Socioeconomic Status and Stress-Related Biological Responses Over the Working Day

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Objectives: The influence of low socioeconomic status on cardiovascular disease may be mediated in part by sustained activation of stress-related autonomic and neuroendocrine processes. We hypothesized that low socioeconomic status would be associated with heightened ambulatory blood pressure and cortisol output over the working day. **Methods:** One hundred eight men and 94 women from the Whitehall II epidemiological cohort participated. Blood pressure and heart rate were monitored every 20 minutes over a working day and evening, and salivary cortisol was sampled on waking up and at 2-hour intervals. Measures were also taken under resting laboratory conditions. Socioeconomic status was indexed by grade of employment. **Results:** Resting blood pressure, heart rate, and cortisol did not differ by grade. Ambulatory systolic pressure was greater in the morning in the lower (128.9 ± 15.7 mm Hg) than the intermediate (122.6 ± 12.5 mm Hg) and higher grades (123.3 ± 12.7 mm Hg) after adjustment for age, sex, smoking, and alcohol intake ($p = .019$). Heart rate was also raised in the morning in the lower grade participants. Differences in morning systolic pressure and heart rate were independent of concurrent physical activity. Cortisol concentration was greater in lower than higher grade men (9.54 ± 4.1 vs. 7.38 ± 2.8 nmol/liter, $p = .008$) but was more elevated in higher than lower grade women (7.84 ± 2.5 vs. 6.35 ± 1.9 nmol/liter, $p = .014$). Differences remained significant after adjustment for age, time of awakening, smoking, and alcohol intake. **Conclusions:** Socioeconomic differences in blood pressure and cortisol may reflect stress-related activation of biological pathways that contribute to variations in disease risk. **Key words:** socioeconomic status, blood pressure, cortisol, ambulatory monitoring, stress, coronary heart disease.

BP = blood pressure; CHD = coronary heart disease; HR = heart rate; SES = socioeconomic status.

INTRODUCTION

There are marked SES inequalities in CHD throughout the western world (1, 2). The effect is graded, with a progressively higher incidence with lower SES as defined by occupational position, income, and education in men and women (3, 4). Lower SES is also associated with more advanced subclinical disease as evidenced by measures of carotid atherosclerosis (5) and aortic and coronary calcification (6, 7).

Lower SES is associated with a range of behavioral and biological risk factors, including cigarette smoking and sedentary lifestyle; increased incidence of diabetes; reduced high-density and raised low-density lipoprotein; increased central obesity, fibrinogen, and procoagulant profiles; and impaired glucose tolerance (8–12). The pathways through which lower SES elevates risk factors and increases incidence of CHD are not yet established. Lifestyle factors contribute, but the social gradient in CHD and in biological risk factors is still present after smoking, alcohol, physical activity, and other health habits are taken into account (13–15). It has been proposed that the experience of low social status elicits sustained activation of stress-related autonomic and neuroendocrine responses that in turn promote atherogenesis (16, 17).

Two methods are commonly used to investigate psychobiological pathways in disease: laboratory studies of acute biological stress reactivity and naturalistic monitoring of physiological functioning in everyday life. Naturalistic monitoring studies using ambulatory and other repeated-sampling methods allow the influence of everyday experience on biological processes related to disease risk to be evaluated. There have been comparatively few studies involving naturalistic monitoring of groups of adults systematically sampled on the basis of SES, although several post hoc analyses of study groups categorized on occupational or educational criteria have been reported (18–21). However, Matthews et al. (22) carried out ambulatory monitoring of BP and HR with 100 men and women occupying higher and lower status jobs in a university setting. No differences in systolic or diastolic BP were observed over the working day; HR was elevated in the lower SES groups, but only in participants who reported negative moods in diary ratings. Findings for salivary cortisol have been inconsistent. A study of more than 750 adults in Germany showed positive associations between cortisol sampled at 07:00 to 08:00 hours and SES defined by education or occupation (23). More recently the salivary cortisol of children aged 6 to 10

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years was found to be inversely associated with parental SES (24).

In the present study we carried out ambulatory monitoring of BP and HR together with repeated sampling of salivary cortisol over a working day in men and women of higher, intermediate, and lower SES as defined by occupational grade. Participants were members of the Whitehall II study, an epidemiological cohort of more than 10,000 civil servants first recruited in 1985 to 1988 (25). Psychosocial, behavioral, and biological risk factors for CHD have been extensively studied in this cohort using grade of employment as the index of SES (8, 25, 26). We hypothesized that systolic BP and HR would be elevated in lower SES participants and that the concentration of salivary cortisol would also be raised. We also hypothesized that the cortisol increase on awakening would be greater in lower SES participants because this response has previously been related to chronic stress (27, 28).

A number of methodological issues affect the interpretation of measures obtained in everyday life conditions. First, it is possible that any differences recorded using ambulatory methods might merely reflect tonic variations in biological activity between groups. For instance, because BP is typically higher in men than women, any sex differences observed during ambulatory monitoring would not demonstrate a differential response to everyday life experience. Accordingly SES groups were compared for BP, HR, and cortisol measured under resting conditions in the laboratory as well as over the working day. Second, ambulatory BP and HR are markedly influenced by physical activity (29), and lower SES individuals may be more be more active at work. The present sample was restricted to nonmanual workers, but variations in the level of energy expenditure during the working day might still be present. We used concurrent diaries of physical activity ratings to monitor this possibility and carried out a validation of this method with accelerometry in a subsample. Smoking and alcohol intake can influence BP, HR, and cortisol, so these factors were included as covariates. An additional issue that may be relevant is the time of awakening because short sleep hours can lead to heightened sympathetic activity early in the day and to elevated evening cortisol (30). Higher salivary cortisol responses to waking and higher subsequent levels over the day have both been associated with early awakening (31). Finally, both cardiovascular and cortisol values over a working day can be affected by the stressfulness of the period (32, 33). Higher status individuals may have more choice over their activities on the day of physiological monitoring, thereby reducing its stressfulness. Ratings were therefore obtained of the stressfulness of the working day in comparison with usual levels.

METHODS

Participants in this study were 227 volunteers (121 men and 106 women) drawn from the Whitehall II cohort (25). They were recruited using the following criteria: age 45 to 58 years, day workers based in the London area, not planning to retire for at least 3 years, no history of CHD, no previous diagnosis or treatment for hypertension, and willingness to take part in laboratory testing (not described here) as well as ambulatory monitoring on a workday. Women were not eligible if they were premenopausal because menopausal status has effects on ambulatory blood pressure (18). Participants were drawn from higher (administrative and professional), intermediate (senior and higher executive officer), and lower (clerical, office support) employment grades. The response rate was 55%.

Ambulatory Monitoring Procedures

Ambulatory blood pressure monitoring was carried out using the SpaceLabs 90217 monitor (Redmond, WA), an instrument that satisfies international instrumentation protocols (34). The monitor was fitted between 07:30 and 09:30 hours on a working day (depending on work schedules) at the participant's place of work or in the laboratory at University College London. After confirmation of accurate functioning, participants wore the monitors for the remainder of the day and evening. Blood pressure was measured at 20-minute intervals throughout the day. Each reading was accompanied by an entry in a diary, in which the participant recorded location, activity over the previous 5 minutes (lying, sitting, standing, or walking), a detailed measure of specific current activities (eg, desk work, preparing food), verbal interactions, and any eating, drinking, smoking, or medication taken since the last reading. At the end of the evening, participants were asked to rate whether their day at work had been less stressful than usual, about average, or more stressful than usual.

Saliva samples were collected using cotton dental rolls (Salivettes, Sarstedt, Leicester, UK) held in the mouth until saturated. Measures were taken on waking up, 30 minutes later, and then within eight 30-minute time windows throughout the day and evening (08:00–08:30, 10:00–10:30 . . . 22:00–22:30). Tubes were returned to the investigators personally or by post, and cortisol was analyzed using a biotin-streptavidin immunoassay (35).

Other Measures

Saliva was sampled and BP was recorded under resting conditions in the laboratory after 30 minutes of inactivity using an A&D UA779 electronic sphygmomanometer. Height, body weight, and waist and hip circumference were measured using standard procedures. Laboratory sessions were carried out in both the morning and afternoon. Smoking, alcohol intake, and the use of hormone replacement therapy were assessed by questionnaire. In relation to alcohol, measures were taken of how much participants had typically drunk over the past year and over the past week.

Data Reduction

The ambulatory records of seven participants were lost before downloading from monitors. The BP and HR readings were reviewed and outliers were excluded using the criteria described by Berardi et al. (36). The number of eligible BP and HR readings averaged 34.3 ± 5.7 but ranged widely between individuals, so it was not possible to compare every time point or even hourly averages without substantial missing data. To make comparisons by SES over the day, it was therefore necessary to average data into four periods: morning (07:50–10:50), midday (11:00–14:00), afternoon (14:00–17:00), and evening (17:00–22:30). The average number of readings in these four periods was 4.61 ± 0.98, 7.27 ± 1.1, 8.17 ± 1.4, and 14.1 ± 4.2, respectively. To ensure robust effects, we decided to include in the analyses only individuals who had at least two readings from each time period. One hundred ninety-nine individuals were included in the BP analyses and 202 in the HR analyses. There were no differences across grades of employment in the number of readings contributing to each time period or in the time of starting monitoring in the morning.

The main BP and HR analyses involved repeated-measures analysis of variance with grade of employment (higher, intermediate, lower) and sex as between-subjects factors and time of day (morning, midday, afternoon, and evening) as the within-subject factor. The Greenhouse-Geisser correction was applied where appropriate, and adjusted p values (but not degrees of freedom) are presented. The influence of physical activity on BP and HR was assessed by dividing the ratings of activity associated with each reading into two categories: sitting and standing/walking (a negligible number of readings were taken while lying). The proportion of readings obtained in each time period when the participants were standing/walking was analyzed and then included as a covariate in the analyses of BP and HR. The impact of smoking status, alcohol intake, hormone replacement therapy, body weight, and stressfulness of the working day were assessed by including these variables as either factors or covariates in the analyses, as detailed below.

Complete saliva free cortisol sequences were obtained from 189 participants. Recent studies indicate that analysis of the cortisol response to awakening may be compromised by the failure of many participants faithfully to obtain samples immediately after waking (37). We did not use electronically timed tubes in this study, so compliance with the waking sampling protocol was judged by computing the difference between the time participants stated they had woken up and the time they stated that the first saliva sample had been taken. Participants showing a difference of more than 10 minutes were excluded. Extreme outliers were also omitted, leaving 163 for analysis. Exclusions did not vary by sex or grade of employment. In view of these limited numbers, we decided to combine the high and intermediate grades of employment and compare them with the lower grade. One hundred fourteen participants (63 men, 51 women) were included in the combined high-grade group and compared with 49 (24 men, 25 women) low-grade participants. Data were analyzed by repeated-measures analysis of variance with grade of employment and sex as between-subjects factors and time (waking, +30 minutes, and eight timed samples) as the within-subject factor. In addition, the response to waking (difference between +30 minutes and waking values), the average of all samples, and the average of the eight timed samples were compared. Because of a small difference between employment grades in age, cortisol analyses were adjusted for age. Data are presented as mean ± SD.

Validation of Diary Ratings

A subgroup of 123 participants in this study had energy expenditure assessed using TriTrac-R3D research ergometers (Reining International, Madison, WI). These solid-state monitors are accelerometers that assess movements in three planes and use the integrated vector magnitude together with information concerning gender, age, weight, and height to calculate estimated energy expenditure in kilocalories. Validations of the TriTrac and related triaxial accelerometers indicate that the instruments provide reliable assessments of energy expenditure (38, 39).

To validate the physical activity ratings, the association between energy expenditure and the index derived from diaries (the proportion of BP readings taken when standing/running) was assessed. The energy expenditure for the 5 minutes preceding each BP reading was computed from accelerometers and averaged for all readings in the day and evening. The sample was then divided into tertiles of low (mean, 11.7 ± 5.0 kcal/5 min), medium (23.9 ± 2.9 kcal/5 min), and high (41.1 ± 9.8 kcal/5 min) energy expenditure. The mean proportion of BP readings taken when standing/walking was compared across tertiles; the results are shown in Figure 1. Analysis of variance confirmed a significant linear trend across energy expenditure categories ($F(2,119) = 2.83$, $p = .019$) with higher objective physical activity being associated with a greater proportion of readings taken when walking/running. This analysis provides some corroboration for the use of diary ratings as indicators of physical activity in the complete sample.

RESULTS

The characteristics of the 202 participants in the three employment grade groups are detailed in Table 1. The grade of several participants had changed because of promotion by the time they were tested compared with the job grades on which invitations were based. There were 81 higher, 66 intermediate, and 55 lower grade participants in the study. The proportion of men and women did not differ between grades. Lower grade participants were slightly older on average ($F(2,196) = 3.45$, $p = .034$), but there were no differences between grades in body mass, waist circumference, waist/hip ratio, or in the proportion of women taking hormone replacement therapy. There were fewer male smokers in the higher than intermediate and lower grades, but the difference was not significant. Alcohol intake was greater in higher grade participants ($F(2,197) = 3.36$, $p = .037$), and the proportion of daily drinkers was greater in the higher grades ($\chi^2 = 14.6$, $p < .001$). As expected, body weight, waist/hip ratio, and resting BP were all higher in men

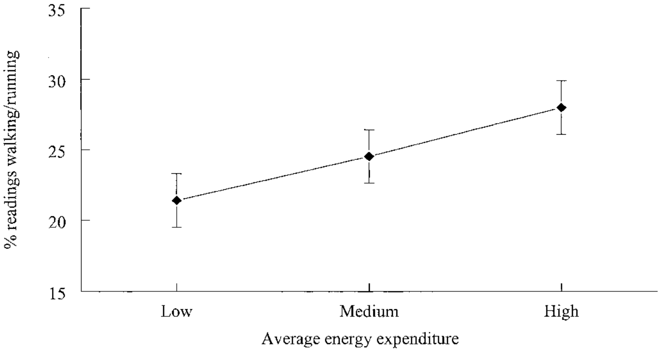

Fig. 1. Mean percentage of BP readings taken when participants were standing or walking in groups with low, medium, and high average energy expenditure. Error bars are SEM.

TABLE 1. Characteristics of Participants in the High, Intermediate, and Low Employment Grades[a]

	High Grade		Intermediate Grade		Low Grade		Statistical Differences
	Men (*N* = 44)	Women (*N* = 37)	Men (*N* = 35)	Women (*N* = 31)	Men (*N* = 29)	Women (*N* = 26)	
Age (y)	52.3 ± 2.7	51.1 ± 2.3	52.1 ± 2.6	52.6 ± 3.0	53.7 ± 2.9	52.2 ± 3.0	Grade, $p = .034$
Weight (kg)	79.4 ± 8.8	71.0 ± 11.1	78.6 ± 14.3	68.0 ± 11.7	77.3 ± 11.9	66.3 ± 11.0	Sex, $p < .001$
Waist/hip ratio	0.913 ± 0.07	0.807 ± 0.10	0.888 ± 0.07	0.797 ± 0.14	0.906 ± 0.07	0.780 ± 0.06	Sex, $p < .001$
Body mass index (kg/m^2)	25.4 ± 2.9	26.1 ± 4.2	25.6 ± 3.8	24.8 ± 3.9	25.5 ± 3.4	25.3 ± 4.3	
Current smoker (%)	2.3	8.1	11.8	6.5	13.8	7.7	
Alcohol intake							
Daily in past year (%)	58.1	41.7	26.5	41.9	21.4	16.0	Grade, $p < .001$
Measures in past week	12.2 ± 9.2	9.3 ± 8.0	8.8 ± 11.7	8.4 ± 6.5	8.2 ± 11.5	5.0 ± 5.8	Grade, $p = .037$
Hormone replacement therapy (%)		27.0		29.0		23.1	
Resting systolic BP (mm Hg)	121.0 ± 10.7	111.1 ± 13.1	120.1 ± 11.7	110.3 ± 12.2	121.8 ± 11.9	115.6 ± 14.9	Sex, $p < .001$
Resting diastolic BP (mm Hg)	74.0 ± 7.2	70.6 ± 9.7	73.7 ± 9.5	69.5 ± 9.4	75.2 ± 9.9	72.5 ± 8.7	Sex, $p = .009$
Resting HR (beats/min)	61.5 ± 9.7	65.3 ± 8.6	61.8 ± 8.2	64.3 ± 6.4	64.6 ± 11.4	64.1 ± 9.7	

[a] Values are mean ± SD, unless otherwise indicated.

than women ($F(1,196) = 7.05–73.1$, $p < .01$). Importantly, resting BP and HR did not differ with grade of employment.

Ambulatory Blood Pressure, Heart Rate, and Grade of Employment

The pattern of systolic BP variation over the day differed by SES, as evidenced by the significant grade of employment–by–time interaction ($F(6,579) = 2.94$, $p = .012$). These results are summarized in Figure 2. Systolic BP was greater in the morning period in the lower grade participants than in the intermediate and higher grade participants. The mean levels of systolic BP in the morning period adjusted for age, sex, smoking status, and alcohol intake averaged 123.3 ± 12.7 mm Hg in the higher, 122.6 ± 12.5 mm Hg in the intermediate, and 128.9 ± 15.7 mm Hg in the lower grade participants ($F(2,191) = 4.04$, $p = .019$). The three SES groups did not differ in systolic BP over the remainder of the day. There was a small rise in systolic BP in the evening in the lower but not the intermediate or higher grade groups. In addition, the main effect of sex was significant ($F(1,193) = 15.7$, $p < .001$), but sex did not interact with grade or time of day.

Ambulatory diastolic BP did not vary with employment grade. There was, however, a significant grade of employment–by–time interaction in the analysis of HR ($F(6,588) = 2.87$, $p = .014$). As shown in Figure 3, the differences by grade were again confined to the

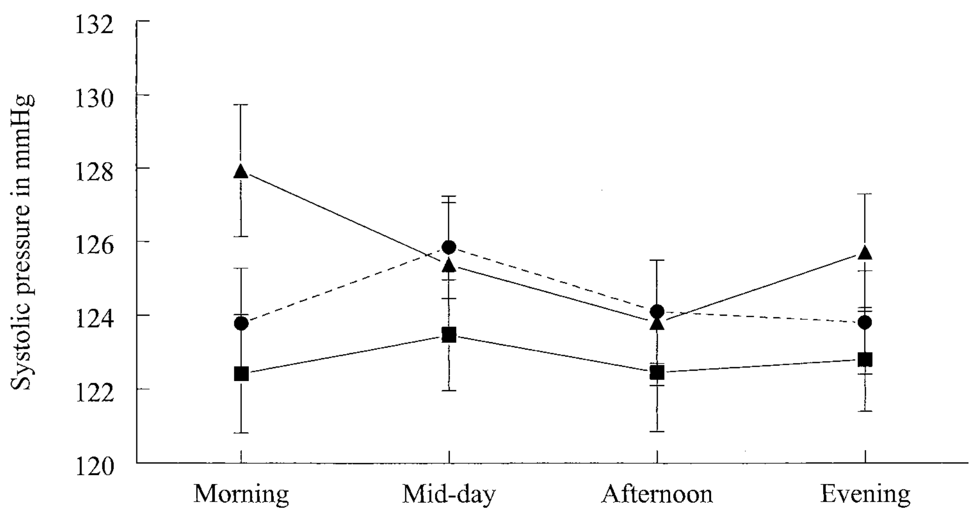

Fig. 2. Mean ambulatory systolic BP in the morning (07:50–11:00), midday (11:00–14:00), afternoon (14:00–17:00), and evening (17:00–22:30) periods of the working day in men and women from higher (●), intermediate (■), and lower (▲) grades of employment. Error bars are SEM.

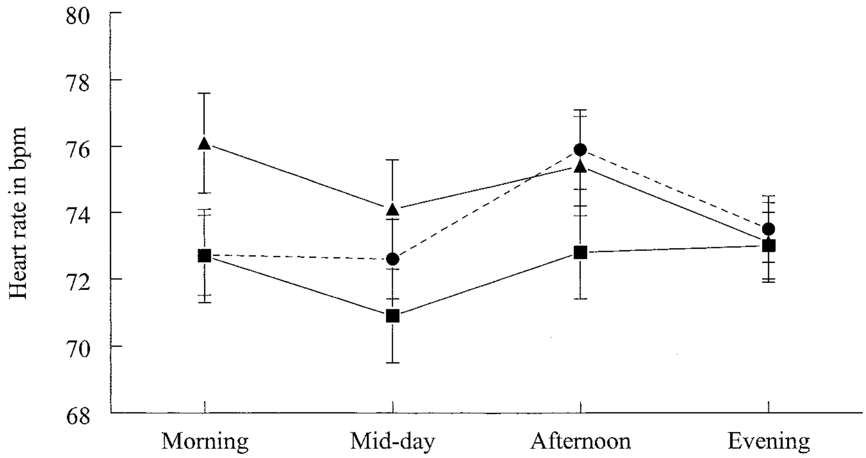

Fig. 3. Mean HR in the morning (07:50–11:00), midday (11:00–14:00), afternoon (14:00–17:00), and evening (17:00–22:30) periods of the working day in men and women from higher (●), intermediate (■), and lower (▲) grades of employment. Error bars are SEM.

morning period. Post hoc tests indicated that the HR of the higher (mean 71.9 ± 10.4 beats/min) and lower (mean 76.7 ± 14.9 beats/min) employment grade groups differed in the morning after adjustment for age, sex, smoking status, alcohol intake, and body weight ($F(1,129) = 4.40$, $p = .038$), whereas the higher and intermediate grade groups and the intermediate and lower grade groups did not differ significantly.

The Influence of Activity Level

The proportion of readings taken when standing/walking averaged 25.2% in the morning, 24.3% in midday, 23.0% in the afternoon, and 30.7% in the evening ($F(3,573) = 6.03$, $p < .001$). There was also a main effect of grade of employment in the analysis of the proportion of readings associated with standing/walking ($F(2,191) = 4.92$, $p = .008$). Across the entire day, 22.6% ± 12.9% of readings in the higher grade, 25.0% ± 12.8% in the intermediate, and 29.7% ± 12.8% in the lower grade participants were taken while standing/walking. Systolic BP and HR were also higher when participants were standing/walking compared with sitting during all phases of the day (data not shown). Nevertheless, the grade–by–time of day interaction remained significant after covarying for activity level in the analyses of systolic BP ($F(6,522) = 2.45$, $p = .031$) and HR ($F(6,561) = 2.62$, $p = .023$). Activity was a significant covariate in these analyses ($p < .001$), indicating that it did covary with cardiovascular activity over the day.

As an additional check we analyzed only the systolic BPs that were recorded after participants had been sitting for 5 minutes ($N = 187$). The grade-by-time interaction remained significant ($F(6,543) = 2.36$, $p = .035$), due as before to elevated levels in lower SES individuals in the morning period. By way of illustration, systolic BP recorded while seated in the morning period averaged 121.3 ± 13.2 mm Hg in higher grade and 128.3 ± 14.9 mm Hg in lower grade participants after adjustment for sex, age, smoking status, alcohol intake, and body weight ($F(1,121) = 7.45$, $p = .007$). In the corresponding HR analysis, the grade-by-time interaction was no longer significant in measures obtained only while sitting ($F(6,552) = 1.33$). There were insufficient participants with data in all four time periods to carry out a similar analysis of BP and HR measures obtained while walking/running.

Cortisol and Grade of Employment

There was no difference in resting cortisol by grade of employment, although resting values were higher in men (10.9 ± 8.3 nmol/liter) than women (7.36 ± 7.9 nmol/liter) in the laboratory ($F(1,179) = 5.79$, $p = .017$) after taking account of the time of day of laboratory sessions. In the analysis of cortisol over the day, the grade of employment–by–sex interaction was significant ($F(1,158) = 10.8$, $p < .001$), suggesting that men and women showed different patterns of response. Separate analyses were therefore performed for men and women.

In the analysis of men, there was a significant effect of grade ($F(1,84) = 5.14$, $p = .026$) together with a quadratic grade-by-time interaction ($F(1,84) = 5.76$, $p = .019$). This result is illustrated Figure 4. Saliva free cortisol showed the expected increase between waking and 30 minutes later, followed by a progressive decline over the remainder of the day. The quadratic effect reflects the fact that higher and lower grade

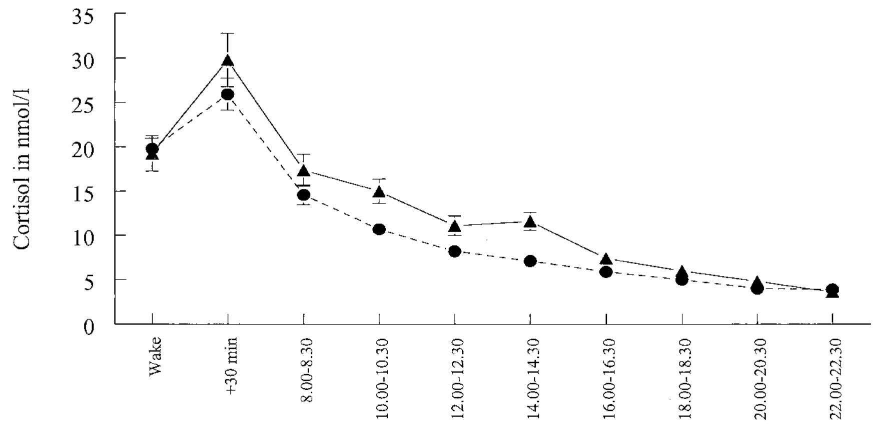

Fig. 4. Mean saliva-free cortisol sampled on waking up, 30 minutes later, and then at 2-hour intervals in men from higher (●) and lower (▲) grades of employment. Error bars are SEM.

groups did not differ on waking or at the end of the day but that differences were present during working hours. The response to waking averaged 6.11 nmol/liter in higher and 10.5 nmol/liter in lower grade men, a difference that was not significant ($F(1,84) = 1.21$). The level of cortisol averaged across all samples of the day was greater in the lower than higher grade men (12.5 ± 4.2 vs. 10.5 ± 3.4 nmol/liter, $F(1.84) = 5.14$, $p = .026$). When the waking and +30-minutes values were omitted, the average cortisol over the day remained greater in the lower grade men (9.54 ± 4.1 vs. 7.38 ± 2.8, $F(1,85) = 7.49$, $p = .008$). This difference remained significant after further adjustment for smoking status and alcohol intake ($F(1,81) = 6.28$, $p = .014$).

Lower grade participants reported waking up at 06:00 hours (±50 minutes), whereas higher grade men and women woke on average at 06:29 hours ± 41 minutes ($F(1,158) = 15.4$, $p < .001$). Time of awakening was not related to waking cortisol level, the cortisol response to waking up, or to cortisol measured through the day and evening. In addition, the difference between higher and lower grade of employment groups remained after adjusting for time of awakening along with other covariates ($F(1,79) = 7.36$, $p = .008$).

The analysis of cortisol in women showed the opposite pattern (Fig. 5). Across the day and evening, there was a main effect of grade of employment ($F(1,73) = 5.57$, $p = .021$), and average cortisol was greater in higher than lower grade women (11.0 ± 3.4 vs. 9.22 ± 2.4 nmol/liter). The difference was also significant when the waking and +30-minutes samples were omitted; the mean cortisol in higher grade women over the day and evening was 7.80 ± 2.5 nmol/liter, compared with 6.39 ± 1.9 nmol/liter in lower grades, after adjustment for age, smoking status, alcohol intake, time of awakening, and hormone replacement therapy ($F(1,69) = 5.33$, $p = .024$). There was no difference between grades in the waking response in women, and no grade-by-time interaction as there was for men.

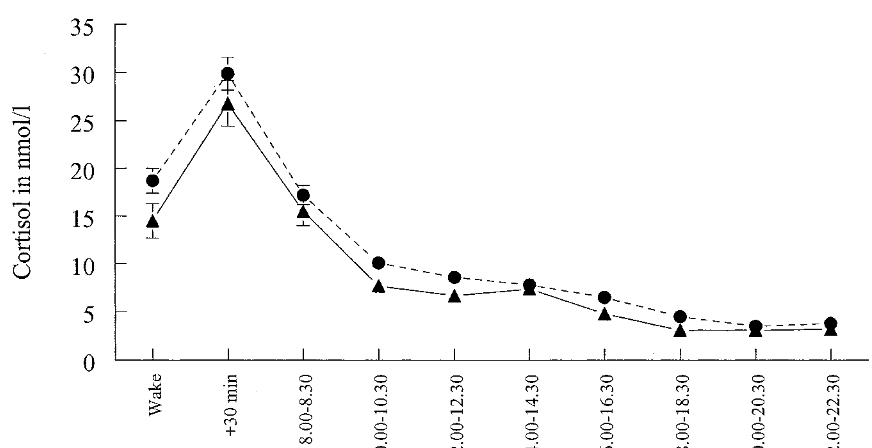

Fig. 5. Mean saliva-free cortisol sampled on waking up, 30 minutes later, and then at 2-hour intervals in women from higher (●) and lower (▲) grades of employment. Error bars are SEM.

Stressfulness of the Working Day

Ratings of the stressfulness of the work day were completed by 165 participants. Of these, 55% stated that the day was less stressful than usual, 36% said that it was average, and 9% reported that it was more stressful than usual. A comparison was made between the proportion of participants in each grade of employment who rated the day as less stressful than usual. There was a significant difference ($\chi^2 = 6.23$, $p = .045$) since 56.1% of the higher and 64.8% of the intermediate grade participants rated the day as less stressful than usual, compared with only 40.0% of the lower grade participants. The stressfulness rating was therefore included as a covariate in the analyses of systolic BP, HR, and cortisol. The grade of employment difference in morning systolic BP remained significant in this reduced sample after covarying for stressfulness along with age, smoking status, alcohol intake, and time of awakening ($F(2,137) = 3.93$, $p = .022$). The cortisol differences by grade of employment also remained significant for men ($F(1,55) = 7.58$, $p = .008$) and women ($F(1,55) = 4.17$, $p = .046$). But the HR differences with grade were no longer significant after the stressfulness of the day of monitoring had been taken into account ($F(2,156) = 0.66$).

DISCUSSION

The main findings of this study are that lower SES was associated with elevated ambulatory systolic BP and HR in the early part of the working day and with heightened cortisol output in men and lower cortisol output in women. The mean difference between higher and lower grades in the morning period was 4.4 mm Hg systolic BP and 4.6 beats/min HR (5.6 mm Hg and 4.8 beats/min after adjustment for covariates). Cortisol output between 08:00 and 23:10 hours was 29% greater on average in the lower than higher grade men and 23% greater in the higher than lower grade women. These differences were independent of waking time, smoking, and alcohol intake. The absence of differences in diastolic BP is consistent with other studies of psychosocial factors, such as job strain and job demands, that also appear to influence systolic BP to a greater extent than diastolic BP (40).

One of the difficulties of integrating psychophysiological methods into the epidemiological framework to investigate broad sociodemographic factors is statistical power. Ambulatory BP and neuroendocrine activity are affected by numerous variables other than SES, including anthropometric, lifestyle, psychosocial, and biological factors. Identifying an independent association with SES therefore requires large-scale studies. The present investigation suffered in this respect in two important ways. First, although our hope had been to analyze BP and HR in hourly averages across the day, missing data meant that it was necessary to divide the monitoring period into four longer time periods. If BP and HR had been averaged into hourly means, only 132 of 220 participants would have had complete data. The result was a loss of precision with which socioeconomic variations over time could be identified. Second, the amount of missing data in the cortisol analyses meant that the three grades of employment had to be collapsed into two. The fact that higher and intermediate grade groups did not differ in systolic BP at any time point provides some justification for combining these groups, but it is nevertheless a limitation that complete cortisol profiles were not obtained from more participants.

Recruitment from the Whitehall II cohort had the considerable benefit of assessing psychobiological pathways in a population in which social inequalities in CHD and risk factors are already established. On the other hand, we were concerned not to place excessive demands on participants in this study in case their continued involvement in the epidemiological follow-up was compromised. Hence, monitoring was confined to a single working day rather than the repeated days included in other studies (22), and we did not continue ambulatory BP monitoring through the night. We were unable therefore to assess the full diurnal profile of cardiovascular function.

We were aware of the possibility that differences in BP and HR across the social gradient might be due to concomitant physical activity. Concurrent diary assessments indicated that even though the lower grade participants were clerical and office support staff rather than manual workers, they were more likely to be physically active at the time of cardiovascular measurements than was the higher grade group. Ergometers were available for only about half of the sample in this study. These measurements were therefore used further to validate the diary rating method of assessing activity rather than to provide objective estimates of energy expenditure in all analyses. The diary ratings of posture activity used in this study have previously been validated against accelerometry (41), but not when categorizing diary data using the method detailed here. The validation analyses indicated that different levels of energy expenditure were reliably distinguished by the diary measure of activity (proportion of readings taken when standing/walking), although the size of the association was not great. The use of diary ratings to account for differences in activity is clearly less satisfactory than objective assessment in all participants. Nonetheless, the analyses of systolic

BP, carried out with diary activity measures as covariates, provide support for the inference that SES differences were not due to physical activity. The conclusions for HR are more marginal; although the SES difference survived adjustment for concomitant physical activity, it was not significant when analyses were restricted to measures taken when seated.

Socioeconomic status was not associated with resting BP, HR, or cortisol in this study but only with values recorded during the working day. This finding is consistent with previous studies of clinic or screening BP, which have shown only modest associations with SES (42). It suggests that the heightened BP and HR of lower grade participants may be biological responses to the actual experience of lower social status (17). The differences observed are relatively small and are not themselves indicative of cardiovascular pathology. However, sustained small variations in cardiovascular and neuroendocrine may accelerate disease progression if maintained in everyday life conditions for prolonged periods (43, 44).

We are not certain why socioeconomic differences in cardiovascular activity were apparent only early in the day. The pattern of results may relate to the nature of the work carried out in this civil service population. More light may be thrown on this issue in the detailed analyses of mood and social interaction recorded in diary ratings that have yet to be carried out. As noted in the "Introduction," to our knowledge only one other published study has assessed ambulatory BP using automated methods in participants systematically sampled from different SES strata (22). In that study, no differences in ambulatory systolic or diastolic BP between men and women in higher and lower status jobs were observed. Our participants were several years older than those in this previous study, and it is possible that the influence of SES on biological responses accumulates through the life course. The impact of working in high-demand/low-control jobs on ambulatory blood pressure is greater in lower status men (21), and lack of control at work is inversely associated with grade of employment in the Whitehall II cohort (25).

The results for cortisol output over the day present a conflicting picture. We hypothesized that cortisol levels would be greater in lower than higher SES groups and that cortisol responses to waking would also be elevated. The anticipated difference in cortisol output over the day was observed in men, but differences in responses to awakening were not confirmed. The lack of a significant difference in waking response may be a direct result of an insufficient sample size; power analyses (45) indicate that 109 men per group would be required to confirm a difference in waking response of the size observed here with 80% power. More importantly, the results for women were opposite to prediction, with elevated cortisol in higher status individuals.

These differences were not related to time of awakening. Because lower SES participants woke up an average 29 minutes earlier than the higher SES group, we thought it possible that they might have been suffering from chronic sleep debt (30). Length of sleep time was unfortunately not assessed. However, the differences in cortisol were maintained after statistical adjustment for time of awakening; indeed, we did not observe any association between time of awakening and the cortisol response to awakening. The explanation for the difference in the association between hypothalamic-pituitary-adrenocortical activation and SES in men and women is not clear. It cannot be assumed that heightened cortisol necessarily has adverse effects and that lower diurnal levels are adaptive because there is evidence that both high and low cortisol are associated with different patterns of disease risk (46, 47). In laboratory studies it has been found that men show greater stress-related cortisol responses than women (48). A number of other sex differences in cortisol activation in response to psychosocial factors have also been described (28, 49). Rohleder et al. (50) recently investigated the impact of psychosocial stress on the glucocorticoid sensitivity of interleukin-6 and tumor necrosis factor-α. Although the free cortisol responses of men and women to psychosocial stress were similar, in men glucocorticoid sensitivity was markedly increased 1 hour after stress, whereas glucocorticoid sensitivity decreased significantly in women.

Another relevant factor may be the experience of women working in higher status jobs. Light et al. (19) reported that women in high-status occupations who also had high scores on the John Henryism Effort-Coping Scale had elevated diastolic BP at work compared with women in low-status occupations. Associations between sustained cardiovascular and neuroendocrine function and high occupational status in female managers in Sweden have also been described (51). However, these investigations did not demonstrate differences in cortisol output of the type found here. Future analyses will address the possible moderating role played by psychosocial work characteristics, John Henryism, family responsibilities, and other factors.

Although volunteers were systematically recruited from different grades of employment, participants were a selected group because a number of civil servants declined to take part. It has previously been shown in the Whitehall II study that grade of employment is associated with body weight and waist/hip ratio, but comparable effects were not observed in this investigation. The difference in smoking prevalence by grade was also smaller than in the complete cohort. The study may therefore have attracted relatively fit lower status participants, underestimating differences between socioeconomic groups.

These results are consistent with the hypothesis that part of the social gradient in disease risk is due to psychobiological factors or variations in biological function stimulated by autonomic, neuroendocrine, and immune activation from the central nervous system (16). Ambulatory monitoring is a powerful tool for assessing the psychobiological pathways because recordings are obtained under naturalistic conditions while participants are going about their everyday lives. Further research is required to delineate SES differences in biological function more fully and to understand the sex differences in cortisol responses. Nevertheless, if the pattern of physiological response recorded during ambulatory monitoring is representative of ordinary life, then people of lower SES may endure heightened cardiovascular activation for several hours each day compared with higher status individuals, with concomitant neuroendocrine responses at least in men. Such a pattern may promote enduring differences in cardiovascular disease risk.

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