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Time course and mechanisms of hemoconcentration in response to mental stress

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Abstract

Hemoconcentration with mental stress exposure may be involved in the triggering of acute cardiovascular events. In the present study, hematocrit was measured repeatedly at baseline, during a 4 min mental stress task and during 20 min of recovery. Blood was sampled every 1–2 min throughout. Blood pressure, heart rate and R-wave to pulse interval, a measure of cardiac contractility, were measured with the same periodicity. The stress task elicited a 1.3% increase in hematocrit, which was sustained with full return to baseline level occurring only after 16 min of recovery. Between-subject correlations between hematocrit and hemodynamic activity were low. Aggregate within-subject coefficients were more impressive; the temporal profile of hematocrit correlated significantly with all hemodynamic variables. Similar within-subject analyses indicated that whereas cardiac contractility was correlated with hematocrit both during stress-related increase and subsequent recovery, blood pressure was related to hematocrit only during the increase. This suggests that stress-induced hemoconcentration may driven by different mechanisms than those which underlie its recovery.

Keywords: Blood pressure; Heart rate; Hematocrit; Hemoconcentration; Mental stress; R-wave to pulse interval; Recovery

1. Introduction

Acute cardiovascular events are a major cause of death (American Heart Association, 2005; European Cardiovascular Disease Statistics, 2005). Survivors of such events frequently identify mental stress as a precipitating factor (Smith and Little, 1992; Tofler et al., 1990). In addition, increased mortality from and/or hospital admissions for acute cardiovascular events have been observed following various environmental stressors, such as earthquakes, terror attacks, and even disappointing outcomes of key soccer matches (Carroll et al., 2002; Kario et al., 2003; Kario and Matsuo, 1995; Leor and Kloner, 1996; Meisel et al., 1991; Smith and Little, 1992; Tofler et al., 1990; Trichopoulos et al., 1983; Witte et al., 2000). Taken together, these studies support a previously proposed concept, which considers that psychological stress may induce physiological changes that can trigger acute cardiovascular events in vulnerable individuals (Muller et al., 1989).

It has been proposed that hemoconcentration, i.e. an increase in hematocrit or decrease in plasma volume, is one physiological change that may account for the link between mental stress and acute cardiovascular events (Allen and Patterson, 1995). Indeed, epidemiological studies have shown rheological variables, such as hematocrit and blood viscosity, to be associated with mortality from acute cardiovascular events, such as myocardial infarction and stroke (Lowe et al., 1997; Woodward et al., 2003). It must be recognized, however, that these studies were concerned with resting rheological status, rather than acute changes with stress exposure. As far as the authors are aware, only one study to date has examined the association between acute changes in hematocrit and cardiovascular events (Kario and Matsuo, 1995); the increased incidence of events following the Hanshin–Awaji earthquake was associated with an increase in hematocrit from 39%, measured 1–3 years prior to the earthquake, to 41% in the days following. However, it is unclear whether this increase in hematocrit was caused by the psychological impact of the earthquake or other factors, such as dehydration resulting from an interrupted water supply.

Nevertheless, laboratory studies have repeatedly demonstrated hemoconcentration with acute mental stress exposure

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(Bachen et al., 2002; Bacon et al., 2004; Jern et al., 1991; Muldoon et al., 1992, 1995; Patterson et al., 1993, 1995a, 1995b, 1998; Veldhuijzen van Zanten et al., 2002, 2004, 2005). However, most of these studies measured hemoconcentration infrequently and there are few data on the time course of mental stress-induced hemoconcentration. If such hemoconcentration constitutes a risk factor for cardiovascular events, it is important to understand its temporal dynamics. An exception here is a study employing a time course design in which blood was sampled every 2 min during a 10 min subtraction task with verbal harassment, and every 3 min during a subsequent 30 min recovery (Patterson et al., 1995b). During the stress task, plasma volume decreased substantially and recovery, defined as being no longer significantly different from baseline, occurred 12 min post task. Thus, a brief stress exposure elicited a sustained reduction in plasma volume. Given the potential clinical significance of such protracted change, replication is warranted.

The underlying mechanisms of stress-induced hemoconcentration remain to be fully elucidated. It is currently believed that such hemoconcentration is a function of increases in arterial pressure that drive increases in capillary pressure (Patterson et al., 1993, 1995a, 1995b, 1998). Capillary pressure is one of the Starling forces that regulate fluid flux along the capillary wall and an increase in capillary pressure, unless matched by changes in its opposing forces, would lead to increased fluid flux out of the inter-vascular compartment into the interstitial space (Starling, 1896), leaving hemoconcentrated blood. Between-subject associations between stress-induced hemoconcentration and blood pressure reactivity have been reported in a number of studies (Patterson et al., 1995a, 1998; Veldhuijzen van Zanten et al., 2002, 2004, 2005). As yet, the within-subject association between hematocrit or plasma volume and blood pressure has been largely ignored. Only a time course approach permits analyses of within-subject as well as between-subject associations.

The present study, then, re-examined the time course of hematocrit during a 20 min baseline, a 4 min mental stress task and a 20 min recovery. Using within-subject analyses, temporal patterns of hematocrit were correlated with contemporary hemodynamic activity to provide a more sensitive test of the mechanisms underlying stress-induced hemoconcentration. It was hypothesized that the brief mental stress task would elicit a sustained increase in hematocrit and that the temporal patterning of hematocrit would be correlated with the temporal patterning of hemodynamic activity, particularly blood pressure.

2. Methods

2.1. Participants

Twenty male students with a mean age of 22.90 (S.D. = 3.21) years and body mass index of 24.04 (S.D. = 2.21) kg/m^2 gave informed consent and participated. None of the participants smoked or had a history of cardiovascular disease. They were asked to abstain from vigorous exercise and alcohol for 24 h, and from food and caffeine for 4 h, prior to testing. The study was approved by the research ethics committee.

2.2. Mental arithmetic stress

The mental arithmetic task was the paced auditory serial addition test, in which participants were presented with a series of single digit numbers and required in each case to add each number to the number presented next. Thus, they not only had to perform simple addition, but also had to retain the latter of two numbers presented in memory for subsequent addition to the next number presented (Gronwall, 1977; Ring et al., 2002). For 4 min, numbers were delivered using an audio tape player and participants had to call out their answers. The presentation rate was 24 digits/min for the first 2 min and 30 digits/min for the last 2 min. While the participants were performing the mental arithmetic task, they were recorded with a video camera. This camera was attached to a television, and the participants were asked to look at themselves on the screen while performing the task. The participants were also informed that the tape would be analysed by two senior academics from the department to look at body and facial composure during the task. In reality, no such analysis was undertaken. Percentage of correct answers was used as an objective measure of performance.

2.3. Hemodynamic measures

An oscillometric monitor (Dinamap Compact T, Critikon) measured systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg) and mean arterial blood pressure (MAP, mmHg) using a cuff around the left ankle (Block and Schulte, 1996). A peripheral pulse was measured using an infra-red photoplethysmograph (1020EC, UFI) attached to the right ear lobe and an electrocardiogram measured using surface electrodes (Invisatrace, Conmed) in a chest configuration and a Grass amplifier. Signals were recorded continuously at 2000 Hz. The cardiac interbeat interval was determined from successive R-waves, and used to calculate heart rate (HR, bpm). R-wave to pulse interval (RPI, ms), an index of cardiac contractility (Obrist, 1981), was calculated as the time between the R-wave and the foot of the systolic upstroke of the ear pulse (Lane et al., 1983).

2.4. Blood sampling

At each blood draw, the first 2–3 ml of blood was discarded, and then a 2 ml sample was collected in a tube containing potassium ethylenediaminetetraacetic acid (EDTA K3E 7.5%, 0.04 ml, Vacutainer, BD) from a vein in the antecubital fossa, using an 18-gauge needle (Insyte, BD) and two-way valve (Posiflow, BD). The catheter was flushed with 3 ml isotonic saline after each blood draw, unless the time between draws was 1 min. For the measurement of hematocrit, the microhematocrit procedure was applied in duplicate; blood was drawn from EDTA tubes into non-heparinized capillary tubes and centrifuged for 5 min at 12,000 × g using a microhematocrit centrifuge (Hawksley). Hematocrit was determined using a microhematocrit reader (Hawksley). In addition, hematocrit was also measured using a Coulter® A^C·T diff™ Analyzer (Beckman Coulter Inc.).

2.5. Procedure

Participants completed a single 2 h session starting between 9:00 a.m. and 1:00 p.m.[1] On arrival at the laboratory, the procedure was explained and demographic information collected. Following the attachment of the electrodes, participants were requested to lie down on a tilt table and the cannula was inserted. An initial blood pressure measure was taken to familiarize participants with cuff inflation and deflation. After a 20 min baseline rest period (baseline) the task was explained and 10 practice trials were presented to make sure the participant understood the instructions. The 4 min mental arithmetic task (task) and the 20 min recovery followed without further interruptions. Blood pressure measurements were initiated and a 2 ml blood sample collected at the start of minutes 1, 3, 5, 7, 9, 11, 13, 15, 17, 18, 19 and 20 of baseline, minutes 1, 2, 3, and 4 of the task, and minutes 1, 2, 3, 4, 6, 8, 10, 12, 14, 16, 18, 20 of recovery. In addition, 4 ml of blood was obtained in a separate EDTA tube at minutes 11, 15 and 20 of baseline, minutes 3 and 4 of task and minutes 12, 16 and 20 of recovery (data not reported here).

[1] There were no time of day effects for hematocrit.