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Family history of cardiovascular disease is associated with cardiovascular responses to stress in healthy young men and women

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Abstract

Heightened cardiovascular stress responsivity is associated with cardiovascular disease, but the origins of heightened responsivity are unclear. The present study investigated whether disturbances in cardiovascular responsivity were evident in individuals with a family history of cardiovascular disease risk. Data were collected from 60 women and 31 men with an average age of 21.4 years. Family history of cardiovascular disease risk was defined by the presence of coronary heart disease, hypertension, diabetes or high cholesterol in participants' parents and grandparents; 75 participants had positive, and 16 had negative family histories. Systolic and diastolic blood pressure (BP), heart rate and heart rate variability were measured continuously for 5 min periods at baseline, during two mental stress tasks (Stroop and speech task) and at 10–15 min, 25–30 min and 40–45 min post-stress. Individuals with a positive family history exhibited significantly greater diastolic BP reactivity and poorer systolic and diastolic BP recovery from the stressors in comparison with family history negative individuals. In addition, female participants with a positive family history had heightened heart rate and heart rate variability reactivity to stressors. These effects were independent of baseline cardiovascular activity, body mass index, waist to hip ratio and smoking status. Family history of hypertension alone was not associated with stress responsivity. The findings indicate that a family history of cardiovascular disease risk influences stress responsivity which may in turn contribute to risk of future cardiovascular disorders.

Keywords: Cardiovascular disease; Cardiovascular reactivity; Cardiovascular recovery; Family history; Hypertension; Stress

1. Introduction

Cardiovascular disease is the leading cause of death and morbidity in western countries. Coronary atherogenesis, increased left ventricular mass, plaque rupture, thrombus formation, vasospasm and arrhythmogenesis have all been associated with heightened cardiovascular responsivity to acute stress (Manuck, 1994). It has been argued that heightened cardiovascular reactivity to stress contributes to the development of future cardiovascular disease (Treiber et al., 2003). However, because studies are often carried out among people with existing cardiovascular disease, it is difficult to determine the causal order between heightened reactivity and disease onset. It is also uncertain what causes heightened cardiovascular responses.

Cardiovascular diseases have strong heritable components and young people whose parents suffer from these conditions are at elevated risk. Family history may contribute to heightened cardiovascular stress reactions, and a family history design makes it possible to determine whether physiological dysfunction precedes cardiovascular disease onset. A large and complex literature has investigated whether normotensive individuals with a positive family history of hypertension display greater cardiovascular responses to stress than persons with a negative family history of hypertension (Pierce et al., 2005). Early meta-analytic reviews of family history of hypertension indicated that individuals with a positive family history have greater physiological reactivity to a stressor than those with no family risk (Fredrikson and Matthews, 1990; Manuck et al., 1993). Healthy offspring of hypertensive individuals have also been found to exhibit slower and less

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complete recovery from acute laboratory stress (Hocking Schuler and O'Brien, 1997; O'Brien et al., 1998; Schneider et al., 2003).

A positive family history of cardiovascular disorders other than hypertension is strongly associated with future incidence of cardiovascular disease, even when environmental risk factors are taken into account (Williams et al., 2001; Andresdottir et al., 2003). To date, few studies have investigated cardiovascular reactivity to stress and family history of cardiovascular disease risk defined more broadly. There is evidence that normotensive individuals with a family history of myocardial infarction exhibit greater blood pressure increases or less attenuation of total peripheral resistance following stress than those with a negative family history (Stoney et al., 1988; Treiber et al., 1991, 1993). However, to our knowledge, no studies have examined the relationship between cardiovascular responsivity to stress and family history of cardiovascular disease risk defined in broader terms, including such factors as diabetes and high cholesterol as well as hypertension and coronary heart disease. A criticism of previous literature relating family history of hypertension with stress reactivity is that family history has been reported by offspring who may not be aware of their parents' health status, and that risk has been defined by a single generation (Schneiderman et al., 2000). As a result, it is now recommended that studies should obtain reports from parents, with information from at least two generations (Silberberg et al., 1999).

The present study investigated whether disturbances of cardiovascular stress responsivity were evident in persons with a raised family risk of cardiovascular disease defined broadly. We tested a sample of young male and female healthy normotensive volunteers, and hypothesised that participants with a positive family history of cardiovascular disease risk (including high cholesterol, coronary heart disease, diabetes and hypertension) would show larger cardiovascular responses (reactivity and recovery) to two behavioural challenges in comparison with participants with negative family histories. The analyses controlled for possible confounders such as participant's own baseline physiological activity, body mass index, abdominal adiposity and smoking status. In addition, we examined the relationship between cardiovascular responsivity and family history of hypertension as an individual risk factor.

2. Materials and methods

2.1. Participants

One hundred and three young adults aged between 18 and 25 years were recruited through email notices to academic departments in University College London. Participants were screened by structured interview to ensure that they were generally healthy, not taking any medication (including antidepressants), were without cold or flu symptoms, were not taking antibiotics, and had at least one contactable blood-related parent. Participants were asked to avoid aspirin or ibuprofen for 10 days prior to the session, and caffeine and alcohol 12 h before the session. Thirty-four participants were male (33%) and 69 were female (67%). The majority of participants were university students. Written informed consent was gained from each participant and ethical approval was granted by the University College Hospital Medical Research Ethics Committee.

2.2. Mental stress tasks

Two mental stress tasks were administered in a fixed order. First, a modified computerised version of the Stroop colour–word interference task was administered for 5 min. During this task participants were presented with a target word in the centre of the screen which was printed in an incongruent colour (green, red, blue, yellow). The participant was then asked to match the colour that the target word was printed in with the correct word from four options at the bottom of the screen. The presentation rate varied with task performance in order to keep pressure constant throughout the testing period. Participants were given a 30 second practice period and were instructed that accuracy and speed of response would be recorded. In the second task participants were presented with a hypothetical situation describing someone who had to defend themselves to the police after being wrongly accused of shoplifting. Participants were instructed that they would have 2 min to construct a response to the scenario before delivering a 3 min video recorded speech focusing on their feelings and emotions surrounding the situation.

2.3. Measures

Heart rate and heart rate variability (HRV) were assessed by the electrocardiogram of an impedance cardiography device (VU-AMS, Amsterdam, Holland) as described by Willemsen et al. (1996). The VU-AMS uses six disposable pre-gelled Ag/AgCl electrodes (ReddotTM 2239–50, 3M Health Care, Germany) to record both electronic and impedance cardiogram signals (ECG/ICG), but only the ECG-based measures are presented here. Heart rate variability was assessed using time domain measures. During a 5 min period the difference between each inter-beat interval was squared, the mean of these squared intervals was then derived and the square root of this mean was calculated as the root mean square successive difference (rMSSD).

Systolic and diastolic blood pressure (BP) was measured using the Portapres Model-2 device (TNO-TPD Biomedical Instrumentation, Amsterdam, Holland). The Portapres system comprises a control unit, front-end unit, two finger cuffs, height correction unit, AC adapter and interface cable. The participant is fitted with two small cuffs attached to the control unit on the middle and ring finger of their non-dominant hand. Each finger cuff is then pressurised and inflated for alternate 30 min periods to continuously read blood pressure on a beat-to-beat basis.

Cardiovascular data for this study were collected continuously and then averaged over specified 5 min trials. A single-item Likert scale was used to measure subjective stress; scores could range from 1 (no stress) to 7 (very high stress). During a structured interview, the number of cigarettes smoked per day, hours of exercise undertaken in a four week period and units of

alcohol consumed in a typical week were recorded. Body weight was measured to the nearest 0.1 kg with participants in underwear, and height was measured to the nearest 0.1 cm. Waist circumference was measured horizontally midway between the lowest rib and iliac crest. Hip circumference was measured as the widest part in the gluteal region. Body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared. Waist–hip ratio (WHR) was calculated by dividing waist by hip circumference.

2.4. Procedure

Participants were individually tested in a purpose-built temperature controlled laboratory. All sessions began at 12:30 pm. A brief structured interview examining participant's current state of health and previous day's events was completed, followed by measurement of WHR and BMI. The VU-AMS and Portapres-2 devices were then fitted. Participants were left to relax for 30 min. The last 5 min of this rest period constituted the baseline trial for continuous BP, heart rate and HRV, and participants completed the first subjective stress scale. They then performed the two mental stress tasks and completed the first post-task subjective stress scale. VU-AMS and Portapres recordings were taken throughout the task period. Following completion of the tasks participants were instructed to relax for the next 45 min. During this recovery period, subjective stress scales and 5 min of continuous VU-AMS/Portapres recordings were completed at 10–15, 25–30 and 40–45 min post-task.

2.5. Family history measures

Family history information was obtained from participants' parents by means of a short questionnaire. Factors included in the questionnaire were based on recommendations by Higgins et al. (1996). Parents were asked to provide details of their own age, weight, height, waist circumference and smoking history. They were also asked whether they had ever been told by a doctor that they had high blood pressure, heart disease, diabetes or high cholesterol; age of diagnosis was subsequently noted. Parents provided details of the health status of their parents, including history of diabetes, heart disease, high cholesterol or high blood pressure.

In total, 88 (85.4%) participants provided contact details for both parents and 15 (14.6%) provided details for just one parent. A total of 191 questionnaires were posted and 156 were returned, yielding a response rate of 81.7%. Of these returned questionnaires, family history data from at least one parent was available for 91 (88.3%) of the sample, while 63.1% of participants had family history data available from both blood-related parents. To avoid a reduction in statistical power which would result if only subjects with two parents had been assessed, non-responding partners of parents that did respond were classified with a negative family history. The offspring ($n=12$) of parents who did not respond to the questionnaire had similar WHR, BMI, heart rate, HRV, systolic and diastolic BP baseline, reactivity and recovery levels, to those who did return the parent questionnaire. χ^2 analyses also revealed no gender difference between participants whose parents responded and those who did not. All parents who returned their questionnaire provided information about one set of participant's grandparents. From a potential total of 412, details were gained for 316 (76.7%) grandparents, and 88.3% of these participants had information from at least two grandparents.

2.6. Family history questionnaire scoring

Family history of cardiovascular disease was calculated by summing the total number of cardiovascular-related risk factors for parents (multiplied by 2), with the total number of cardiovascular-related risk factors for grandparents, as recommended by Silberberg et al. (1999). For example, if a participant's mother had heart disease and diabetes, and father had no history of any of the four disorders (i.e., hypertension, heart disease, diabetes, high cholesterol), the individual would receive a parental score of 4. If the same person had two grandparents with high cholesterol, they would be given a grandparent score of 2, making their total family history score 6. Family history of cardiovascular disease scores ranged from 0 to 15 out of a theoretical maximum of 32. Scores were dichotomised using a conservative classification criterion so that two groups with a divergent family history were created. Participants were defined as having a negative family history of cardiovascular disease if neither parent nor any of the four grandparents had evidence of cardiovascular disease risk factors, or if the four grandparents collectively reported just one cardiovascular disease risk factor (i.e., the total score was 0 or 1) ($n=16$). They were defined as having a positive family history of cardiovascular disease if the total number of cardiovascular disease-related risk factors presented by both parents and grandparents exceeded two (i.e., total score was 2 or more) ($n=75$). The 12 participants who had neither parent respond were eliminated from the analyses.

Family history of hypertension was scored in a similar way. A participant was defined as having a positive history of hypertension if at least one parent or at least two grandparents reported a history of raised blood pressure. A participant was defined as having a negative history of hypertension if neither of their parents, and one (or none) of their four grandparents reported high blood pressure. In total, 64 participants had a negative history of hypertension, while 27 participants had a positive history of hypertension. Of the 75 participants classified with a positive risk of cardiovascular disease, 27 (36%) had a positive risk of hypertension.

2.7. Data reduction and statistical analyses

Cardiovascular data (systolic BP, diastolic BP, heart rate and HRV) were averaged into six 5 min trial periods (baseline, task 1, task 2, 10–15 min post-task, 25–30 min post-task and 40–45 min post-task). Heart rate variability was defined as the root mean square of successive differences between inter-beat intervals (rMSSD). Data were screened for technical errors, equipment failure and for cardiovascular responses which fell outside possible parameters. Participants with

Table 1
Sample characteristics (unadjusted means±sd)

	Cardiovascular disease FH positive (male=26, female=49)	Cardiovascular disease FH negative (male=5, female=11)	Hypertension FH positive (male=11, female=16)	Hypertension FH negative (male=20, female=44)
Age (years)	21.29±2.1	21.69±2.3	20.70±1.8	21.64±2.2
Ethnicity (% Caucasian)	55 (73.3%)	12 (75%)	19 (70.4%)	48 (75.0%)
Waist to hipratio	.790±.12	.750±.10	.168±0.03	.763±0.08
Body massindex (kg/m^2)	23.57±3.7	23.23±3.6	23.95±4.5	23.32±3.23
Exercise level (hours per 4 weeks)	31.17±27.4	34.50±24.4	23.50±18.1	34.30±28.4
Alcohol consumption (units/day)	2.95±1.1	2.62±1.1	2.78±.95	2.94±1.2
Cigarette smokers (%)	13 (14.3%)	0	9 (9.9%)	4 (4.4%)
Baseline systolic blood pressure (mmHg)	115.24±11.2	110.51±13.2	116.04±11.8	113.77±11.6
Baseline diastolic blood pressure (mmHg)	65.67±8.3	63.84±9.1	65.10±8.5	65.53±8.5
Baseline heart rate (bpm)	71.27±9.4	70.16±11.0	73.11±8.6	70.22±9.9
Baseline heart rate variability (ms)	59.18±31.6	52.78±26.9	57.38±36.4	58.23±28.5

erroneous data were subsequently removed from the analyses. Results were based on the full sample ($n=91$) for heart rate and heart rate variability analyses, 87 participants for systolic BP and 85 for diastolic BP analyses; the missing blood pressure data were due to technical problems with the Portapres-2 device, which was functioning incorrectly for a period of data collection. Cardiovascular reactivity was defined as task value minus baseline level for each of the cardiovascular parameters during tasks 1 and 2; higher scores indicate greater task reactivity. Cardiovascular recovery was defined as values 45 min post-task minus baseline level for each cardiovascular parameter; greater scores indicate poorer task recovery, covarying for magnitude of task responses.

Comparisons of participants' and parents' background characteristics by gender and family history status were made using *t*-tests. χ^2 tests were used for comparison of participants' and mothers' and fathers' smoking status and incidence of parental and grandparent cardiovascular risk factors. Physiological and subjective stress profiles over the session were assessed using repeated measures analysis of variance, with gender as the between-subject factor and trial as the within-subject factor. *Post hoc* comparisons were made using Tukey's LSD test. Univariate analysis of variance, with family history and gender as the between-subjects factors were used to assess physiological reactivity to and recovery from the two tasks, controlling for the person's own smoking status, BMI, WHR and cardiovascular baseline levels.

3. Results

3.1. Sample characteristics

The characteristics of the sample are summarised in Table 1. Average hours of exercise taken per week were above the UK government's recommended level, only 15.5% smoked, and alcohol consumption was low. Comparisons showed that family history (FH) positive and FH negative individuals (for both cardiovascular disease risk and hypertension risk alone) were of a similar age and ethnicity, had comparable BMIs, drank a similar amount of alcohol per week and reported similar amounts of exercise. There were no smokers in the FH negative group, preliminary analyses revealed that exclusion of smokers from the FH positive group did not alter results. Consequently, smokers were included in the final analyses. Men had greater WHR than women ($t=4.38$, $p=.001$). No other gender differences were found.

3.2. Parent and grandparent sample characteristics

Characteristics of the parent and grandparent sample are summarised in Table 2. Few of the parents smoked, but half reported at least one cardiovascular-related condition. Gender comparisons showed that mothers were significantly younger ($t=3.60$, $p=.001$) and had smaller waist circumferences ($t=5.23$, $p=.001$) than fathers, while BMI was marginally lower in mothers than fathers ($t=1.96$, $p=.052$). A similar number of mothers and fathers were smokers, and incidence of high blood pressure, heart disease and diabetes did not differ significantly by gender. χ^2 analysis revealed that fathers had a greater incidence of high cholesterol than mothers ($\chi^2=4.34$, $p=.037$), but comparison of overall incidence of cardiovascular-

Table 2
Parent and grandparent characteristics (unadjusted means±sd)

	Mother ($n=87$)	Father ($n=71$)	Grandparent
Age	51.5±4.7	54.4±5.5	
Body mass index (kg/m^2)	25.12±4.1	26.44±4.3	
Waist measurement (cm)	77.73±13.8	91.02±15.8	
Cigarette smokers (%)	7 (8.0%)	13 (18.3%)	
High cholesterol (%)	13 (14.9%)	20 (28.6%)	38 (12.4%)
High blood pressure (%)	17 (19.5%)	14 (20.0%)	92 (30.2%)
Heart disease (%)	1 (1.1%)	4 (5.6%)	71 (23.4%)
Diabetes (%)	3 (3.4%)	7 (9.9%)	45 (14.6%)
Total incidence (%)	34 (39.1%)	45 (63.4%)	157 (50.8%)

Table 3
Cardiovascular and subjective stress responses to the experimental procedure (unadjusted means±sd)

		Baseline	Task 1 (Stroop)	Task 2 (Speech)	15 min post-task	30 min post-task	45 min post-task
Subjective stress ratings (0–7; low–high)	Male	2.21±1.2[a]	4.41±1.3[b]	3.97±1.5[b]	1.82±.72[c]	1.53±.62[d]	1.59±.78[d]
	Female	1.96±1.1	4.64±1.1	4.42±1.3	1.91±.72	1.62±.69	1.67±.82
Systolic BP (mmHg)	Male	122.95±11.9[a]	141.71±24.5[b]	151.68±28.2[c]	133.65±14.1[d]	131.30±14.0[e]	128.67±15.7[f]
	Female	111.55±10.0	118.94±16.7	129.68±21.4	118.61±13.6	116.40±14.0	112.39±14.1
Diastolic BP (mmHg)	Male	65.66±6.9[a]	78.37±11.1[b]	85.05±11.1[c]	73.37±8.7[d]	73.15±8.3[d]	71.01±9.3[e]
	Female	65.11±8.8	72.32±12.7	78.67±12.9	71.30±12.1	69.65±11.3	67.11±10.8
Heart rate (bpm)	Male	69.0±11.1[a]	74.83±13.3[b]	84.82±16.3[c]	67.55±10.5[d]	67.18±10.1[d]	66.52±10.3[d]
	Female	72.11±8.7	79.50±10.5	87.64±14.2	70.60±9.6	70.62±9.3	70.88±9.0
Heart rate variability (ms)	Male	59.77±33.6[a,d]	48.87±27.3[b]	39.26±18.4[c]	59.24±30.4[a]	63.50±31.9[d]	64.59±30.9[d]
	Female	57.13±29.4	39.41±18.5	36.88±18.6	55.74±27.3	57.13±30.9	56.22±29.00

Values on each row that have different superscripts are significantly different from each other ($p<.05$).

related conditions did not differ by gender. One hundred fifty-seven (50.8%) of the grandparents were reported to have one or more cardiovascular-related disorder. Seventy-one (23.4%) grandparents suffered from heart disease, 38 (12.4%) suffered from high cholesterol, 92 (30.2%) had high blood pressure, and 45 (14.6%) had diabetes. No difference in condition incidence was observed between maternal and paternal grandparents.

3.3. Subjective and physiological responses during the study

Physiological and subjective responses to the tasks are summarised in Table 3. Repeated measures analyses of variance showed that subjective stress ratings changed significantly over the 6 trials ($F_{6,505}=198.9$, $p<.001$). Stress ratings rose sharply following tasks before returning to levels slightly below baseline during the recovery period. Responses for men and women were similar throughout the procedure. A significant main effect of trial was discovered for systolic and diastolic BP (systolic BP, $F_{5,420}=75.45$, $p=.001$; diastolic BP, $F_{5,410}=77.39$, $p=.001$). *Post hoc* LSD tests, detailed in Table 3, indicated a significant increase from baseline in both systolic and diastolic BP during the first task, followed by a further increase from task 1 to task 2. A decline was then observed with the onset of the recovery phase. *Post hoc* tests indicated that for systolic BP all recovery trials were significantly different from one another. For diastolic BP, the 45 min trial had lower values than the 15 and 30 min recovery trials. Thus for both systolic and diastolic BP, levels continued to decline until 45 min post-task. There was a significant gender difference in reactions to task 1 (systolic BP, $F_{1,81}=3.99$, $p=.049$; diastolic BP, $F_{1,79}=6.64$, $p=.012$) and task 2 (systolic BP, $F_{1,81}=5.40$, $p=.023$; diastolic BP, $F_{1,79}=5.61$, $p=.020$), with men being more reactive to both tasks. No gender difference was found for systolic or diastolic BP recovery.

The main effect of trial was significant in the analyses of heart rate ($F_{5,505}=163.78$, $p=.001$) and HRV ($F_{5,475}=46.25$ $p=.001$). *Post hoc* LSD tests indicated a rise in heart rate during task 1, followed by an additional increase from task 1 to task 2. A significant decrease in HRV was recorded between baseline and task 1 and between task 1 and task 2. Heart rate and HRV had returned to baseline by the first recovery period, and fell to levels below baseline for the remaining two recovery periods. No trial by gender interaction or main effect of gender was present for either variable. It should be emphasised that individual differences in cardiac responses were substantial for both tasks. For example, blood pressure responses for task 1 ranged from −17.78 to +65.02 mmHg for systolic BP and −12.07 to +32.95 mmHg for diastolic BP, and ranges of recovery were equally large.

3.4. Family history of hypertension and physiological responsivity

We found no evidence that participants with a positive family history of hypertension had heightened cardiovascular stress reactivity or slower recovery. There were no effects of family history of hypertension on diastolic BP, heart rate or HRV. The only significant finding was the reverse of that predicted, in that male participants with a negative FH of hypertension had stronger systolic BP reactions to task 1 and task 2 than participants with a positive FH of hypertension ($F_{1,16}=4.64$ and 5.64 respectively, $p<.05$). No associations between FH of hypertension and systolic BP were discovered for female participants, and there were no differences in subjective stress responses related to family history.

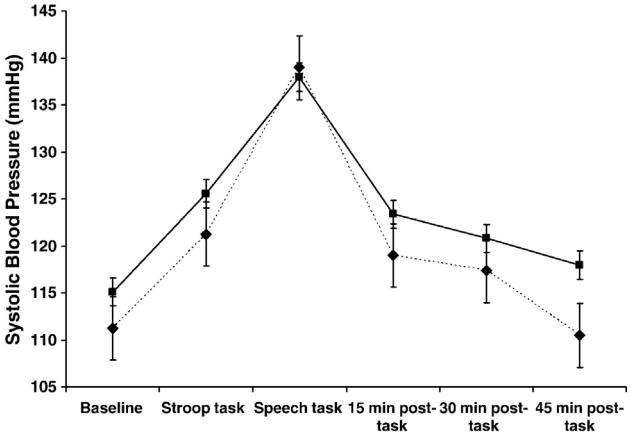

Fig. 1. Mean systolic blood pressure over the study period for participants with positive (solid line) and negative (dashed line) family histories of cardiovascular disease. Mean values are adjusted for participant's own baseline systolic blood pressure, body mass index, waist to hip ratio, gender and smoking status. Error bars are standard error of the mean.

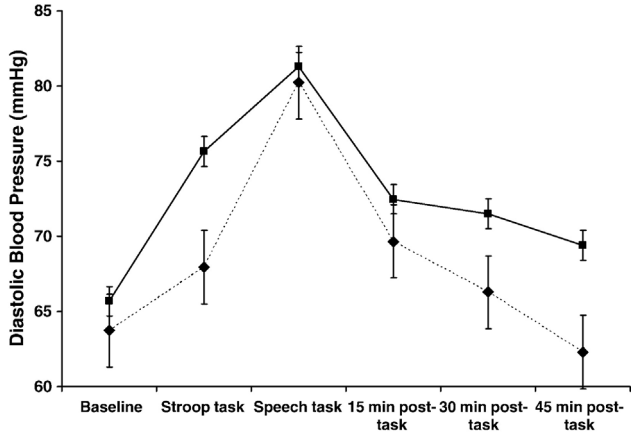

Fig. 2. Mean diastolic blood pressure over the study period for participants with positive (solid line) and negative (dashed line) family histories of cardiovascular disease. Mean values are adjusted for participant's own baseline diastolic blood pressure, body mass index, waist to hip ratio, gender and smoking status. Error bars are standard error of the mean.

3.5. Family history of cardiovascular disease risk and physiological responsivity

There was no difference in systolic BP task reactivity between participants with a positive and negative FH of cardiovascular disease risk. However, an effect of family history was found for task recovery, since participants with a positive FH of cardiovascular disease had slower systolic BP recovery ($F_{1,70}=4.42$, $p=.039$). Systolic BP averaged 3.36 mmHg (±11.1) above baseline in the final (40–45 min) recovery trial in the positive FH group, compared with a decrease of 3.11 mmHg (±12.6) in the negative FH group, after adjusting for baseline systolic BP, smoking status, WHR and BMI (see Fig. 1). This effect remained significant when the systolic BP response to task 2 was included as a covariate ($F_{1,69}=6.04$, $p=.017$), indicating that the recovery effect was independent of stress reactivity.

Participants with a positive FH of cardiovascular disease risk had a significantly stronger diastolic BP reaction to task 1 ($F_{1,68}=7.76$, $p=.007$) and significantly poorer recovery ($F_{1,68}=7.06$, $p=.010$) after controlling for participants' own baseline diastolic BP, smoking status, WHR and BMI. These data are shown in Fig. 2. The mean increase in diastolic BP during task 1 adjusted for covariates was 10.23 mmHg (±8.1) in the positive and 2.58 mmHg (±9.6) in the negative FH groups. During the final recovery trial, diastolic BP remained an average of 3.85 mmHg (±8.4) above baseline in the positive FH group, while falling 2.22 mmHg (±7.9) below baseline in the negative FH group. The difference in recovery response remained significant after the diastolic BP response to task 2 was included as a covariate ($F_{1,67}=8.04$, $p=.006$), indicating that the effect of recovery was independent of stress reactivity.

Univariate analysis of covariance revealed a significant gender by FH interaction for task 1 heart rate reactivity ($F_{1,83}=5.69$, $p=.019$). Female participants with a positive FH of cardiovascular disease risk were more reactive to task 1 ($F_{1,54}=8.74$, $p=.005$) than those with a negative FH, with mean increases of 8.33 bpm (±5.8) and 3.18 bpm (±3.9) respectively, adjusted for baseline heart rate, smoking status, WHR and BMI. No difference was found for male participants, and there were no FH effects for heart rate recovery or reactivity to task 2. There was also a significant gender by FH interaction for HRV task reactivity ($F_{1,31}=4.48$, $p=.026$). When the sample was split by gender, female participants with a positive FH of cardiovascular disease risk were marginally more reactive to task 1 ($F_{1,19}=3.37$, $p=.082$; positive FH=−19.85, ±20.5; negative FH=−8.61, ±15.1) and significantly more reactive to task 2 ($F_{1,19}=7.52$, $p=.013$; positive FH=−22.67, ±20.3; negative FH=−9.91, ±16.7) than those with a negative FH of cardiovascular disease risk. Male participants did not differ in terms of HRV and family history risk, and no family history differences in HRV recovery were found. Subjective stress responses did not vary with family history of cardiovascular disease risk.

4. Discussion

In the present study it was hypothesised that participants with a positive family history of cardiovascular disease risk would exhibit greater physiological responses and impaired recovery from two laboratory-based mental stress tasks. Using a cumulative score for parents and grandparents, the results revealed that a positive family history of hypertension was not associated with exaggerated cardiovascular response in young adults. However, a positive family history of cardiovascular disease risk defined more broadly was associated with slower systolic and diastolic BP recovery, with heightened diastolic BP reactivity to one of the two tasks, and with heightened heart rate and HRV reactivity to the stressors in women. These effects were independent of baseline physiology, WHR, BMI and smoking status.

The lack of association between cardiovascular responses and family history of hypertension is contrary to some previous studies. However, the literature on this topic is mixed, and Pierce et al. (2005) have argued that differences are more pronounced in studies in which cardiovascular stress reactions are relatively small. Our protocol generated large responses on average. Additionally, studies that have defined hypertensive history objectively rather than by participants' reports have also shown limited differences (De Visser et al., 1995; Manuck et al., 1996).

Reliable associations were observed between family history of cardiovascular disease risk in general and stress reactivity and recovery. This classification was based on parental reports of high cholesterol, high BP, diabetes and coronary heart disease. Parents also provided information about their own parents, so that two generations of risk could be analyzed. The most consistent effect was for BP recovery, which was slower in the positive family history group (Figs. 1 and 2). De Visser et al. (1995) observed slower recovery in the offspring of hypertensive parents, though this was secondary to differences in stress reactivity. In the present study, effects persisted after reactions to task 2 were included as covariates, so were independent of reactivity effects. The finding adds to recent literature emphasising variations in post-stress recovery as determinants of cardiovascular risk. Thus slow recovery has been associated with psychosocial risk factors such as

low socioeconomic status (Steptoe et al., 2002), and predicts progression in clinic BP levels longitudinally (Steptoe and Marmot, 2005; Stewart et al., 2006). The mechanisms driving this response are unclear. Slow recovery may reflect dysregulation of homeostatic mechanisms, or acute behavioural responses such as rumination may be responsible (Glynn et al., 2002). No family history group differences were found for recovery of heart rate or HRV. This may be because these variables are typically much swifter to return to baseline than blood pressure (Linden et al., 1997). It is striking in the present study that heart rate and HRV had returned to baseline by the 15 min post-task trial, while BP remained elevated (Table 3).

The fact that heightened cardiovascular reactivity and slow recovery in participants with a positive family history of cardiovascular disease risk were independent of WHR, BMI, baseline cardiovascular levels and smoking status indicates that effects were not secondary to risk factors already present in this group. The investigation also revealed that men showed greater blood pressure reactivity and poorer recovery than women. If elevated cardiovascular responsivity is related to increased risk of cardiovascular disease (as this study suggests) this may help to explain why men have a higher risk of cardiovascular disease (Stoney et al., 1988).

Family history differences were only found for heart rate, systolic and diastolic BP in response to task 1. The absolute BP and heart rate levels were greater during task 2 than task 1, so it is possible that a ceiling effect prevented group differences from emerging. Against this, however, is the fact that family history differences in HRV during task 2 were found.

The results of the study support the notion that cardiovascular reactivity may mediate associations between genetic or family environment factors and the development of cardiovascular disease (Turner and Hewitt, 1992). Individual differences in cardiovascular function arise from polymorphisms in the genes encoding elements of the adrenergic and serotonergic systems. These result in aberrations in transmitter synthesis, transmitter release and reuptake, enzymatic degradation and receptor activation, all of which may lead to individual genetic susceptibility to heightened cardiovascular reactivity and ultimately cardiovascular disease (McCaffery et al., 2002, 2003; Snieder et al., 2002).

The strengths of this study include obtaining cardiovascular risk information directly from participants' parents, and indexing risk on the basis of two generations. However, the reliability of parental reports is uncertain. The incidence of grandparents with reported cardiovascular disorders was very low in this sample. For example, the 12.4% high cholesterol incidence reported for grandparents in the present study is lower than that reported for parents, and different from the 2003 UK national average (Joint Health Survey Unit, 2005). It is likely that grandparent cardiovascular risk factors were under-reported. Similarly, it is not possible to ascertain how accurate parents' own details were. There were also a number of non-responders to the parental questionnaires. Statistical power would have been reduced substantially if only subjects with two parents had been assessed. It was decided, therefore, to classify the non-responding partners of parents that did respond with a negative family history. This meant that the negative family offspring group may have contained false positives which could have diluted responsivity differences. Finally, although the findings suggest that responsivity precedes cardiovascular disease onset, the cross-sectional nature of the design means that the causal direction of this relationship cannot be confirmed. Future investigations should include longitudinal assessment and would benefit from the use of experimental and pharmacological manipulations to determine whether interruption of proposed pathways could alter health outcomes.

The findings from this study suggest that family history of cardiovascular disease risk contributes to individual differences in stress responsivity in healthy young adults. The use of a family history design indicates that physiological stress responsivity could contribute to the future development of cardiovascular disease. In accordance with the model of allostatic load, it can be theorised that, over time repeated heightened cardiovascular stress responsivity may result in cumulative detrimental alterations in cardiovascular structure and function which could result in increased cardiovascular disease incidence in those most at risk (McEwen, 1998). It should however be recognized that this experimental design is only valid if the heightened cardiovascular risk associated with stress is due to genetic and familial effects. If increased responsivity derives from other sources (such as current life stress), then family history classification will be irrelevant; nevertheless, the study does suggest that the use of a family history design is valuable when identifying individuals most at risk, and may provide an opportunity for early interventions and improved control of hypertension, high cholesterol, diabetes and heart disease in the future.

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