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Cortisol patterns and brachial artery reactivity in a high stress environment

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ABSTRACT

Chronic stress can result in frequent or persistent challenges of the hypothalamic-pituitary-adrenal (HPA) axis resulting in abnormal cortisol patterns and increased risk for cardiovascular disease (CVD). Police work is an environment replete with stress. The present article describes associations between cortisol, a biomarker of stress, and brachial artery flow mediated dilation (FMD) in police officers. A random sample stratified on gender ($n = 100$, 33% women) was generated from officers in a mid-sized urban department. Four salivary cortisol parameters were derived: after awakening, following a standardized high protein meal challenge, during the entire day, and after a dexamethasone suppression test. Continuous scan B-Mode ultrasound was used to measure percent change in brachial artery FMD following occlusion and release. Elevated cortisol secretion after awakening was significantly associated with impaired FMD in women, reflected by an inverse trend. Adjustment for age, smoking, and alcohol consumption did not appreciably alter this trend. A similar result was not evident among male officers. Responses of other cortisol challenges to the HPA axis were not associated with FMD. In conclusion, increased cortisol secretion after awakening was independently associated with impaired FMD in female police officers only, indicating a possible link between HPA axis stress response and subclinical CVD. However, because associations were not found with other cortisol parameters and were not evident in male officers, replication of these findings with a prospective study design may be warranted.

1. Introduction

Stress may be described as a biosocial process that places undue strain on persons resulting in psychological and biological changes which increase the risk for disease (Cohen et al., 1997). The hypothalamic-pituitary-adrenal (HPA) axis is central to the body's responses to stress and consequently is often a focal point in research concerning stress. The status of the HPA axis can be assessed by measurements of cortisol secretion using various challenge procedures (McEwen, 2000; Rosmond et al., 1998). A normal cortisol pattern may be described as having a high degree of variation, with a morning peak, an evening nadir, and an appropriate response to challenges. HPA dysregulation due to prolonged or extreme stress has been associated with inefficient turning on or shutting off of the cortisol response (McEwen and Seeman, 1999; McEwen, 2004). It has been suggested that abnormal cortisol patterns can result from frequent or persistent challenges of the HPA axis and constitute a major risk for disease including central obesity, insulin resistance, cardiovascular problems, hypertension, and depression (Chrousos, 1998; Haddy and Clover, 2001; McEwen, 1998).

Psychological stress has been associated with an increased risk of cardiovascular events (McEwen, 1998). However, the effect of stress and implications for cardiovascular risk are not well understood. Endothelial dysfunction is an important early stage in atherogenesis, and brachial artery flow mediated dilation (FMD) is endothelium-dependent (Widlansky et al., 2003). The physiology of FMD and methodologic guidelines for its measurement have been discussed (Adams et al., 1996; Corretti et al., 2002; Herrington et al., 2001). Brachial ultrasound measurements of arterial diameter are taken before and during a transient increase in blood flow. This increase in blood flow is caused by the inflation and subsequent release of a blood pressure cuff on the forearm. This procedure provides a noninvasive evaluation of brachial artery flow mediated vasodilation (FMD) (Corretti et al., 2002). Under these experimental conditions the FMD response is a marker for the endothelial response to flow induced shear stress which includes the release of nitric oxide (NO) leading to vasodilation. The magnitude of endothelial dysfunction in coronary arteries has been linked with the degree of coronary atherosclerosis detected by angiography (Zeiher et al., 1991). The presence of endothelial dysfunction has been associated with increased risk of cardiovascular disease (Verma et al., 2003). Although the underlying biologic mechanisms have not yet been established, HPA axis dysfunction and the associated cortisol dysregulation have been linked to endothelial

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dysfunction in two experimental studies in humans. In one study, endothelial dysfunction resulting from an acute mental stress challenge was prevented by blocking the production in cortisol with a pharmacological agent (Broadley et al., 2005). In a second study by Broadley et al. (2006), blocking cortisol production attenuated the endothelial dysfunction seen in patients with treated major depression. The ability of the HPA axis to respond to challenge may be compromised by chronic stress such as that experienced in a high stress occupation like policing.

Hans Selye (1984) recognized police work as highly stressful. Police work has been described as "civilian combat" (Violanti, 1996). Police officers face the distinct possibility of exposure to psychologically disturbing events in their work including shootings, physical assault, witnessing violence and familial abuse, handling dead bodies, and disaster scenes such as 9/11 or Hurricane Katrina in New Orleans (Paton and Smith, 1996). Although police officers are considered a healthy working population, notably higher mortality rates for cardiovascular disease (CVD) have been found in police cohorts when compared to the general population. CVD has occurred at a higher rate in policemen with fewer years of service, suggesting that work-related factors such as stress may play a part (Violanti et al., 1998). In one of the few large prospective studies of police officers, the Helsinki Police Study identified a number of independent risk factors for coronary heart disease (CHD) (Pyorala et al., 1998). A study of Iowa state police officers found that public safety officers had a higher probability of developing CHD than did the Framingham study population (Franke et al., 1997). Additional studies have found police to have higher rates for heart disease, homicide, and suicide (Forastiere et al., 1994; Dubrow et al., 1988; Quire and Bluont, 1990).

The Buffalo Cardio-Metabolic Occupational Police Stress (BCOPS) baseline study was conducted to establish a population-based sample designed to identify stress and subclinical cardiovascular biomarkers in police work (Violanti et al., 2006). The present article describes findings from the BCOPS study concerning associations between the stress biomarker cortisol and FMD in a sample of police officers.

2. Methods

2.1. Sample

The Buffalo, New York Police Department, an urban force of 934 officers at the time of data collection, was the selected sample site. A random sample stratified on gender ($n=100$) was generated from all police officers in the department using a computer-generated random number table. Female officers were oversampled (42 females, 58 males). No specific inclusion criteria were used for the study, other than the participant would be a sworn police officer and willing to participate in the study. One hundred percent of the originally selected sample participated in the study. None of the selected participants reported taking specific steroid medications. However, seven participants with the following conditions were excluded from brachial ultrasound measures: Raynaud's syndrome ($n=2$), prior myocardial infarction ($n=1$), cardiac pacemaker ($n=1$), hypertension ($n=1$), sprained wrist ($n=1$), and patient discomfort ($n=1$). In addition, participants must not have been taking blood thinners or high doses of aspirin. Among the remaining 93 participants, 12 additional brachial scans were not of sufficient quality to be read due to participant movement, recording problems and inaccessible artery position. In total, 81 participants had acceptable brachial scans for analysis. Additionally, the 12 officers with inadequate brachial scans in this present study were similar to the 81 officers with acceptable brachial scans with respect to demographic and lifestyle characteristics. Six additional subjects were excluded from analyses due to missing salivary cortisol data, leaving 75 participants with complete data on both brachial reactivity and cortisol measures. Demographic and lifestyle characteristics were not significantly different for the 75 participants and the 25 who were excluded or had missing values.

The Center for Preventive Medicine, State University of New York at Buffalo, School of Public Health and Health Professions, Buffalo, NY, served as the data collection site. All phases, testing, and reports of the study were approved by the State University of New York at Buffalo Internal Review Board and the National Institute for Occupational Safety and Health Human Subjects Review Board.

2.2. Measures

2.2.1. Salivary cortisol

Cortisol was measured in saliva samples. Although cortisol can feasibly be measured in blood, urine and saliva, its measurement in saliva has come to be preferred because the cortisol present is unbound thus providing the level of biologically active hormone and the small amounts present in saliva can be easily detected and quantified by immunoassay. Officers were provided with Salivettes (Sarstedt, USA), a commercially available collection device consisting of a dental roll and a centrifuge tube, for the collection of saliva samples. At the designated collection time, the officers removed the dental roll from the centrifuge tube and placed it in their mouth for approximately 2 min allowing for saturation of the roll. Once in the laboratory, the tube was centrifuged to provide a nonviscous saliva sample for assay; centrifuged samples are maintained at −20 °C until assayed for cortisol by a commercially available chemiluminescence immunoassay (IBL, Hamburg, Germany) at the Technical University of Dresden. All specimens collected had sufficient quantity and quality to conduct assays at each time point.

Four salivary cortisol parameters were measured in the present study. Table 1 provides the cortisol saliva testing schedule. The first measure involved cortisol response to awakening which normally increases rapidly within the first 30 min after awakening, remains elevated for at least 60 min, and then decreases. In chronic stress, this pattern may change, so that levels of cortisol are not elevated upon awakening, and/or are elevated yet fail to return to baseline within a period of several hours. Secondly, a standardized high protein meal challenge is administered at midday in the clinic. The meal challenge consisted of a baseline saliva sample followed by the high protein shake (55 g of protein) and four additional saliva samples at 15-min intervals thereafter (Rosmond and Bjorntorp, 2000). A third measure was diurnal (whole day) cortisol levels, obtained from saliva samples the next day after the clinic visit. The fourth measure was a dexamethasone suppression test (DST), obtained by self-administration of a 0.5-mg dexamethasone tablet taken at bedtime on day 2 after a saliva sample. One additional morning saliva sample was taken the following morning of the third day.

2.2.2. Brachial FMD

The use of ultrasound to measure endothelial function in the systemic arteries has become an important method for the detection of early arterial abnormalities (Kumiko et al., 2004). Brachial artery

Table 1
Timing of salivary cortisol sampling, BCOPS Pilot Study.

Cortisol sample number	Day	Approximate time	Cortisol sample characteristics
1	1	11:10 am	Baseline (prior to protein lunchtime challenge)
2	1	11:20–12:30	15 min after lunchtime challenge
3	1	11:20–12:30	30 min after lunchtime challenge
4	1	11:20–12:30	45 min after lunchtime challenge
5	1	11:20–12:30	60 min after lunchtime challenge
6	2	Awakening	First awakening sample
7	2	Awakening	15 min after awakening
8	2	Awakening	30 min after awakening
9	2	Awakening	45 min after awakening
10	2	Lunchtime	Immediately before eating midday meal
11	2	Dinnertime	Immediately before eating evening meal
12	2	Bedtime	Before bedtime and before taking dexamethasone tablet
13	3	Awakening	Post dexamethasone awakening sample