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## Does mental arithmetic before head up tilt have an effect on the orthostatic cardiovascular and hormonal responses?

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#### ABSTRACT

Passive head up tilt (HUT) and mental arithmetic (MA) are commonly used for providing mental and orthostatic challenges, respectively. In animal experiments, even a single exposure to a stressor has been shown to modify the response to subsequent stress stimulus. We investigated whether MA applied before HUT elicits synergistic responses in orthostatic heart rate (HR), cardiac output (CO), heart rate variability and arterial blood pressure. The 15 healthy young males were subjected to two randomized protocols: (a) HUT and (b) HUT preceded by MA, with sessions randomized and  $\geq 2$  weeks apart. Beat to beat continuous hemodynamic variables were measured and saliva samples taken for hormonal assay. HUT alone increased HR from  $59\pm 7$  (baseline) to  $80\pm 10$  bpm (mean $\pm SD$ ) and mean blood pressure (MBP) from  $88\pm 10$  to  $91\pm 14$  mmHg. HUT results after MA were not different from those with HUT alone. The activity of alpha amylase showed differences during the experiments irrespective of the protocols. We conclude that mental challenge does not affect orthostatic cardiovascular responses when applied before; the timing of mental loading seems to be critical if it is intended to alter cardiovascular responses to upright standing.

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#### 1. Introduction

A common physical stress to the human body is standing, which may lead to dizziness in normal persons. When a healthy person stands, there is 10–15% (approximately 600–700 ml) of the blood being redistributed to the legs. This leads to decreases in venous return (cardiac pre-load), cardiac filling pressure and output. With normal regulatory capability, arterial pressure at heart level remains unaltered or even is slightly increased. Passive head up tilt (HUT) is used regularly as an orthostatic loading tool.

The neurovascular responses to mental stress can take varied shapes: Mental challenge activates the sympathetic system, increases heart rate, cardiac output and blood pressure [1]. Mental arithmetic (MA) is applied routinely to provide mental challenge.

While central drive induced by mental challenge adds to physiologically mediated cardiovascular reflexes and affects orthostatic responses [30], are these changes present when additional mental loading is applied before orthostatic challenge? From animal experiments, it has been shown that even a single exposure to a stressor may modify the response to a subsequent stress stimulus [2,3]. For example, repeated exposure to some but not all stress stimuli may lead to a desensitization of responses to the primary persistent stress, but hyperresponsiveness to a novel stimulus [4,5]. We, therefore, hypothesized that

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mental challenge preceding HUT would also affect the orthostatic cardiovascular responses. This would have practical value since if this is right, it would imply that mental challenge could be applied in subjects even before they stand up, and the resulting cortical activation would improve the orthostatic cardiovascular responses upon standing up. We investigated this using HUT alone and HUT preceded by MA. Stress application was randomized and separated by two weeks.

#### 2. Materials and methods

#### 2.1. Participants

The study was carried out with healthy, non-obese, non-smoking, non-medicated men who were free from any somatic or mental condition. Because gender and age may affect orthostatic and stress responses (reviewed in [6]), we focused on young healthy men whose physical characteristics were homogeneous. The study criteria were met by 15 subjects of age  $27\pm5$  years, weight 74+8 kg and height 179+5 cm (mean+SD).

Subjects 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

The subjects served as their own controls. An online randomizer (http://www.randomizer.org/) was used to allocate the subjects to each protocol. We asked participants to abstain from coffee for 2 days before the test sessions. Since there is an influence of salt intake on baroreceptor sensitivity and because the person's volume status influences hormonal basal levels as well as responses to orthostatic stress [7], test persons were asked not to change their fluid and salt intake as governed by their usual dietary habits.

To compensate for random and unavoidable climatic effects on the cardiovascular system, every day two subjects did either of the two protocols (at 9–11 AM; 11 AM–1 PM). The two protocols were randomized, open and separated by two weeks (Fig. 1): 10 min of HUT and 10 min of MA in supine position followed immediately by 10 min of HUT (HUT preceded by MA). Part of the HUT alone data has been used in the study of Goswami et al. [30] to investigate interaction of mental and orthostatic challenges.

To remove any effects of intravenous cannulation on physiological responses [8], no invasive procedure was done. Saliva was sampled for cortisol and alpha amylase.

#### 2.2.1. Head up tilt (HUT)

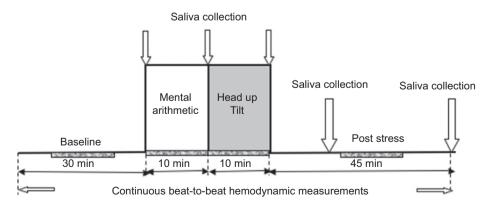
Each experiment was preceded by 30 min supine rest. At minute zero, the tilt table was brought to 70° HUT position and after 10 min, table was returned to supine position (Fig. 1). During the test, subjects were supported by an adjustable footrest, and were instructed to avoid undue movements of the lower limbs and to breathe normally. Test persons were secured and had access to an emergency shutdown (automatic return to supine position) at all times.

Since the aim of the experiment was to induce orthostatic stress without inducing syncope, criteria for termination included *any* of the following [9]: (a) blood pressure fell below systolic 80 mmHg, or that it dropped rapidly (systolic (SBP) by  $\geq 20$  mmHg/min, diastolic (DBP) by  $\geq 10$  mmHg/min), or heart rate dropped by  $\geq 15$  bpm; (b) Lightheadedness, dizziness, visual disturbances, nausea, stomach awareness, clammy skin, excessive sweating, or skin pallor. These were the criteria of termination but all the subjects went through all the protocols with no problems.

The test was carried out in a semi-dark and quiet room, maintained at 24 °C and humidity at 55%, using the Automatized Human Multi-Stimulation Test Device [9].

#### 2.2.2. Mental arithmetic

MA was administered by a method similar to that used by Carter and colleagues [1]. Subjects subtracted continuously the numbers 6 or 7, randomly, from a 2 or 3 digit



**Fig. 1.** MA was applied before HUT. Saliva collection was done (a) prior to MA and HUT (sample 1), (b) after finishing MA and/or HUT (sample 2) and at 15 (sample 3) and 45 min (sample 4) after termination of challenges. Rectangular hatched areas represent durations (10 min each) during which data were analyzed.

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