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Cerebral blood flow modulations during proactive control in chronic hypotension

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ABSTRACT

In addition to complaints including fatigue, mood disturbance, dizziness or cold limbs, chronic low blood pressure (hypotension) is associated with reduced cognitive performance. Deficiencies in cerebral blood flow regulation may contribute to this impairment. This study investigated cerebral blood flow modulations during proactive control in hypotension. Proactive control refers to cognitive processes during anticipation of a behaviourally relevant event that allow optimization of readiness to react. Using functional transcranial Doppler sonography, bilateral blood flow velocities in the middle cerebral arteries were recorded in 40 hypotensive and 40 normotensive participants during a precued Stroop task. Hypotensive participants exhibited smaller bilateral blood flow increases during response preparation and longer response time. The group differences in blood flow and response time did not vary by executive function load, i.e. congruent vs. incongruent trials. Over the total sample, the flow increase correlated negatively with response time in trials with a higher executive function load. The findings indicate reduced cerebral blood flow adjustment during both the basic and more complex requirements of proactive control in hypotension. They also suggest a general deficit in attentional function and processing speed due to low blood pressure and cerebral hemodynamic dysregulations rather than particular impairments in executive functions.

1. Introduction

Chronic hypotension refers to a persistent state of low blood pressure independent of the occurrence of other pathological conditions (De Buyzere, Clement, & Duprez, 1998). Associated complaints include fatigue, reduced drive, impaired mood, dizziness, and cold limbs (Duschek, Hoffmann, & Reyes del Paso, 2017a; Pilgrim, 1994; Rosengren, Tibblin, & Wilhelmsen, 1993). According to WHO (1978) criteria, hypotension is diagnosed when systolic blood pressure falls below 100 mmHg in women and 110 mmHg in men. The prevalence of this condition has been estimated at 2–3% in the general population, with younger women being especially affected (Duschek & Schandry, 2004). Abnormalities in autonomic cardiovascular control have been well-established in chronic hypotension, suggesting involvement of autonomic nervous system dysregulations in its etiology (Covassin, Zambotti, Cellini, Sarlo, & Stegagno, 2013; Duschek, Dietel, & Schandry, 2008).

In addition to bodily symptoms and mood disturbance, there is evidence of cognitive impairment in chronic hypotension. Various studies have documented prolonged simple reaction times (Duschek & Schandry, 2004; Duschek, Meinhardt, & Schandry, 2006), as well as deficits in attentional functions such as tonic and phasic alertness or selective, divided and sustained attention (Duschek, Matthias, & Schandry, 2005; Costa, Stegagno, Schandry, & Bitti, 1998). Memory impairment has been suggested by lower recall performance of verbal material (Costa et al., 1998). In contrast, higher cognitive domains, i.e. executive functions, have barely been investigated in hypotension. Moreover, the available studies revealed mixed results. While one study documented reduced task switching ability (Weisz, Schandry, Jacobs, Mialet, & Duschek, 2002), both positive and negative results were seen for working memory updating (Duschek et al., 2005; Duschek, Hoffmann, Reyes del Paso, & Ettinger, 2017b; Sarlo, de Zambotti, Gallicchio, Devigili, & Stegagno, 2013). Further studies failed to find differences between individuals with low and normal blood pressure in performance on arithmetic tasks (Duschek & Schandry, 2006; Covassin et al., 2013).

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Disturbance in cerebral blood flow regulation has been considered to mediate cognitive impairments in chronic hypotension (Duschek & Schandry, 2004; Sarlo et al., 2013). Due to the close coupling of neural activity and brain metabolism, cerebral activation processes are accompanied by transient increases in cerebral blood flow (Iadecola, 2017). In hypotension, this mechanism may not be sufficient to ensure optimal perfusion. Research concerning this hypothesis has been conducted in the field of preparatory cognitive processing using a cued reaction time task (Duschek & Schandry, 2004). Paradigms of this type focus on the attentional function of phasic arousal, namely a short-term increase in attentional tone the anticipation of a significant event (Johnson & Proctor, 2004; Posner & Rafal, 1987). Using functional transcranial Doppler sonography (fTCD), blood flow modulations in the middle cerebral arteries (MCA) of both hemispheres were recorded during the task. A right-dominant blood flow increase was seen, which was far smaller in individuals with hypotension than in those with blood pressure in the normal range. This has been interpreted as indicative of insufficient adjustment of brain perfusion to cognitive demands. Moreover, longer response times arose in hypotensive individuals, as well as a positive correlation between reaction speed and the magnitude of blood flow increase, which underlines the significance of hemodynamic adjustment in task performance (Duschek, Schuepbach, & Schandry, 2008; Duschek, Heiss, Schmidt, Werner, & Schuepbach, 2010).

Though phasic alertness such as addressed by cued reaction time tasks is doubtlessly crucial in everyday life, it is important to note that response preparation commonly involves more complex cognitive processes. These processes have been conceptualized as proactive control and may include the maintenance of goal-relevant information, response selection or inhibition of inappropriate behavior (Aron, 2011; Braver, 2012; Connolly, Goodale, Menon, & Munoz, 2002). Complex preparatory processes and the psychophysiological mechanisms involved therein have not yet been investigated in chronic hypotension. To address this research gap, we studied cerebral blood flow modulations during preparation of responses in the Stroop task (MacLeod, 1991). In the Stroop task, the participant has to name the font color of different color words, while ignoring the word meaning. The font color may match the word meaning (congruent condition) or differ from word meaning (incongruent condition). During the incongruent condition, interference occurs between font color and word meaning, which is associated with increased cognitive load and longer response times. In the present study, a precued Stroop task was applied to study cerebral blood flow modulations during complex preparatory processes in chronic hypotension. In a Stroop task, proactive control especially implies interference anticipation and prevention (Manard, Francois, Phillips, Salmon, & Collette, 2017). Considering the required overriding of the dominant response of word reading, proactive inhibition is also likely to be involved, that is, control mechanisms preventing an inappropriate response from occurring in an anticipated situation (Ballanger, 2009).

Evidence from fMRI studies suggests that, on a neural level, proactive control is mainly represented in the lateral prefrontal cortex (Braver, 2012; Chambers, Garavan, & Bellgrove, 2009). In addition, precued tasks involve substantial load with respect to phasic alertness, which is associated with a network including the lateral prefrontal and inferior parietal cortex, in addition to the reticular formation (Paus et al., 1997). The previously documented deficiencies in cerebral blood flow adjustment during cognition in chronic hypotension may also emerge during complex preparatory processes, resulting in suboptimal task performance (Duschek & Schandry, 2004; Sarlo et al., 2013). In contrast to incongruent trials of the Stroop task, the preparation of congruent trials is widely restricted to basic attentional processing. As such, comparison between both types of trials allows evaluation as to the degree to which the expected differences between hypotensive and normotensive individuals in cerebral blood flow and performance vary according to task difficulty, as well as the involvement of executive functions. Though available knowledge about executive functions in hypotension is still scarce, as a working hypothesis, we predicted that both the reduction in cerebral blood flow adjustment and reaction speed are greater for incongruent trials, indicating reduced proactive control of interference.

In the study, fTCD was applied to measure blood flow velocities in the MCA of both cerebral hemispheres. This technique enables continuous recording at a high temporal resolution, which in turn allows analysis of distinct periods of the hemodynamic response (Duschek & Schandry, 2003; Schuepbach, Boeker, Duschek, & Hell, 2007; Schuepbach et al., 2009; c.f. Wecht et al., 2012 for application of fTCD during a Stroop paradigm). fTCD studies using precued tasks revealed biphasic courses of blood flow modulations, with the first component associated with response preparation and the second with response execution (Duschek & Schandry, 2004; Duschek, Heiss, Schmidt, Werner, & Schuepbach, 2010; Montoro et al., 2015). However, based on previous observations, we presently hypothesized that only the magnitude of the first component varies according to blood pressure and is linked to task performance (Duschek & Schandry, 2004; Duschek, Schuepbach, et al., 2008; Duschek et al., 2010; Montoro et al., 2015).

This study investigated cerebral blood flow modulations during proactive control in chronic hypotension. Cerebral blood flow modulations may be relevant as a mediator of the associations among cardiovascular regulation, neural activity and cognition, where cognitive impairments may be mediated by insufficient neural activation, associated with reduced blood flow adjustment (Duschek, Schuepbach, et al., 2008; Duschek et al., 2010). The following hypotheses were tested: (1) Individuals with chronic hypotension exhibit smaller bilateral MCA blood flow increases during the preparation of congruent and incongruent trials of the Stroop task than those with normal blood pressure. (2) Moreover, hypotensive participants show longer response times in both types of trials. (3) In the entire sample, the magnitude of the preparatory blood flow increase is positively associated with response speed. (4) Incongruent trials are associated with stronger MCA blood flow increases during response preparation and longer response times than congruent trials. (5) Finally, as a result of greater color word interference in hypotension, differences in the preparatory blood flow increase and response speed between both conditions are larger in hypotensive than in normotensive participants.

2. Methods

2.1. Participants

In total, 40 individuals with hypotension according to WHO criteria (WHO, 1978) and 40 normotensive control persons participated. The sample included five men (two in the hypotensive sample, three in the control group). Participants were recruited via e-mail distribution lists of the local universities that addressed students and their friends and families. Persons suffering from a relevant physical disease or mental disorder were excluded from participation. Health status was assessed by means of an anamnestic interview and a questionnaire covering diseases of the cardiovascular, respiratory, gastro-intestinal and urogenital systems, the thyroid and liver, and metabolic diseases and psychiatric disorders. In addition, none of the participants used any kind of medication affecting the cardiovascular or central/peripheral nervous system. In both groups, 34 participants were university students; the remaining participants were in the workforce. Seventy-six participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) (38 in both groups); 17 participants were smokers (six in the hypotensive group, 11 in the control group). Table 1 provides information about age, body mass index (BMI), extent of education, physical activity, and blood pressure and heart rate (as recorded at the beginning of the experimental procedure).