, suggesting that the parasympathetic nervous system mainly regulates autonomic function in response to head-up tilting. Thus, PTSD should damage autonomic modulation and also contribute to the pathogenesis of PTSD symptoms. In addition, it is possible link to increased cardiovascular disease in PTSD.

Declaration of interest statements

All the authors have no conflict of interest.

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