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Hemodynamic, hemostatic, and endothelial reactions to psychological and physical stress in coronary artery disease patients

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Abstract

Episodes of psychological and physical stress may elicit thrombotic cardiac events, such as myocardial infarction. These events are triggered when there are concurrent hemodynamic, hemostatic, and endothelial abnormalities. Hemodynamic, hemostatic, and endothelial reactions of 72 (15 women, 57 men) coronary artery disease patients to psychological and physical stress were examined. Blood pressure, electrocardiography, and impedance cardiography were recorded during rest, mental arithmetic, and exercise. Blood was collected, via catheter, at rest and after each task. Mental arithmetic elicited increases in blood pressure, heart rate, cardiac output, and cardiac contractility, but no consistent changes in hemostatic and endothelial markers. In contrast, exercise, in addition to increasing blood pressure, heart rate, cardiac output, cardiac contractility, and lowering peripheral resistance, elicited increases in plasma viscosity, hematocrit, platelets, and tissue plasminogen activator together with a decrease in plasminogen activator inhibitor. This pattern of hemodynamic, hemostatic, and endothelial reactions suggests that acute psychological and physical stress influence the thrombotic system differently in these high risk patients. Future research is needed to investigate how these stress responses are prospectively related to acute cardiac events.

Keywords: Endothelial; Exercise; Hemodynamic; Hemostatic; Mental arithmetic

1. Introduction

Coronary artery disease (CAD) is the leading cause of death in the Western world. One of the most significant events contributing to cardiac morbidity and mortality is a myocardial infarction (MI). A MI occurs when a clot (thrombus) occludes a coronary artery, decreasing blood flow to an area of the myocardium. For a thrombus to occur there must be a ''pro-thrombotic'' state in the artery, which involves concomitant disturbances in blood flow (hemodynamics), irregularities in blood constituents (hemostatics), and abnormalities of the vessel wall (endothelial dysfunction) (Lee and Lip, 2003b; Virchow, 1856). Therefore, an examination of these three components may be useful in elucidating the underlying mechanisms responsible for cardiac events.

Acute bouts of both physical and psychological stress have been shown to precipitate MI and ischemia in CAD patients (e.g., Brown, 1999; Gabbay et al., 1996; Tofler et al., 1990). However, caution has to be exercised in interpreting these results. Although patients may have engaged in such activities prior to MI, contingency is not a guarantee of causality. It is necessary to identify plausible pathways via which these kinds of acute events could trigger MIs. There is reasonable evidence which suggest that exercise triggers a pro-thrombotic state in patients with CAD or its risk factors (El-Sayed et al., 2000; Lee and Lip, 2003b). However, the evidence is less clear for mental stress. For example,

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psychological stress has been shown to induced disruptions in hemodynamic (e.g., Obrist, 1981), hemostatic (e.g., Broijersen et al., 1996; Grignani et al., 1992; Musumeci et al., 1987), and endothelial markers (e.g., Cardillo et al., 1998; Musumeci et al., 1987), while other have not found such perturbations (Broijersen et al., 1995; Gebara et al., 1996; Wallen et al., 1997). As disturbances in all three-component systems are thought to produce a pro-thrombotic state it is important to simultaneously study the effects of stress on this triad. However, at the same time, we know of no studies that have reported such data.

In order to elucidate the mechanisms underlying stress-induced thrombotic events, the present study examined the effects of exercise (submaximal cycling) and mental stress (mental arithmetic) on hemodynamic (blood pressure (BP), heart rate (HR), cardiac output (CO), and total peripheral resistance (TPR)), hemostatic (plasminogen activator inhibitor-1 (PAI-1), platelet factor 4 (PF4), and fibrinogen) and endothelial components (tissue plasminogen activator (tPA)) in patients with documented CAD. We hypothesized that both psychological and physical stress would induce a pro-thrombotic state via perturbation of the three-component systems.

2. Methods

2.1. Participants

Between January 1998 and April 2000, all patients admitted for elective cardiological angiography or percutaneous transluminal coronary angioplasty at City Hospital NHS Trust, Birmingham, UK, were eligible for inclusion in the study. Patients were excluded for the following reasons: MI or stroke in the last three months, currently on warfarin, renal or liver impairment, current active bleeding, and unable to speak or read English. There were no age or gender restrictions. Of the 170 eligible patients, 98 (59%) refused to participate. The remaining 72 (42%; 57 men, 15 women) gave written informed consent and constituted the effective study sample. The research protocol was approved by the local research ethics committee of City Hospital NHS Trust, Birmingham. All participants were tested a minimum of four weeks after either angiography or angioplasty. Participants continued normal medication regimes prior to testing.

2.2. Assessment of coronary artery disease severity

All angiograms and angioplasties were carried out by a senior cardiologist in the cardiology theatre at City Hospital. The coronary angiogram involved the routine examination of the left and right coronary arteries, in both the right anterior and left anterior oblique views (Hamsten et al., 1986). If necessary, additional views were taken to achieve the optimal overall view of the arteries. The presence of CAD was scored as the number of coronary arteries (0, 1, 2, or 3) classified as having at least one stenosis which was $\geq$50% across the vessel's lumen. This procedure was conducted blind of all other variables and data, and was scored by a senior cardiologist.

2.3. Stress testing procedure

Participants completed a single stress testing session in the Cardiovascular Psychophysiology Unit, City Hospital NHS Trust, Birmingham. On entry to the unit, the protocol was described, and the participant connected to the equipment. The protocol comprised the following: an initial formal 20-min rest period, the paced auditory serial addition task (PASAT), a second formal 20-min rest period, the exercise task, and a final 20-min formal rest period. During formal rest periods, participants were encouraged to relax. At the end of each formal rest period and task, a blood sample was collected and processed, which lasted approximately 5 min. In line with other similar studies (Goldberg et al., 1996; Jiang et al., 1996), exercise was performed last to minimize carryover effects since delayed recovery from exercise has been reported in other studies (Krum et al., 1991). Blood pressure measurements were initiated at the start of minutes 12, 15 and 18 of the formal rest periods, and at the start of minutes 2, 5 and 8 of the tasks. Impedance cardiography and electrocardiography were recorded during minutes 11–18 of the formal rest periods and throughout the tasks (minutes 1–8).

Using data obtained at the beginning of the study regarding the half-lives and mental stress induced values, in healthy participants, of tPA ($t_{1/2}$ = 6 min (Biessen et al., 1997; Lijnen and Collen, 1995)); average stress increase of 32% (Jern et al., 1989)), PAI-1 ($t_{1/2} < 10$ min (Loskutoff and Samad, 1998); average stress decrease of 9% (Jern et al., 1989)), and PF4 ($t_{1/2}$ = 3 min (Walz and Hung, 1985); average stress increase of 106% (Naesh et al., 1993; Patterson et al., 1995; Patterson et al., 1994; Wallen et al., 1997)), we estimated that a formal 20-min rest period would be long enough for any venipuncture or PASAT induced increases to return to baseline.

2.4. Mental arithmetic and exercise tasks

In the 8-min PASAT, participants were required to add two sequentially presented single-digit numbers, while retaining the latter of the two numbers in memory for subsequent addition to the next number presented (Gronwell, 1977). Numbers, ranging from 1 to 9, were delivered using a tape player (Sony CFS-E14L). Participants were instructed to add each number they heard to the immediately preceding number and to call out the answer. The experimenter sat in front of the participant and scored the responses. If performance broke down, participants were told to continue with the next digit presented. The task consisted of four 2-min series of 29, 34, 40, and 48 digits at