Delayed Blood Pressure Recovery After Psychological Stress Is Associated With Carotid Intima-Media Thickness
Whitehall Psychobiology Study

Andrew Steptoe, Ann E. Donald, Katie O’Donnell, Michael Marmot, John E. Deanfield

Objective—Delayed blood pressure (BP) recovery after psychological stress is associated with low socioeconomic status (SES) and prospectively with increases in clinic BP. We tested whether poststress BP recovery was related to carotid atherosclerosis.

Methods and Results—Psychophysiological stress testing was performed with a healthy subgroup of the Whitehall II epidemiological cohort, and recovery systolic BP was monitored 40 to 45 minutes after stressful behavioral tasks. Carotid ultrasound scanning was conducted on 136 men and women (aged 55.3 ± 2.7 years) 3 years after stress testing. Participants were divided into those whose systolic BP had returned to baseline in the recovery period (adequate recovery, n = 37), and those whose BP remained elevated (delayed recovery, n = 99). Systolic BP stress responses did not differ in the 2 groups. Carotid intima-media thickness (IMT) was associated with delayed recovery in lower SES (means 0.78 versus 0.65 mm) but not higher SES participants (means 0.75 versus 0.74 mm) after adjustment for age, gender, baseline systolic BP, and resting BP, smoking, body mass and fasting cholesterol at the time of ultrasound scanning (P = 0.010).

Conclusions—Variations in poststress recovery reflect dysfunction of biological regulatory processes, and may partly mediate psychosocial influences on cardiovascular disease. (Arterioscler Thromb Vasc Biol. 2006;26:2547-2551.)

Key Words: atherosclerosis ■ blood pressure ■ recovery ■ socioeconomic status ■ stress

Low socioeconomic status (SES) and psychosocial factors such as chronic work stress, social isolation, and depressed mood predict the development of coronary heart disease (CHD) in initially disease-free individuals.1,2 Associations are evident not only for clinical manifestations of CHD but also for subclinical disease markers such as carotid intima-media thickness (IMT).3–5 The pathways responsible are not fully understood, because effects persist after controlling statistically for standard risk factors. One possibility is that psychosocial adversity is associated with sympathoadrenal and neuroendocrine activation that promotes progression of atherosclerosis.6

Stress-related cardiovascular activation can be assessed by measuring responses to standardized behavioral challenges in the laboratory. Stress responses have 2 components, the magnitude of increase during stressful challenges (reactivity) and the rate of poststress recovery. Blood pressure (BP) stress reactivity has been positively associated with carotid atherosclerosis both cross-sectionally and longitudinally.7–10 The contribution of poststress recovery has not previously been evaluated. Delayed poststress BP recovery is more common in adults of lower than higher SES,11 is associated with psychosocial risk factors such as social isolation,12 and predicts increases in clinic BP prospectively.13,14 In this study, we tested the hypothesis that carotid IMT in middle-aged men and women without any manifest cardiovascular disease is greater in individuals showing delayed poststress BP recovery independently of any association with stress reactivity or with resting BP or lipid levels. We also assessed whether the relationship between poststress recovery and carotid IMT might be greater in lower SES individuals.

Materials and Methods

Participants
Data were collected in a follow-up to the psychobiology substudy of the Whitehall II study. The Whitehall II study involves 10 308 London-based civil servants originally recruited in 1985 to 1988 to investigate psychosocial, biological and demographic risk factors for CHD.15 The psychobiology substudy involved 228 volunteers (123 men, 105 women) who underwent psychophysiological stress testing in 1999 to 2000.11 Participants were of white European origin, aged 45 to 59 years, lived in the London area, in full-time work, and had no history or objective signs of CHD and no previous diagnosis or treatment for hypertension. Selection was stratified by grade of employment (as a marker of SES) to include higher and lower status participants. Carotid ultrasound scanning was performed on 141
Characteristics of the Study Population

<table>
<thead>
<tr>
<th></th>
<th>Adequate Systolic BP Recovery</th>
<th>Delayed Systolic BP Recovery</th>
<th>$P$ for Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men/Women</td>
<td>22/15</td>
<td>56/43</td>
<td>0.76</td>
</tr>
<tr>
<td>Age, y</td>
<td>52.5±3.2</td>
<td>52.3±2.5</td>
<td>0.71</td>
</tr>
<tr>
<td>Grade of employment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher</td>
<td>70.3%</td>
<td>74.7%</td>
<td>0.60</td>
</tr>
<tr>
<td>Lower</td>
<td>29.7%</td>
<td>25.3%</td>
<td></td>
</tr>
<tr>
<td>Educational attainment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>32.4%</td>
<td>48.4%</td>
<td>0.022</td>
</tr>
<tr>
<td>High school</td>
<td>14.7%</td>
<td>23.2%</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>52.9%</td>
<td>28.4%</td>
<td></td>
</tr>
<tr>
<td>Personal income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;£20 000</td>
<td>11.7%</td>
<td>20.0%</td>
<td>0.004</td>
</tr>
<tr>
<td>£20 000–35 000</td>
<td>35.0%</td>
<td>49.1%</td>
<td></td>
</tr>
<tr>
<td>&gt;£35 000</td>
<td>53.3%</td>
<td>30.9%</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress testing</td>
<td>25.1±3.5</td>
<td>25.5±3.6</td>
<td>0.53</td>
</tr>
<tr>
<td>Ultrasound scanning</td>
<td>25.1±3.6</td>
<td>25.6±3.9</td>
<td>0.49</td>
</tr>
<tr>
<td>Smoking, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress testing</td>
<td>5.4%</td>
<td>4.0%</td>
<td>0.73</td>
</tr>
<tr>
<td>Ultrasound scanning</td>
<td>5.4%</td>
<td>7.1%</td>
<td>0.73</td>
</tr>
<tr>
<td>GHQ cases, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>21.2%</td>
<td>21.1%</td>
<td>0.98</td>
</tr>
<tr>
<td>Mental health (SF36)</td>
<td>76.6±14.3</td>
<td>77.3±12.3</td>
<td>0.79</td>
</tr>
<tr>
<td>Systolic BP, mm Hg, ultrasound scanning</td>
<td>118.2±10.6</td>
<td>117.6±13.8</td>
<td>0.81</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg, ultrasound scanning</td>
<td>69.6±7.4</td>
<td>70.0±10.8</td>
<td>0.87</td>
</tr>
<tr>
<td>Fasting total cholesterol, mmol/L, ultrasound scanning</td>
<td>5.82±1.1</td>
<td>5.80±1.0</td>
<td>0.90</td>
</tr>
</tbody>
</table>

individuals 3 years after the psychophysiological stress testing (62% response rate). Of those not tested, 1 had died, 4 were lost to follow-up, 3 had withdrawn from the Whitehall II study, 9 had moved out of London, and 70 were unable or unwilling to undergo ultrasound scanning. There were no differences between participants and nonparticipants in terms of gender, age, grade of employment, body mass index (BMI), or the proportion of individuals who showed delayed poststress recovery, but smokers were less likely than nonsmokers to participate in ultrasound scanning ($P=0.011$). Four participants tested were taking antihypertensive medication at the time of carotid scanning and were excluded from analysis, and data were incomplete in another individual, leaving 79 men and 57 women aged 55.3±2.7 years. The characteristics of the study population are detailed in the Table.

Psychophysiological Stress Testing

Participants were tested either in the morning or afternoon in a light and temperature-controlled laboratory. They were instructed not to have drunk tea, coffee, or caffeinated beverages, or to have smoked for at least 2 hours before the study, and not have consumed alcohol or exercised on the evening before or on the day of testing. Blood pressure and heart rate were monitored continuously from the finger using a Portapres-2 device (Finapres Medical Systems, Amsterdam, Netherlands). After the insertion of a venous cannula for the periodic collection of blood samples (not described here), participants rested for 30 minutes. Blood pressure and heart rate were recorded for the last 5 minutes of this period (baseline trial). Two behavioral tasks were then administered in random order with a 5-minute inter-task interval. The tasks were a computerized color-word interference task and mirror tracing, both of which have been used extensively in cardiovascular stress research. Each task lasted for 5 minutes, during which BP and heart rate were recorded continuously. Participants rested quietly after tasks, reading, or watching wildlife videos, and poststress recovery was assessed with a 5 minutes recording made after 40 to 45 minutes. The study was approved by the UCL/UCLH Committee on the Ethics of Human Research.

Carotid Ultrasound Assessment

Ultrasound scanning was performed 3 years after psychophysiological stress testing using methods described previously. The right and left common carotid arteries were scanned with a 5- to 10-MHz probe (Alokia Prosoun 2000). The carotid bulb was identified, and longitudinal 2-dimensional ultrasonographic images of the common carotid artery 1 to 2 cm proximal to the carotid bulb were obtained. The optimal longitudinal image was acquired on the R-wave of the ECG, and continuously recorded on video tape for 5 seconds. Measurements of the posterior wall of the artery were made from stored images with electronic calipers. Carotid IMT was calculated as the distance between the first bright light (lumen-intima interface) and the leading edge of the second bright light (media-adventitia interface). The 3 maximum measures from the right carotid artery in 3 different frames, and the 3 maximum measures from the left common carotid artery in 3 different frames, were averaged. On a separate session performed within 2 weeks of carotid assessment, resting BP (mean of 3 values) and fasting cholesterol were measured.

Other Measures

Weight and height were measured both at the time of stress testing and ultrasound scanning, so that BMI could be calculated. We recorded educational attainment and income as additional measures of SES. The sample was divided into 3 categories of education: basic education, high school or equivalent, and college and above, and 3 categories of income: <£20 000, £20 000 to 35 000, and >£35 000. Mental health was assessed with 2 measures. The first was the General Health Questionnaire (GHQ), a screening instrument for psychiatric problems. The 30-item version was used with standard scoring, such that individuals with scores of 5 or more were defined as GHQ cases (psychological distress). Second, the mental health scale from the Short Form 36 (SF36) health status instrument was administered. This consists of 5 items, summed and scaled so that 100 represents the best and 0 the worst mental health.

Statistical Analysis

Delayed poststress BP recovery was taken to be failure of systolic BP to return to baseline or to fall below baseline 40 to 45 minutes poststress, as defined previously by our group. Comparisons were made between the 37 individuals with adequate recovery and 99 with delayed BP recovery. Repeated measures analysis variance was used to compare the BP and heart rate response profiles of the groups. The association between carotid IMT and BP recovery was analyzed after controlling for factors that might be potentially related to IMT, including gender, prestress baseline BP, and smoking.

Results

There were no differences between the delayed and adequate poststress recovery groups in age, grade of employment, BMI, or the proportion of men and women (Table). However, participants in the delayed recovery group tended to be of lower SES than the adequate recovery group in terms of educational attainment ($P=0.022$) and income ($P=0.004$).
Few participants were smokers, and this proportion did not differ between groups. Resting BP and fasting cholesterol measured at the time of ultrasound scanning did not differ in the delayed and adequate recovery groups.

Mean systolic BP increased from 113.9±12.1 mm Hg at baseline to 137.5±18.9 mm Hg during tasks, decreasing to 118.8±12.8 mm Hg 40 to 45 minutes poststress. The delayed and adequate recovery groups did not differ in baseline levels or in task reactions (mean increase of 24.5 and 21.0 mm Hg, respectively), but by the end of the recovery period, systolic BP had fallen by an average of 5.47±4.5 mm Hg below baseline in the adequate recovery group, while remaining 8.91±6.2 mm Hg above baseline in the delayed recovery group (P<0.001; Figure 1). Diastolic BP averaged 69.0±9.6, 82.9±11.5, and 73.6±11.0 mm Hg in the baseline, task and 40 to 45 minutes recovery periods, but task reactions and recovery values did not vary in relation to the systolic BP recovery grouping. Heart rate increased from 64.4±8.7 bpm at baseline to 71.4±10.2 during tasks, returning to 62.5±8.1×40 to 45 minutes poststress.

Carotid IMT averaged 0.74±0.12 mm, ranging from 0.50 to 1.07 mm. IMT did not differ between men and women, but was positively correlated with BMI (r=0.19), age (r=0.16), and systolic BP at follow-up (r=0.26). It was not related to smoking or total cholesterol either at the time of stress testing or ultrasound scanning. The association between carotid IMT and poststress systolic BP recovery is shown in Figure 2. The difference between adequate and delayed recovery groups was significant, with mean IMT levels of 0.76 versus 0.70 mm after adjustment for age, gender, prestress baseline systolic BP, and smoking, clinic BP, fasting total cholesterol and BMI at the time of ultrasound scanning (P=0.022). In addition, the recovery grouping by SES interaction was significant (P=0.010), because systolic BP recovery was related to IMT only in lower and not higher SES participants. Carotid IMT adjusted for covariates averaged 0.78 mm in the lower SES delayed recovery group, and 0.65 mm in the adequate recovery group. The association persisted after additional control for systolic BP during tasks (P=0.016), so was independent of stress reactivity.

Inspection of Figure 2 suggests that people in the lower SES/adequate recovery group had particularly low levels of carotid IMT. We tested whether this group was stress resilient by comparing it with the lower SES/delayed recovery and the higher SES/adequate recovery groups. There were no differences in demographic or clinical risk factors. However, the lower SES/adequate recovery group appeared to be psychologically very robust. None of the participants in the lower SES/adequate recovery group had GHQ scores above threshold for psychological distress compared with 20% of the lower SES/delayed recovery (P=0.046) and 29.6% of the higher SES/adequate recovery groups (P=0.012). Similarly, scores on the SF36 mental health scale averaged 81.6±7.1 in the lower SES/adequate recovery compared with 69.8±18.0 in the lower SES/delayed recovery group (P=0.02), and 73.1±17.2 in the higher SES/adequate recovery group (P=0.078); higher scores on this scale represent better mental health.

Carotid IMT was positively associated with systolic BP reactions to the color/word task after controlling for age, gender, and SES (P=0.038). However, this effect did not survive further adjustment for prestress baseline systolic BP and smoking, clinic BP, fasting total cholesterol and BMI at the time of ultrasound scanning. There was no relationship between carotid IMT and systolic BP reactivity to the mirror tracing task, diastolic BP task recovery or recovery, or heart rate reactivity or recovery.

**Discussion**

Exposure to psychological stress elicits acute cardiovascular and neuroendocrine activation, followed by return toward baseline levels after the challenges terminated. Slow poststress recovery is thought to be indicative of chronic allostatic load, or the failure of biological regulatory processes resulting from sustained or repeated challenges to the system over extended periods. Less effective poststress recovery may also be linked with perseverative cognitions and ruminative thoughts about task performance. Delayed poststress recovery has been associated with a positive family history of cardiovascular disease and increased BP levels over 3 to 5
distress.15 However, not all lower SES individuals develop mental health in the lower but not higher SES groups.

This is consistent with higher levels of stress resilience. If lower SES/adequate recovery subgroup had a more favorable mental health profile compared with others, and this is consistent with higher levels of stress resilience. If prompt BP recovery is characteristic of resilient individuals and has a stress-buffering effect, then it will be particularly relevant to people exposed to high levels of chronic life stress. As noted, lower SES groups typically experience greater life stress in relation to work and financial pressures, while having reduced social support. Higher SES groups have less chronic stress exposure, so this buffering resource is not mobilized. This may be the reason why prompt BP recovery was associated both with greater carotid IMT and better mental health in the lower but not higher SES groups.

An association between carotid IMT and BP stress reactivity during tasks has been detailed in three previous studies. Two reports from the Kuopio Ischemic Heart Disease study showed that exaggerated systolic BP responses to mental stress were related to carotid atherosclerosis cross-sectionally7 and prospectively over a 7-year period in middle aged men.10 Barnett et al8 reported a positive relationship between systolic BP stress reactivity and changes in carotid plaque area over a 2-year period in 136 cardiology outpatients and volunteers. A third study involving healthy postmenopausal women showed an association between IMT and pulse pressure but not systolic BP stress responses.9 None of these investigations included the extended poststress recovery period monitored here, or assessed associations with SES. However, Lynch et al27 analyzed another indicator of systolic BP stress reactivity, namely the BP increase that occurs in anticipation of physical exercise, and showed an association with carotid IMT that was greater in lower than higher SES participants.

There was a modest association between systolic BP reactivity to the color word task and carotid IMT in the present experiment, but the effect was not independent of the baseline BP, so was less robust than the recovery difference. The tasks administered in this study were only moderately stressful, and more intense challenge may be required to identify reactivity effects. The associations between systolic BP recovery and IMT were not duplicated in analyses of diastolic BP or heart rate. A similar pattern has previously been described for stress reactivity measures,10 and it would appear that systolic BP is a more reliable marker of psychobiological dysregulation. Carotid scanning was performed 3 years after psychophysiological stress testing, but because there were no IMT measures at the time of stress testing, our results cannot be interpreted as demonstrating prospective associations.

Acute emotional stress elicits a range of biological responses implicated in atherogenesis, including increased lipid levels, endothelial dysfunction, inflammatory cytokine release, and hemostatic responses.28–30 Individual differences in poststress recovery may be associated with heightened or prolonged activation of these processes.12 Our results that suggest that one of pathways through which stress-related factors influence the development of CHD is through disturbances of homeostatic regulation leading to delayed or ineffective poststress recovery of cardiovascular function.

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Disclosures
None.

References
5. Haas DC, Davidson KW, Schwartz DJ, Essickmann N, Roman MJ, Pickering TG, Gerin W, Schwartz JE. Depressive symptoms are indepen-
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