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Cortical and cardiovascular responses to acute stressors and their relations with psychological distress

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ABSTRACT

The purpose of this study was to assess the interrelation between cortical, cardiovascular, behavioural, and psychological responses to acute stressors in a large sample of healthy individuals. To date, there are only preliminary evidences for a significant association among these psychophysiological indexes during a stress task.
65 participants completed psychological questionnaires (Beck Depression Inventory and State-Trait Anxiety Inventory) and underwent a psychosocial math stress task, consisting of a control and an experimental (i.e. stressful) condition. Prefrontal and autonomic activities were recorded using respectively a 2-channel near-infrared spectroscopy (NIRS) device and a portable ECG monitoring system.
Results evidenced an increased activation of both frontal areas assessed by NIRS, and a positive association between the right NIRS channel and heart rate changes from baseline, during both control and experimental conditions. Subjective stress increased during the procedure, reaching its maximum during the experimental condition. Behavioural performances during the task (e.g. response time) did not correlate with anxiety or depression. Autonomic data evidenced, as expected, an overall reduction of vagal tone during the experimental condition. Finally, severity of depressive and anxious symptoms predicted an increase in parasympathetic activity both at rest and during the task, even when controlling for respiration rate.
Results support the hypothesis of an integration between right sectors of frontopolar or dorsolateral PFC and cardiac regulation. Trait anxiety and depression predicted an increase in vagal tone during the entire procedure. The implication of these findings is discussed.

1. Introduction

Stress responses aim at maintaining the homeostasis of the organism in reaction to environmental stressors and preparing it to action (Carroll et al., 2012; Ulrich-Lai and Herman, 2009). Nevertheless, prolonged stress responses could lead to adverse medical conditions (e.g. hypertension) through several physiological mechanisms (Segerstrom and Miller, 2004). However, further studies are required to clarify the interrelation between physiological, behavioural and cognitive aspects of stress, which seem to be strictly related to state and trait psychological conditions.

From a general point of view, stress results in complex activation/deactivation patterns of various cerebral structures (Kogler et al., 2015) as well as to the activation of the Autonomic Nervous System (ANS) and of neuroendocrine systems, such as the hypothalamic–pituitary–adrenal axis (Ulrich-Lai and Herman, 2009). Among cortical structures, Prefrontal Cortex (PFC) seems one of the most implicated in stress responses (Brugnera et al., 2016; Doi et al., 2013; Kern et al., 2008; Kogler et al., 2015; Takizawa et al., 2014). Near-Infrared Spectroscopy (NIRS) is a recent non-invasive technology based on the properties of light; it allows assessing PFC activation patterns during a stress task in terms of concentration changes in cortical haemoglobin. Past NIRS studies suggested that stress is associated with an hyperactivation of right sectors of prefrontal cortex (Sakatani et al., 2010; Tanida et al., 2007; Tanida et al., 2004), even if some papers reported a general frontal activation (Takizawa et al., 2014; Yang et al., 2009).

It is well known that emotive, cognitive and affective information could be processed asymmetrically (Seghier, 2008). Indeed, differences among left and right hemispheres (e.g. during stress or affective tasks) has been widely reported in functional neuroimaging studies (Seghier, 2008): language, for example, is a widely recognized asymmetrical

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cognitive function (Benn et al., 2012; Seghier, 2008). The hemispheric dominance could be investigated using a measure called Laterality Index (LI), that is the index of the left or right asymmetry of PFC activity. This measure is particularly suitable to investigate prefrontal asymmetries using 2-channel NIRS devices (Tanida et al., 2004). For example, Tanida et al. (2004) using a Laterality Index found that individuals with higher HR increases had a large activity in right prefrontal cortex than in the left one, during a stress task.

Right prefrontal cortex, according to the so-called "approach-withdrawal hypothesis" of emotions processing (Brugnera et al., 2017), seems to have a key role in mediating withdrawal behaviours and negative emotions, as supposedly experienced during stress responses (Davidson et al., 1990). This hypothesis is supported by evidence that higher state anxiety is associated with higher right PFC activation (Ishikawa et al., 2014; Takizawa et al., 2014). However, few NIRS studies have investigated the role of psychological distress (e.g. depression or trait anxiety) on prefrontal cortex activity during a stress task. These relations, considering the negative effect of psychological distress (in particular anxiety) on attentional control and working memory system (Attentional Control Theory; Eysenck et al., 2007), deserve more attention. Preliminary evidence suggests that cognitive performance could also be reduced in individuals without psychological distress, in case of they show high stress responses or if they perceive the stressor as uncontrollable (Henderson et al., 2012).

Evidence suggests also a different hemispheric lateralization of systems that control the autonomic nervous system. Indeed, left hemisphere seems to regulate the parasympathetic activity of the autonomic nervous system (Wittling et al., 1998), while right hemisphere appears to be dominant in the control of the emotion processing (e.g. Heilman and Gilmore, 1998) and the sympathetic activity (Critchley et al., 2000; Heilman et al., 1978; Wittling and Genzel, 1995). For example, past NIRS studies showed that a right PFC activity was correlated with increased heart rates and parasympathetic withdrawal during stressful tasks (Sakatani et al., 2010; Tanida et al., 2007; Tanida et al., 2004). According to the model of neurovisceral integration (Thayer et al., 2009; Thayer and Lane, 2000), the central autonomic network (CAN) is a functionally integrated system through which specific brain areas (such as ventromedial PFC and amygdala) control visceromotor, neuroendocrine, and behavioural responses that are critical for goal-directed behaviours and adaptability (such as responses to stressful stimuli; Thayer et al., 2009). In addition to the main CAN areas, other anatomical regions selectively regulate one of the two branches of the autonomic nervous system, such as right dorsolateral PFC (Beissner et al., 2013). The final cerebral structure of the CAN is the brainstem, that directly regulates the heart rate as well the Heart Rate Variability (HRV; Thayer et al., 2009). HRV, the physiological phenomenon of variation in the beat-to-beat interval, is considered the principal index of central–peripheral neural feedback and of central-autonomic nervous system integration (Thayer and Lane, 2000).Specific analyses of Heart Rate Variability can provide useful information about the cardiac ANS modulation: for example, frequency domain analyses of fixed frequency bands of HRV (i.e. High Frequencies, HF) offer a direct index of parasympathetic (or vagal) activity over the cardiac tone (Task Force of the European Society of Cardiology, 1996).

It is well known that cognitive tasks, increases in task difficulty and in attentional demand strongly suppress the parasympathetic influences on the heart, thus leading to increased HR, decreased HRV and lowered High Frequencies (Hansen et al., 2003; Luft et al., 2009; Overbeek et al., 2014; Pendleton et al., 2016). Moreover, a recent meta-analysis has evidenced that stress responses alter ANS, leading to sympathetic activation and parasympathetic withdrawal (Castaldo et al., 2015). Castaldo et al. (2015) concluded that during stress tasks High Frequencies are significantly depressed.

High Frequencies seem also to be related to state and trait psychological conditions. High levels of psychological distress (i.e. state and trait anxiety; depression) are associated with reduced HRV both at rest and in response to stressors (Chalmers et al., 2014; Kemp et al., 2012; Kemp et al., 2010). These results are important because a lower overall HRV at rest is considered a maladaptive stress response which could constitute a risk factor for increased adverse cardiac events (Porges, 2007). The association between psychological distress and reduced Heart Rate Variability can also be interpreted taking into account the above mentioned model of neurovisceral integration (Thayer and Lane, 2000). Central autonomic network is impaired in distressed individuals and this impairment leads to a reduction of both parasympathetic tone and behavioural flexibility (Thayer et al., 2009). Indeed, distressed individuals are more likely to be worried and hypervigilant even when no real threat exists as well unable to disengage threat detection (Thayer et al., 2009). However, the debate about the link between psychological distress and stress responses is still open: few other studies have found, for example, a relationship between high levels of psychological distress and increased vagal tone or lower sympathetic activation during a stress task (Liang et al., 2015; Sanchez-Gonzalez et al., 2015; Shinba et al., 2008; Traina et al., 2011).These results could be explained taking into account the conservation-withdrawal pattern, considered the counterpart of fight-flight reactions (Buerki and Adler, 2005). To date, few studies found evidence of conservation-withdrawal pattern in humans (Bosch et al., 2001).

A critical aspect of the reviewed literature on responses to stress tasks, is the presence of a number of limitations: for example, NIRS literature is characterized by the lack of a control condition, the use of a single-gender sample, and usually small sample sizes.

This study aimed to address most of these gaps and clarify response patterns to psychosocial stress, integrating information from cortical (i.e. PFC), autonomic (i.e. HR and HRV), psychological (i.e. anxiety and depression) and behavioural data (i.e. performance to math task). In order to achieve these goals, we performed a study with a large sample of healthy individuals of both sexes, using a computerized and standardized procedure called Montreal Imaging Stress Task (MIST). MIST allows to administer both an experimental and a control condition, that are respectively with and without a social and time stressful pressures; during the procedure, individuals have to solve arithmetic operations. Cognitive performances could be collected on both conditions (Dedovic et al., 2005). Past literature has shown that MIST is a reliable protocol to induce physiological stress at CNS level (Kogler et al., 2015), even if ANS changes during this procedure have been underexamined. To the best of our knowledge, only 3 studies investigated vagal reactivity during this specific stress task, showing mixed results (Janka et al., 2015; La Marca et al., 2011; Monge et al., 2014).

Therefore, in this study we tested the hypotheses that (i) the procedure will be effective and will induce significant changes in perceived stress (as assessed by manipulation checks); (ii) the experimental condition (i.e. stress task) will lead to increased heart rates and parasympathetic withdrawal, as supported by the meta-analysis of Castaldo et al. (2015); (iii) the experimental condition will lead to increased activity of right PFC, as partly supported by previous NIRS studies (Sakatani et al., 2010; Tanida et al., 2007); (iv) ANS and PFC activity will be positively and significantly correlated, as suggested by the model of neurovisceral integration (Beissner et al., 2013; Thayer et al., 2009; Thayer and Lane, 2000); (v) psychological, cortical and performance outcomes will be significantly and positively correlated, as supported by the Attentional Control Theory (Eysenck et al., 2007) and previous studies (Takizawa et al., 2014); (vi) psychological distress (i.e. depression and trait anxiety) will have a negative predictive value on parasympathetic activity at rest, as supported by two previous meta-analyses (Chalmers et al., 2014; Kemp et al., 2010), and putatively during the entire procedure.

2. Material and methods

2.1. Participants

A total of 65 healthy participants (52.3% females) with a mean age of 24.7 years (SD = 3.9) volunteered for the experiment. Participants were