Chapter 17
Cortical and Autonomic Stress Responses in Adults with High Versus Low Levels of Trait Anxiety: A Pilot Study

A. Brugnera, C. Zarbo, R. Adorni, A. Compare, and K. Sakatani

Abstract Stress responses are mediated by complex patterns of cortical and autonomic activity. Earlier studies showed increased recruitment of the right prefrontal cortex (PFC) and parasympathetic withdrawal during a stress task; however, it remains unclear whether these responses change in relation to different levels of psychopathological symptoms, such as trait anxiety. The present study examines the effect of a mathematical task (with a control condition and a stressful/experimental condition) on the PFC and autonomic activity, using a two-channel near infrared spectroscopy (NIRS) and an ECG monitoring system. After a preliminary screening of 65 subjects, a sample of 12 individuals (6 with the highest and 6 with the lowest scores on an anxiety questionnaire, i.e. the STAI trait) was selected. The two groups were similar regarding demographic variables (age, sex, body mass index) and baseline STAI-state scores. Repeated measures ANOVAs were used to compare changes from baseline in oxyhemoglobin (oxy-Hb), heart rate (HR) and root mean square of successive differences (RMSSD) between the two groups. Individuals affected by high levels of trait anxiety showed a reduced bilateral PFC activity during the entire experimental procedure compared to those with low anxiety. No differences in NIRS channels were found between the two groups. During both conditions, RMSSD was lower among individuals affected by high levels of anxious symptoms. Finally, throughout the procedure, changes in HR were higher in the anxious group. Overall, these findings suggest a reduced PFC activity and a larger parasympathetic withdrawal during a stress task in individuals with high levels of trait anxiety compared to those with low anxiety. These results could represent a starting point for future NIRS and ECG studies on the relationship between mental disorders and acute stress responses.

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1 Introduction

Stress response involves the activation of the central and autonomic systems, that are known to be interconnected by the central autonomic network (CAN) [1]. Through this network, several neuroendocrine, behavioral and visceromotor reactions are controlled by specific brain areas, such as the prefrontal cortex (PFC). During psychosocial stress, the PFC processes emotions and subjective feelings and regulates cardiac reactivity [1, 2].

Earlier NIRS studies in healthy individuals showed activation of the right PFC [3], increased heart rate (HR) and parasympathetic withdrawal [4] in response to stressors. However, few studies have focused on the psychophysiological stress responses of anxious persons. Takizawa et al. [5] reported a positive correlation between higher levels of trait anxiety and a greater decrease in deoxy-Hb in the frontopolar PFC during a stress task. Moreover, high levels of trait anxiety are associated with reduced vagal cardiac function [6], albeit that contradictory results have also been reported [7]. However, to our knowledge, no studies have explored the role of high and low levels of trait anxiety on both PFC and cardiovascular reactivity to acute stressors.

Investigating psychophysiological responses to stress is important as it has been suggested that persons with anxiety disorders have an impairment of the CAN [1]. Indeed, anxious individuals seem unable to manage threat detection, and this reduced cognitive efficiency can lead to endless states of worry and hypervigilance as well as reduced parasympathetic tone [1]. Moreover, anxious individuals experience deficits in working memory and executive functions, as well as a reduced processing and regulation of affective information [8]. This reduced cognitive efficiency is associated with prefrontal hypoactivity [8].

Therefore, this study investigated both prefrontal and cardiological responses to a psychosocial stressor in individuals with low and high levels of trait anxiety, as assessed by the State-Trait Anxiety Inventory (STAI) [9]. We tested the hyphothesis that, during a stress task, individuals with high levels of trait anxiety, compared to those with low levels, will show: (i) reduced vagal activity and increased HR, as proposed by Chalmers et al. [6], and (ii) reduced PFC activity, as suggested by Thayer et al. [8].

2 Methods

A total sample of 65 right-handed and healthy participants underwent extensive psychological testing as part of a larger experiment. All individuals completed the STAI [9], a 40-item self-report measure to assess both the presence and severity of

Table 17.1 Frequencies, means (SD) and their respective *t*-values and *p*-values of demographic and psychological variables by group

	Low anxiety (n = 6)	High anxiety (n = 6)	*t*-value	*p*-value
Sex (frequency)	3 men	3 men	/	0.99
Age (SD)	26.6 (5.6)	22.3 (2.1)	1.78	0.10
BMI (SD)	21.3 (3.3)	23 (4.5)	−0.76	0.54
STAI-Trait (SD)	30 (3.1)	58 (3.1)	−18.3	>0.001
STAI-State (SD)	31.5 (4.8)	37 (4)	−2.16	0.055

the usual propensity to be anxious (Trait scale) and current symptoms of anxiety (State scale). The total score for both scales ranges from 20 to 80, with higher total scores representing higher anxiety severity. Six individuals from the lowest quartile of the distribution of the trait anxiety scores, and six from the highest quartile of the trait anxiety scores, were recruited to participate in the present study, following the procedure suggested by Shapiro et al. [10]. The mean age of the 12 individuals was 24.5 (SD 4.6) years, and six of them were females (i.e. 3 per group). The mean body mass index (BMI) was 22.1 (SD 3.9). All 12 individuals were university students.

Demographic and psychological data of the two groups are reported (separately) in Table 17.1. None of the participants was affected by neurological, psychiatric or other medical (e.g. cardiologic) illnesses as assessed by means of a semi-structured interview.

This study was conducted in accordance with the ethical standards of the American Psychological Association (1992) for the treatment of human experimental volunteers. Each participant provided written consent in compliance with the Declaration of Helsinki (BMJ, 1991; 302:1194).

Participants were seated in a comfortable chair, in a silent room. During the psychophysiological recording they were instructed to avoid any movement of the body and to minimize those of the head. A 5-min rest period (baseline) was followed by completion of a randomized controlled stress task, i.e. the Montreal Imaging Stress Task [11], that is designed to evoke stress responses in the subjects. After a 2-min training phase, participants were randomized to start with a 5-min control condition or with a 5-min experimental (stressful) condition. All participants completed both conditions. Details on the entire procedure can be found in [11].

For measurement of changes in concentrations of oxy-Hb, de-oxy-Hb, and total-Hb in the PFC, a portable Bluetooth® CW-NIRS system was used (PocketNIRS Duo, DynaSense, Japan). This system uses light emitting diodes of three different wavelengths (735, 810, and 850 nm) as light source and one photodiode as a detector, and has two channels (one left and one right). The sampling rate was set to 10.2 Hz. Changes in concentration of hemoglobin are expressed in arbitrary units (a.u.). Optodes were fixed to the individual's forehead using adhesive patches. The NIRS montage replicated the one adopted by Tanida et al. [3]. For the present study, we focused on changes in oxy-Hb only. The signal was post-processed using a freely available MATLAB toolbox (N.A.P., NIRS Analysis Package).

For autonomic measurements we used the Pulse Sensor, a wearable Bluetooth® device (produced by STMicroelectronics and manufactured by MR&D, Italy), that continuously monitors heart activity. The device was positioned on the person's chest by means of an elastic band; the ECG of each individual was visually inspected in order to correct missing beats and artifacts. Time domain (i.e. root mean square of successive differences; RMSSD) analysis of HR variability was performed using a freely available MATLAB toolbox (Kubios HRV). RMSSD is a well-established index to evaluate parasympathetic activity.

Differences between demographic and psychological variables were assessed using independent samples t-tests, or Fisher's exact test. Regarding physiological data, for each task condition we analyzed changes in hemoglobin concentration, HR and RMSSD in relation to differences from the mean baseline value. The mean Δoxy-Hb, mean ΔHR and mean ΔRMSSD were subjected to repeated measures ANOVA. For Δoxy-Hb, the factors were Group (Low and High Trait Anxiety), Condition (Control and Experimental) and Channel (Left and Right). For ΔHR and ΔRMSSD, the factors were Group and Condition. Post-hoc analysis was performed using Tukey's test.

A p-value ≤ 0.05 was considered statistically significant. All analyses were performed with SPSS 23 (IBM, USA) and STATISTICA 12.5 (StatSoft Inc., USA).

3 Results

Preliminary data analysis showed that the RMSSD variables were positively skewed: a log transformation corrected the non-normality. Other variables were normally distributed. Because no differences in behavioral data (i.e. response times to MIST) were found between the two groups, these data are not reported. Table 17.1 shows that the two groups were similar with regard to demographic variables.

ANOVA performed on ΔHR showed an effect of the Group ($F1,10 = 5.92$; $p = 0.003$. Low Anxiety: M = 0.92, SE = 1.92; High Anxiety: M = 7.53, SE = 1.92). Other effects and interactions were not significant.

ANOVA performed on ΔRMSSD showed an effect of the Group ($F1,10 = 7.92$; $p = 0.02$. Low Anxiety: M = 0.11, SE = 0.09; High Anxiety: M = −0.21, SE = 0.09). Other effects and interactions were not significant.

Lastly, ANOVA performed on ΔOxy-Hb (Fig. 17.1) showed an effect of the Group ($F1,10 = 15.02$; $p = 0.003$. Low trait Anxiety: M = 0.051, SE = 0.0008; High trait Anxiety: M = 0.005, SE = 0.008) and an effect of the Condition ($F1,10 = 14.69$; $p = 0.003$. Control: M = 0.002, SE = 0.0006; Experimental: M = 0.004, SE = 0.007). Other effects and interactions were not significant.

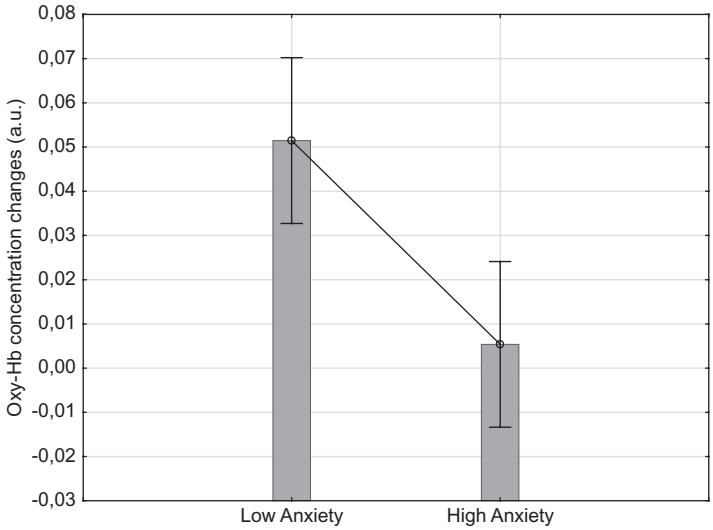

Fig. 17.1 Changes in oxy-Hb concentration in the two groups throughout the procedure. The overall cortical activity in both channels of the High Anxiety group was lower than that of the Low Anxiety group ($p = 0.003$). Vertical bars denote 0.95 confidence intervals

4 Discussion

In summary, these results showed significant cortical and cardiovascular differences between individuals with high and low levels of trait anxiety during the entire procedure (i.e. the cognitive and stressful conditions). Individuals with high trait anxiety compared to individuals with low trait anxiety, showed higher HR as well as reduced PFC activity and parasympathetic withdrawal.

For cortical response, the results show increased PFC activity in the experimental condition compared with the control condition, irrespective of the group; this is attributed to the fact that experimental condition was stressful and more cognitively challenging. The lack of right lateralization during the stressful condition does not allow to confirm earlier findings [3]. Moreover, our results show that individuals with a high level of trait anxiety were characterized by reduced PFC activity throughout the procedure. Probably, as reported by Thayer et al. [8], anxious individuals experience a reduced cognitive efficiency, which could lead to a generalized prefrontal hypoactivity.

Regarding autonomic responses, individuals with high levels of trait anxiety compared to those with low levels, experienced decreased RMSSD and increased HR during the entire procedure; this is partly in accordance with a previous meta-analysis [6].

These specific patterns of autonomic and cortical activity suggest that individuals with high levels of trait anxiety, even without a diagnosis of anxiety disorder, might be affected by a less efficient CAN activity when compared to those with low

levels. According to the CAN model, disrupted CAN activity results in reduced frontal activity that could lead, in turn, to exaggerated sympathetic responses and rigid behaviors (such as hypervigilance, defensiveness, and perseveration), which are typical of anxiety disorders [8]. Indeed, it is known that anxious individuals are characterized by cognitive deficits (i.e. in detecting and managing environmental stimuli) [8].

In conclusion, this is the first NIRS study to investigate both PFC and cardiovascular responses to psychosocial stress in individuals with different levels of trait anxiety but comparable with regard to demographic variables. Despite the limitations of this explorative study (i.e. small sample size, use of a 2-channel NIRS device) some important inferences can be drawn regarding cortical and autonomic changes, in both the cognitive and stressful conditions, in individuals with high anxiety traits. However, additional larger studies are required to further elucidate these findings.

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