Work stress, socioeconomic status and neuroendocrine activation over the working day

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Abstract

Socioeconomic status (SES) differences in cardiovascular and metabolic disease risk may be mediated in part by differential activation of neuroendocrine pathways. We have previously found that salivary cortisol levels over the working day are greater in lower than higher SES men, but that cortisol output is greater in higher than lower SES women. This study investigated the role of work stress in generating these patterns, analysing cortisol output in relation to job demands and job control. Participants were 97 men and 84 woman from the Whitehall II cohort, London, UK, recruited from higher and lower grades of employment. Saliva samples were obtained on waking and 30 min later to assess the cortisol waking responses, and at two hourly intervals over a typical working day. Cortisol responses to waking were positively associated with high job demands, but this effect was attenuated by higher SES. In women but not men, cortisol levels over the remainder of the day were elevated in lower SES participants who experienced high job demands, but depressed in lower status women who reported low job demands. Job control did not influence cortisol responses to waking, but in men cortisol levels over the remainder of the day were inversely related to job control. These cortisol differences were independent of age, smoking status and time of waking up. Subjectively, the most stress was reported by higher SES individuals who experienced low job control. We conclude that work stress and SES are related differently to cortisol responses to waking and cortisol output over the day. Job control may partly mediate SES differences in cortisol in men, while job demands are more relevant for women. Analyses of psychobiological pathways must take account of variations in exposure to chronic stressors as well as differences in responsivity to stressors.

Keywords: Socioeconomic status; Cortisol; Work stress; Whitehall II study; UK

Introduction

The processes through which socioeconomic status (SES) influences health can be investigated at several levels, and important insights have been obtained from socio-cultural, economic, developmental, and behavioural studies. When the impact of SES on the development of cardiovascular and metabolic disease is considered, it is crucial to study the social-biological interface, and understand exactly how SES affects the biological factors involved in disease aetiology. Lower SES is associated with a range of biological risk factors, including adverse lipoprotein profiles, increased central obesity, impaired glucose tolerance, insulin resistance, raised levels of fibrinogen, abnormalities of cardiac rhythm, and procoagulant blood clotting profiles (Matthews, Kelsey, Meilahn, Kuller, & Wing, 1989; Brunner, 1997; Liao et al., 1997; Wamala et al., 1999). Unfortunately, the pathways through which lower SES causes these changes are still not well understood. Lifestyle factors contribute, but the social gradient in cardiovascular mortality and biological risk persists after smoking, lack of physical activity, alcohol consumption, and other health behaviours are taken into account (Lynch, Kaplan, Cohen, Tuomilehto, & Salonen, 1996; Wamala, Mittleman, Schenck-Gustafsson, &
Orth-Gomér, 1999; Steenland, Henley, & Thun, 2002). It has therefore been argued that low SES may activate psychobiological processes, or neuroendocrine, autonomic and immune responses that in turn promote atherogenesis and the development of high risk profiles (Steptoe & Marmot, 2002).

Psychobiological processes can be studied in laboratory settings by assessing physiological responses to stressful stimuli (Carroll, Davey Smith, Sheffield, Shipley, & Marmot, 1997; Steptoe et al., 2002). A limitation of laboratory studies is that only acute responses to brief stimuli are measured, and the way these translate into every day life conditions is uncertain (Turner et al., 1994). An alternative is to assess physiological function with repeated measurements during everyday life. This method allows biological responses to naturally occurring life experiences to be investigated. The measurement technique needs to be unobtrusive and non-invasive, or else it may interrupt normal patterns of behaviour, disturbing the very processes that are being monitored (Costa, Steptoe, Cropley, & Griffith, 1999). At present, the measures that have been used most widely in psychobiological research are ambulatory blood pressure monitoring (Pickering, 1998), 24 h electrocardiography for assessing heart rate (Horsten, Mittleman, Wamala, Schenck-Gustafsson, & Orth-Gomér, 1999), and cortisol assays from saliva (Kirschbaum & Hellhammer, 2000). Cortisol is particularly interesting, since it is a key stress hormone involved in a range of pathologies including hypertension, insulin resistance, abdominal obesity, diabetes, impairment of immune function, infectious illness, and depressive disorder (McEwen et al., 1997; Walker et al., 1998; Goodyer, Park, Netherton, & Herbert, 2001).

This article describes the use of salivary cortisol to investigate psychobiological aspects of low SES. The hypothesis underlying this work is that cortisol secretion is heightened, or its diurnal rhythm is disrupted, in people in low socioeconomic positions, and that these disturbances contribute to increased cardiovascular and metabolic disease risk. The use of salivary cortisol to study SES has been relatively limited thus far. An early study in a large German adult sample showed that cortisol sampled at 7.00–8.00 a.m. was positively related to SES as defined by education or occupation (Brandstätter, Baltes-Götz, Kirschbaum, & Hellhammer, 1991). In contrast, an investigation of salivary cortisol in children aged 6–10 years found an inverse association with parental SES (Lupien, King, Meaney, & McEwen, 2000). We have recently completed a study involving a subsample of the Whitehall II epidemiological cohort recruited from different grades of employment. Cortisol was measured repeatedly over a working day, in the expectation that lower SES would be associated with chronic neuroendocrine activation (Steptoe et al., 2003). The results were only partly consistent with this hypothesis. In men, cortisol output over the day was greater in the lower SES (lower grade) participants, indicating chronic neuroendocrine activation. But in women, the reverse was true, with more cortisol in the higher SES group. These differences were not accounted for by age, smoking status, alcohol use, time of waking up, the stressfulness of the day, or hormone replacement therapy (in women).

What might be responsible for these sex differences in SES and cortisol? One possibility is that they relate to the experience of work stress in different socioeconomic groups. Two separate components of the cortisol profile over the day can be identified. The first is the waking response, defined as the change in cortisol over the first 30–60 min of the day. Most people show an increase in salivary cortisol peaking at about 30 min after waking, and this response is partly genetically determined (Wüst, Federenko, Hellhammer, & Kirschbaum, 2000). The second component is cortisol output across the day. Contrary to what might be expected, cortisol output over the day does not seem to be a consistent marker of work stress (Pollard, Ungpakorn, Harrison, & Parkes, 1996). On the other hand, the cortisol response to waking appears to be positively associated with chronic stress (Schulz, Kirschbaum, Pruessner, & Hellhammer, 1998; Wüst et al., 2000). For instance, Steptoe, Cropley, Griffith, and Kirschbaum (2000) found in a sample of school teachers that high job strain (high demands and low control) was associated with elevated cortisol at 8.00–8.30 a.m., but not at later times of the day.

The purpose of the present study was to discover whether differences in perceived job demands and perceived job control accounted in part for the SES differences in cortisol over the working day in the men and women of our Whitehall II sub-study. Separate analyses were carried out with job demands and job control, since in the Whitehall study it has been found that demands are greater in higher SES respondents, while control is less in lower SES groups (Bosma et al., 1997); combining the two in the construct of job strain (high demand/low control) would therefore confuse the phenomena. We also analysed the cortisol response to waking separately from cortisol over the remainder of the day, in case different associations emerges in the two situations. In addition to cortisol, we analysed subjective stress over the day, as it pertained to job demands, job control and SES.

Method

Participants

The participants in this study were 227 volunteers (121 men and 106 women) drawn from the Whitehall II cohort (Steptoe et al., 2003). They were recruited on the
following criteria: aged 45–58 years, based in the London area, not planning to retire in the next 3 years, and no history of cardiovascular disease. Women were not eligible if they were premenopausal. They were drawn from high (administrative and professional), intermediate (senior and higher executive officer), and low (clerical, office support) employment grades, and the response rate was 55%. Two hundred and five provided useable saliva samples for cortisol analysis. However, 24 were excluded as being non-compliant with the timing of waking samples on criteria detailed below. The remaining 181 individuals were divided for analysis into a higher SES category, composed of 70 men and 56 women from high and administrative grades, and 27 men and 28 women from clerical and office support grades classified as being of lower SES.

Cortisol sampling methods

Saliva samples were collected using cotton dental rolls held in the mouth until saturated, and then stored in Salivette tubes (Sarstedt, Leicester, UK). Participants were instructed to take 10 samples over a single working day, with measures on waking up, 30 min later, and then within eight 30-min time windows space at two hourly intervals through the day and evening (08.00–08.30, 10.00–10.30 … 22.00–22.30). Each sample was accompanied by an entry on a diary in which the participant reported the time, stress over the last 20 min on a 5-point scale (1 = no stress to 5 = high stress), and other ratings not analysed here. The time of waking up was also recorded. Tubes were returned to the investigators personally or by post, and cortisol was analysed using a biotin-streptavidin fluorescence immunoassay (Dressendörfer, Kirschbaum, Rohde, Stahl, & Strasburger, 1992).

Work stress measures

Job demands and control were assessed with measures developed for the Whitehall II study from the demand/control model (Karasek & Theorell, 1990), as described by Bosma et al. (1997). Four job demand items (e.g. ‘Do you have to work very intensively?’) and nine job control items were administered (e.g. ‘Do you have a choice in deciding how you do your work?’), each of which was rated on a 4-point scale ranging from 0 (often) to 3 (never/almost never). Scores were converted to a scale from 0 to 100, where 100 indicates maximum demands or control. The Cronbach \( \alpha \) for the scales in this study were 0.70 and 0.73 for demands and control at work.

Statistical analysis

Cortisol responses to waking can be erroneously measured if people fail to take the first sample immediately after waking. Since the rise is rapid, a delay in the first sample means that the “waking” sample is taken on this upward curve, and that the overall increase may be correspondingly reduced. Kudielka, Broderick, and Kirschbaum (2003) have recently used electronically tagged sampling tubes to show that a proportion of individuals do delay their sampling. Electronic tubes were not available in the present study, so compliance with the waking sampling protocol was judged by calculating the difference between the time participants stated they woke up, and the time they stated that the first saliva sample had been taken. Individuals with time differences of more than 10 min were excluded. Exclusions did not vary by sex or grade of employment.

Cortisol responses to waking were analysed by computing difference scores between waking and 30 min later. Cortisol over the remainder of the day was analysed by averaging the eight timed samples; individuals with any missing values were excluded. Subjective stress ratings were generally low, with few maximum ratings. Analysis was therefore carried out on the proportion of timed saliva samples that were accompanied by a rating of 3–5. The job demand and job control measures were divided into low and high categories on the basis of median split of the complete sample who took part in this psychobiology substudy. Because of ties and the exclusion of participants with missing data, this resulted in 37.1% of participants reporting high job demands and 62.9% with low job demands, and 53.2% with high job control and 46.8% with low job control.

Data were analysed using analysis of covariance, with SES, sex, and job demands or job control as between-subject factors. The covariates were age, smoking status, and time of waking up, since each of these has been shown in other studies to influence cortisol (Kirschbaum, Scherer, & Strasburger, 1994; Van Cauter, Leproult, & Kupfer, 1996; Edwards, Evans, Hucklebridge, & Clow, 2001). Data are presented as means ± standard deviation.

Results

The background characteristics of participants are summarised in Table 1. The lower SES group was slightly older on average \( F (1,177) = 8.36, p = 0.004 \), and the male were older than the female participants \( F (1,177) = 6.69, p = 0.01 \). The grade of employment groups did not differ in body mass index, waist-hip ratio, or in use of hormone replacement therapy. There were more smokers in the lower SES group. The higher SES group woke up an average 30 min later than the lower SES group \( F (1,168) = 16.7, p < 0.001 \), with no differences between men and women. As expected,
ratings of job demands and job control were greater in the higher SES group ($F(1,166)=23.0$ and $15.1$, respectively, $p<0.001$). Consequently, higher SES participants were overrepresented in the high job demand category, while the lower SES respondents dominated the low job control category. Men and women did not differ in job demands, but there were more higher SES women than men in the low job control category ($\chi^2=7.05, p=0.012$).

The mean level of cortisol on waking averaged $18.9 \pm 10.5 \text{nmol/l}$, increasing to $28.0 \pm 13.6 \text{nmol/l}$ 30 min later. The increase did not differ by SES or sex. As described previously, the average cortisol level over the rest of the day was greater in lower than higher SES men ($9.65 \pm 4.1$ vs. $7.52 \pm 2.8 \text{nmol/l}$) after adjustment for age, smoking status and time of waking. By contrast, adjusted cortisol levels in lower SES women averaged $6.53 \pm 2.0 \text{nmol/l}$, compared with $7.59 \pm 2.6 \text{nmol/l}$ in higher SES women (Steptoe et al., 2003).

### Job demands, SES, and cortisol

In the analysis of the cortisol waking response, there was a significant interaction between SES and job demands, controlling for age, smoking status and time of waking up ($F(1,151)=5.50, p=0.020$). This effect is illustrated in Fig. 1. The waking cortisol response was greatest in the lower SES participants who reported high job demands. High job demands did not have an impact on cortisol waking responses in the higher SES group. This SES effect was present both in men and women. Levels of cortisol on waking itself did not differ by SES, sex or job demand category, and adding the waking cortisol value to the analysis as a covariate did not alter the strength of the relationship between SES and job demands.

Job demands also influenced cortisol levels over the remainder of the day, but only in women. In women, there was an interaction between SES and job demands, after controlling for age, smoking, and time of waking up ($F(1,67)=5.29, p=0.025$). The highest average cortisol values over the day were produced by lower SES women with high job demands (Fig. 2). The cortisol levels in the lower SES women who did not report high job demands were less than those of higher SES women ($p=0.025$). Thus in both the analyses of waking cortisol responses and cortisol over the working day, high job demands appear particularly problematic to lower SES participants.

### Job control, SES, and cortisol

Low levels of job control had no impact on cortisol responses to waking in men or women. The mean increase from waking to 30 min later averaged 10.5 and 7.7 nmol/l in the low and high control categories, but the difference was not significant ($p=0.30$). However, over the remainder of the day, cortisol levels were inversely associated with job control in men ($F(1,75)=4.92$, ARTICLE IN PRESS

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Higher grade</th>
<th>Lower grade</th>
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<tbody>
<tr>
<td></td>
<td>Men ($n=70$)</td>
<td>Women ($n=56$)</td>
</tr>
<tr>
<td>Age</td>
<td>52.1 (2.7)</td>
<td>51.6 (2.5)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>25.5 (3.4)</td>
<td>25.7 (4.1)</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.903 (0.07)</td>
<td>0.804 (0.13)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4 (5.8%)</td>
<td>4 (7.1%)</td>
</tr>
<tr>
<td>Hormone replacement therapy (% women)</td>
<td>17 (30.4%)</td>
<td>6 (21.4%)</td>
</tr>
<tr>
<td>Time of waking up</td>
<td>06:30 (44)</td>
<td>06:30 (43)</td>
</tr>
<tr>
<td>Job demands</td>
<td>66.8 (18.0)</td>
<td>69.2 (17.8)</td>
</tr>
<tr>
<td>High job demand category</td>
<td>32 (48.5%)</td>
<td>24 (45.3%)</td>
</tr>
<tr>
<td>Job control</td>
<td>71.9 (11.7)</td>
<td>68.0 (16.4)</td>
</tr>
<tr>
<td>Low job control category</td>
<td>16 (21.2%)</td>
<td>23 (41.1%)</td>
</tr>
</tbody>
</table>
The results are illustrated in Fig. 3, where it can be seen that low job control was associated with elevated cortisol production throughout the day. This pattern did not vary with SES, and was not present among women.

**Stress ratings, work stress, and SES**

The final set of analyses concerned the proportion of cortisol samples over the day that were associated with perceived stress. Overall, 12.5% of cortisol samples were accompanied by perceived stress ratings of 3–5. Women reported more stress than men (18.0% vs. 6.6%), and stress ratings were more frequent among participants with high than low job demands (19.5% vs. 9.0%), and in those with low compared with high job control (16.0% vs. 8.2%). In addition, SES groups differed in their subjective experience of stress, depending on levels of job control ($F(1,153)=4.19$, $p=0.042$). This interaction was due to the greater stress levels reported by higher SES/low job control participants (Fig. 4). These individuals reported substantially more subjective stress than the remainder ($p<0.001$), while job control had no impact on the experience of stress in the lower SES group. The results of the analyses of stress ratings did not interact with sex, so were similar in men and women.

**Discussion**

This study set out to discover whether variations in work stress accounted for the differences in cortisol recorded over the working day in higher and lower SES men and women. Both the demand/control and effort-reward imbalance models of work stress have been related to cardiovascular disease risk in the Whitehall II cohort (Bosma et al., 1997; Bosma, Peter, Siegrist, & Marmot, 1998). Effort–reward imbalance was not measured in the study group at the time of cortisol monitoring, so the analyses were restricted to job demands and job control. High demands, low control and their combination have been associated with coronary heart disease in case-control and longitudinal studies from many countries (Schnall, Landsbergis, & Baker, 1994; Belkic et al., 2000). In the Whitehall II study, low job control but not demands were associated prospectively with self-reported and physician diagnosed coronary heart disease independently of standard risk factors and grade of employment (Bosma et al., 1997). However, Marmot, Bosma, Hemingway, Brunner, and Stansfeld (1997) demonstrated that the excess coronary heart disease rates in lower SES groups were substantially reduced when job control was taken into account, suggesting that work stress factors contribute to SES variations in health outcome. We therefore reasoned that job demands and job control might mediate SES variations in cortisol secretion.

We separated out cortisol responses to waking from cortisol output for the remainder of the day. Cortisol responses to waking are individually timed according to the pattern of waking, while output over the day is measured through sampling at fixed times of day. The
justification for this division is that different factors might influence the two phenomena. A twin study has indicated that the cortisol response to waking is partly under genetic control, while levels over the remainder of the day are not (Wüst et al., 2000). Mineralocorticoid receptors in the central nervous system seem responsible for the regulation of circadian rhythms of hypothalamic-pituitary-adrenocortical activity, while glucocorticoid receptors mediate responses to stress and other perturbations (De Kloet, Vreugdenhil, Oitzl, & Joels, 1998). Cortisol responses to waking have only inconsistently been associated with levels over the rest of the day (Schmidt-Reinwald et al., 1999; Edwards et al., 2001). Chronic stressors such as long-term unemployment have little effect on cortisol over the day, although negative mood and transient perceived stress raise cortisol levels (Ockenfels et al., 1995; Van Eck, Berkhof, Nicolson, & Sulon, 1996; Smyth et al., 1998). By contrast, chronic stressors of varying types appear to increase cortisol responses to waking (Schulz et al., 1998; Wüst et al., 2000). The data in this study confirm the value of analysing the two components separately, since different aspects of job stress had variable relationships with cortisol responses to waking and to cortisol levels over the day.

Cortisol responses to waking were affected by job demands but not job control. The impact of high job demands varied with SES, leading to greater waking responses only in lower SES participants (Fig. 1). The result is not due to differences in cortisol concentration on waking up, or to variations in time of waking, age, or smoking status. The impact of high job demands on cortisol responses to waking is consistent with previous literature concerning other forms of chronic stress. A new finding is that high SES appears to buffer the impact of job demands on cortisol responses. However, the effect did not lead to an overall difference in cortisol responses to waking between participants in higher and lower socioeconomic positions. The reason is that job demands were generally rated as greater in higher SES groups, so the proportion of lower SES participants experiencing high job demands was small in this sample (Table 1).

Job demands influenced cortisol over the remainder of the day, but only in women. The greatest cortisol output was recorded from lower SES women who experienced high job demands (Fig. 2). But it should be noted that only 16% of lower SES women were in the high job demand category, and lower SES women who did not report high job demands actually had diminished cortisol output compared with higher SES women. This factor might therefore have contributed to the greater cortisol output in higher than lower SES women outlined in the Introduction. It illustrates an important point concerning exposure as opposed to responsivity to life stress in relation to SES (Steptoe & Marmot, 2002). Although lower SES women were more responsive to job demands than higher SES women, their exposure to high job demands was infrequent. Eighty-four per cent of lower SES women did not experience high job demands, so the overall level of cortisol output over the day in lower SES women in general was low. When lower SES women do experience high job demands, the resulting elevation in cortisol may be compromising to health. An additional issue that was not addressed in this study is the contribution of non-paid work demands, which can be considerable among working women (Barnett & Hyde, 2001).

In contrast to women, the cortisol levels of men over the day were influenced by job control rather than job demands. As can be seen by Fig. 3, low job control was associated with elevated cortisol throughout the day. This is consistent with laboratory data showing that low control enhances cortisol stress responses (Breier et al., 1987), and with other findings linking low control with adverse physiological consequences (Steptoe, 1983). Low job control was more common in lower than higher SES men (51.9% vs. 21.2%). Consequently, low job control may be one of the factors contributing to the heightened cortisol levels of lower SES men that we have observed in this sample.

Job control also affected the amount of subjective stress reported by participants. As might be expected, more stress was experienced by people with high job demands and low job control, and stress ratings were also more common in women than men. But the analyses also revealed that higher SES participants who experienced low job control had particularly elevated levels of subjective stress over the working day (Fig. 4). Interestingly, women were twice as likely to fall into the high SES/low job control category than were men (Table 1). The subjective data therefore indicate that perceptions of low job control may be especially problematic for higher SES individuals (Stansfeld, Head, & Marmot, 1998).

Our study showed differences between subjective stress outcomes and cortisol responses. This is a typical finding in psychobiological research, since physiological responses and affective changes are only loosely coupled (Feldman et al., 1999). This means that subjective ratings cannot be employed as proxies for biological responses, and that objective measures are needed to document associations between psychosocial and biological outcomes.

The study was restricted to middle-aged working men and women. The sample was also limited in the range of socio-economic status positions, so that even the lower SES group worked predominantly in non-manual clerical jobs. The inclusion of a broader range of lower status occupations might have increased the proportion of low SES individuals who experienced high job demands. Cortisol responses were assessed over a single...
working day, so their generalisability is uncertain. Nevertheless, the results go some way towards explaining why patterns of cortisol output vary with SES in men and women. Men appear to be particularly vulnerable to the effects of low job control, while lower SES women are affected by high job demands. Higher SES buffers the impact of job demands on cortisol responses to waking. These findings indicate that frequency of exposure to work stress, as well as the magnitude of responses to work stress, is an important determinant of SES differences in psychobiological responses implicated in risk of chronic disease.

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References


