International Journal of Psychophysiology 75 (2010) 54–62

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Rate of cardiovascular recovery to combined or separate orthostatic and mental challenges

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ARTICLE INFO

Article history:
Received 20 August 2009
Received in revised form 19 November 2009
Accepted 24 November 2009
Available online 3 December 2009

Keywords:
Mental arithmetic
Head up tilt
Cardiovascular reactivity
Blood pressure
Heart rate
Sympathovagal balance
Hypertension

ABSTRACT

Post stress neurovascular responses induced by physical and mental stress are poorly understood. We investigated the time course of cardiovascular and autonomic recovery, induced by orthostatic and mental challenge, using passive head up tilt (HUT) and mental arithmetic (MA), respectively, when applied singly (MA, HUT) or in combination (MA + HUT). Fifteen healthy males participated in three protocols: HUT, MA and combined MA + HUT, with sessions randomized and 2 weeks apart. Post stress responses were studied in the first 10 min (early; cardiovascular only) and 30 min (late), in 2.5 min epochs. A detailed analysis of early period was done in 30 s epochs. Within the first 2.5 min recovery, time courses of heart rate, stroke volume and cardiac output differed significantly, particularly when comparing HUT vs. MA and MA + HUT vs. MA. Additionally, heart rate response differed in HUT vs. MA + HUT. No differences in hemodynamic recovery were seen during the next 2.5 min. Late responses of heart rate and cardiac output showed significantly lower values as compared to baseline, especially for HUT and MA + HUT. Recovery of hemodynamic responses, either due to single or combined stress challenges, showed stressor- and time-dependent patterns. Our data provide useful information regarding why longer recovery periods must be assessed and provide novel insights regarding recovery of physical and mental stressors. This may have clinical implications in the development of cardiovascular diseases such as hypertension or myocardial ischemia.

1. Introduction

In recent years, physiological recovery after stressors has gained recognition as a decisive element in theories that explain the link between stress and disease, specifically cardiovascular disease (e.g. Pieper, 2005 #1930}). Nevertheless, as opposed to the conventional reactivity hypothesis that emphasizes responses during stressors (Lovallo and Gerin, 2003), to date only a small proportion of research has explicitly addressed the issue of recovery (Chida and Hamer, 2008; Linden et al., 1997; Papousek et al., in press; Pieper and Brosschot, 2005). Among other things, this may be due to the fact that relatively little is known about the behavior of different physiological variables after termination of a stressor (Linden et al., 1997). For instance, little detailed information regarding different time courses of physiological variables is available to date, and it has not been investigated in detail whether recovery of cardiovascular and hypothalamic pituitary adrenal (HPA) activities might not only differ in duration, but also in their time courses during the first few minutes. In addition, as the regulation mechanisms during psychological stressors are fundamentally different from those during physical stressors (Berntson et al., 1994; Cacioppo et al., 1994; Lovallo, 1997; Sawchenko et al., 2000), their time-dependent behavior during recovery, too, may differ. Moreover, many people are subjected to combinations of physical and psychological stress in their working lives (e.g., Corneil et al., 1999). The combination of stressors has not been well examined, yet. While there are some studies on reactivity to combined stressors (Durocher et al., 2009; Webb et al., 2008), detailed analysis of the pattern of recovery has been rare to date.

Recovery of physical stress induced responses, particularly following exercise, has been documented (Freeman et al., 2006). The recovery of neurovascular responses following orthostatic stress, however, has been sparsely reported. Knowledge of typical time courses is relevant, for instance, to the selection of appropriate time windows for the analysis of recovery processes. Thus, there seems to

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doi:10.1016/j.ijpsycho.2009.11.005

be a relative lack of basic research on the issue of physiological recovery altogether.

Although responses to acute stress in the laboratory are not of clinical importance in themselves, they may index the way that individuals respond to ordinary psychological demands in daily life, and accumulation of inadaptive responses may eventually have pathophysiological significance (Chida and Hamer, 2008). This was shown in prospective studies; late heart rate recovery, for instance, was associated with higher carotid atherosclerosis 2 years later (Heponiemi et al., 2007). Meta-analyses showed that dispositional negative affect, a well-recognized factor for the development of coronary artery disease (Frasure-Smith and Lesperance, 2005; Kubzansky et al., 2005), is associated with poor cardiovascular recovery, independently of reactivity (Chida and Hamer, 2008). Thus, inefficient recovery may eventually result in unfavorable physical sequelae. On the other hand, the observation of bradycardia below pre-stimulus levels after the removal of mental challenge (Callister et al., 1992) might also have cardiological implications, because myocardial infarction often occurs at low heart rates (Deanfield et al., 1984). In this connection, it seems relevant to also describe typical patterns of recovery in young and healthy individuals. We believe that the rate of recovery to these orthostatic and mental challenges may have practical implications, particularly in the treatment, prognosis and outcome of patients with cardiovascular diseases and myocardial ischemia.

The mechanisms of cardiovascular regulation have been reported to be different under orthostatic and mental stress. We hypothesized that a different pattern of early term recovery responses between these stressors, when done singly or in combination, would be seen. In addition, we hypothesized that cardiovascular responses would not return to baseline for prolonged periods following the stress applications and that the effects of these stressors would continue up to at least 30 min.

We investigated the time course of recovery of the cardiovascular (early and late) and autonomic (late) responses, induced by orthostatic and mental challenge, when applied singly or in combination. Participants were drawn from our previous study (Lackner et al., in press in which we studied *reactivity* responses to HUT, MA and MA + HUT. In this companion paper, we investigated the *recovery* responses, particularly as there is evidence that hemodynamic responses due to stressors (in other words, physiological mechanisms activated during stress) may not be the same as recovery patterns (Gregg et al., 1999). The responses analyzed include heart rate, stroke volume, cardiac output, blood pressures and autonomic activity. In most studies, recovery was followed for 5–10 min only (Boutcher et al., 2001; Gregg et al., 1999). Individual differences in recovery at more extended periods are probably even more relevant to possible health related effects than those very shortly after the stressor (Gregg et al., 1999). To our knowledge, only one study has examined the post stress responses for longer than 10 min (Steptoe et al., 2003). As considerable individual differences in cardiovascular recovery can be well expected until 10 min after termination of the stress situation (Key et al., 2008; Linden et al., 1997), we obtained measures of cardiovascular recovery for 30 min after termination of the stress.

2. Methodology

2.1. Participants

We focused on healthy men whose age and physical characteristics were homogeneous because gender, age and athletic training may affect orthostatic stress responses (Goswami et al., 2008). Participants abstained from coffee and other stimulants for 2 days before the test sessions, as well as unusual exercise activities in the week prior to the study. The study was carried out in 15 healthy, non-obese, non-smoking, non-medicated Caucasian men of moderate physical fitness, free from any somatic or mental condition (25 ± 3 years, 73 ± 7 kg, 180 ± 7 cm, supine resting heart rate 60 ± 6 bpm; mean $\pm$ SD). Each participant was paid 40 Euro per session.

Participants were familiarized with the test protocol and gave written informed consent to participate in the study. The study was approved by the Graz University Ethics Board and was performed in accordance with the 1989 WMA Declaration of Helsinki.

2.2. Study design

We used a symmetric, crossover within-subjects design and the participants were randomly allocated to each protocol. The participants served as their own control. We asked participants to abstain from coffee and other stimulants for 2 days before the test sessions.

Every day two participants did one of the three protocols (at 9–11 AM; 11 AM–1 PM). The protocols were randomized, open and separated by 2 weeks: a) head up tilt (HUT) alone, b) mental arithmetic (MA) in supine position and c) MA + HUT. Stress application was for 10 min in all the protocols.

The test was carried out in a semi-dark and quiet room, maintained at 24 °C and humidity at 55%.

2.3. Protocol HUT

The orthostatic challenge was provided for 10 min by HUT. A 30 min supine rest preceded each experiment. At minute zero, the tilt table was brought to 70° head-up position and after 10 min the table was returned to supine position. During the test participants were supported by an adjustable footrest and were instructed to avoid undue movements of the lower limbs and to breathe normally.

Since the aim of the experiment was to induce orthostatic stress without inducing syncope, the protocol was terminated if any of the following occurred (Goswami et al., 2009b): a) blood pressure fell below systolic 80 mm Hg, or that it dropped rapidly (systolic by $\geq$20 mm Hg/min and diastolic by $\geq$10 mm Hg/min), or heart rate dropped by $\geq$15 bpm; and b) lightheadedness, dizziness, visual disturbances, nausea, stomach awareness, clammy skin, excessive sweating, or skin pallor. However, all participants went through all the protocols with no problems.

2.4. Protocol Supine MA

MA was provided by mental arithmetic. Participants added or subtracted continuously the numbers 6 or 7, randomly, from a 2 or 3 digit number while lying supine. A new number was provided every 5 s to add or subtract from on a computer screen fixed at the eye of participants.

At the beginning of the selection process, participants were informed about the three protocols; however, participants were not notified in advance which protocol they would encounter on a given test day. During their first visit, the participants were familiarized with the laboratory, personnel and equipment. They received standardized verbal instructions about the protocol, tasks, and computer administered mental arithmetic at the beginning of the first session. Participants were told to solve the tasks as accurately and as fast as possible and that their answers were recorded. A timer applied additional pressure. Halfway through the mental arithmetic, they were asked to answer more correctly, irrespective of their correct answers. These procedures were designed to help reduce adaptation to the stress condition. No external feedback regarding performance during the mental arithmetic was provided during the study.

2.5. MA + HUT protocol

MA was started immediately upon assumption of the upright posture (HUT), and was ended when subject returned to supine position.