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Perceived stress as a risk factor for changes in health behaviour and cardiac risk profile: a longitudinal study

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Abstract. Rod NH, Grønbæk M, Schnohr P, Prescott E, Kristensen TS (University of Copenhagen; University of Southern Denmark; Bispebjerg University Hospital; and Task-Consult, Copenhagen, Denmark). Perceived stress as a risk factor for changes in health behaviour and cardiac risk profile: a longitudinal study. *J Intern Med* 2009; doi: 10.1111/j.1365-2796.2009.02124.x

Objective. The aim of this study was to evaluate the long-term effects of stress on changes in health behaviour and cardiac risk profile in men and women.

Design. A prospective cohort study.

Setting. The Copenhagen City Heart Study, Denmark.

Subjects. The analyses were based on 7066 women and men from the second (1981–1983) and third (1991–1993) wave of the Copenhagen City Heart Study. All participants were asked questions on stress and health behaviour and they had their weight, height, blood pressure and level of blood lipids measured by trained personnel.

Main outcome measures. Changes in health behaviour (smoking, physical activity, alcohol consumption, overweight) and cardiac risk profile (cholesterol, HDL cholesterol, blood pressure, diabetes).

Results. Individuals with high levels of stress compared to those with low levels of stress were less likely to quit smoking (OR = 0.58; 95% CI: 0.41–0.83), more likely to become physically inactive (1.90; 1.41–2.55), less likely to stop drinking above the sensible drinking limits (0.43; 0.24–0.79), and stressed women were more likely to become overweight (1.55; 1.12–2.15) during follow-up. Men and women with high stress were more likely to use antihypertensive medication (1.94; 1.63–2.30), and stressed men were more than two times as likely to develop diabetes during follow-up (2.36; 1.22–4.59).

Conclusion. This longitudinal study supports a causal relation between stress and cardiovascular diseases mediated through unfavourable changes in health behaviour and cardiac risk profile.

Keywords: cardiovascular diseases, health behaviour, psychological stress.

Introduction

Psychological stress is becoming an established risk factor for cardiovascular disease [1–4]. In a recent large case–control study that included cases and controls from 52 countries, a higher risk of myocardial infarction was reported amongst individuals who experienced stress at home or at work, were under severe financial stress, had experienced stressful life events within the last year or were depressed [5]. Evidence of mechanisms linking stress to cardiovascular disease is important in making causal inference, but only few studies have tried to disentangle the complex relations between stress and the mediating factors. It is often assumed that a relation between psychological stress and risk of cardiovascular disease

is partly mediated by changes in health behaviour [6]. Accordingly, stress has been found to be associated with adverse health behaviour such as physical inactivity and smoking in several cross-sectional studies [7–9]. However, it is difficult to tell the cause apart from the effect in such studies and longitudinal changes in health behaviour may be of more interest. Stress could also affect the risk of cardiovascular disease by repeated activation of the autonomic nervous system and the hypothalamic–pituitary–adrenal (HPA) axis, which may lead to more direct pathophysiological changes in cardiac risk profile such as alterations in blood lipids and blood pressure [6, 10]. The relation between stress and cardiac risk profile has mainly been evaluated in laboratory settings with individuals exposed to acute stressors such as performing a speech or taking a test, and the relation between stress of everyday life and long-term changes in risk profile has not been studied as extensively. The aim of this study was to evaluate the effect of stress on longitudinal changes in health behaviour and cardiac risk profile in more than 7000 men and women prospectively followed for a decade.

Materials and methods

Study population

The Copenhagen City Heart Study is a longitudinal study initiated in 1976. An age-stratified random sample of 19 698 men and women, 20–93 years of age, were invited to participate in the study. A physical examination was performed and the participants were asked to fill in a questionnaire regarding various risk factors. In 1981–1983, the study population was supplemented with 500 men and women, 20–25 years of age, and additional study assessments were performed for both new and continuing study participants. The study participants were asked about stress only at the second examination; this information was used as baseline for this study. All participants gave written informed consent. A detailed description of the Copenhagen City Heart Study has previously been published [11]. The 12 698 women and men who participated in the second examination constituted a response proportion of 70% and the vast majority of the participants were Caucasians. Participants with ischaemic heart disease or stroke at baseline (n = 664) or with missing information on stress or other covariates (n = 68) were excluded, leaving 11 966 individuals for the baseline analyses. All surviving participants (n = 10 012) were invited to a third wave of the study in 1991–1993 and 7270 men and women participated, constituting a response proportion of 57% of those who participated in the second wave of the study. Participants with ischaemic heart disease or stroke at baseline (n = 175) or with missing information on stress or other covariates (n = 19) were excluded, leaving 4113 women and 2953 men for the longitudinal analyses.

Perceived stress

The study participants were asked about stress in terms of intensity and frequency at baseline in 1981–1983. In the questionnaire, stress was exemplified as the sensation of tension, nervousness, impatience, anxiety or sleeplessness and no time frame was specified. To assess stress intensity, the participants were asked ‘Do you feel stressed?’ and the response categories were: (i) no, (ii) light, (iii) moderate or (iv) high. To assess stress frequency, the participants were asked ‘How often do you feel stressed?’ and the response categories were: (i) never/hardly ever, (ii) monthly, (iii) weekly or (iv) daily. To combine the two dimensions of stress intensity and frequency, the two questions were added and combined into a 7-point stress score ranging from 0 (indicating low stress) to 6 (indicating high daily stress). For example, if a woman reported moderate daily stress, this woman would be given a stress score of 5 (two points for moderate at the intensity dimension plus three points for daily at the frequency dimension). The stress score was categorized into low (0–1 point), medium (2–4 points) and high (5–6 points) stress.

Health behaviour

Measures of health behaviour included smoking, physical activity, alcohol consumption and body mass index. As part of the self-administered questionnaire, the participants were asked about their smoking

habits, their level of physical activity in leisure time and their average weekly consumption of alcohol. These measures were dichotomized into current smoker versus nonsmoker; inactive versus active; drinking above sensible drinking limits versus not drinking above sensible drinking limits. The sensible drinking limits in Denmark are defined as 14 drinks per week for women and 21 drinks per week for men. Height and weight were measured with participants wearing light clothing without shoes. Body mass index was calculated as weight in kilograms divided by height in metres squared (kg/m). Overweight was defined as a body mass index above 25 kg/m.

Cardiac risk profile

Measures of cardiac risk profile included total cholesterol, HDL cholesterol, blood pressure and diabetes in accordance with the factors used in the Framingham risk score [12]. According to this risk prediction algorithm, the following cut-off points constitute high risk of developing coronary heart disease and are therefore used in this study: total cholesterol ≥6.22 mmol L^{-1}; HDL cholesterol ≤1.16 mmol L^{-1}; high blood pressure: diastolic blood pressure ≥90 mmHg or systolic blood pressure ≥140 mmHg; self-reported diabetes. Self-reported use of antihypertensive medication was used as an indicator of treated hypertension.

Statistical methods

First, the associations between stress and health behaviour or cardiac risk profile at baseline were addressed in a cross-sectional study design. Secondly, the longitudinal associations between stress and developing an adverse health behaviour or cardiac risk profile were estimated amongst those without the unfavourable level of the factor in question at baseline. For example, the association between stress and becoming overweight were assessed amongst those with normal weight at baseline. Subsequently, the longitudinal associations between stress and changing adverse health behaviour or risk factor profile were addressed amongst those at high risk at baseline. For example, the association between stress and smoking cessation was assessed amongst those who smoked at baseline. A logistic regression model was fitted to adjust for potential confounding from age (continuous), education (less than 8 years, 8–11 years or 12 or more years) and marital status (married, never married, divorced/separated, widowed). Initially, all analyses were performed separately for men and women, but if the associations were similar in men and women, the analyses were combined to gain statistical power. A Wald test was used to test for effect modification of sex in the sex-specific analyses.

Results

The mean age at baseline was 53 years for women and men who participated in both the second and third wave of the Copenhagen City Heart Study and the baseline characteristics of the population can be seen in Table 1. Individuals who were lost to follow-up between the two waves (n = 5428) were older and had a more adverse risk factor profile than those who participated in both waves (Table 1). We have previously found perceived stress to be associated with higher risk of ischaemic heart disease in both women (hazard ratio = 1.23; 95% CI: 1.01–1.51) and men (1.25; 1.00–1.56) in the Copenhagen City Heart Study [4].

Stress and health behaviour

Individuals with high levels of stress were more likely to smoke at baseline (OR = 1.59; 95% CI: 1.38–1.84) and less likely to quit smoking during follow-up (0.58; 0.41–0.83) compared to those with low levels of stress (Table 2). Those with high levels of stress than those with low levels of stress were also more likely to be physically inactive at baseline (OR = 2.63; 95% CI: 2.25–3.08) and to become physically inactive during follow-up (1.90; 1.41–2.55). There were no differences in the proportions of inactive persons who became active during follow-up according to stress. Individuals with high stress had an OR of 1.87 (95% CI: 1.53–2.27) of drinking above the sensible drinking limits at baseline compared with those with low stress. Those with medium levels of stress compared with those with low levels of stress were slightly more likely to start drinking above the limits (OR = 1.32; 95% CI:

Table 1 Baseline characteristics of 7066 Danish women and men who participated in both the second (1981–1983) and third (1991–1993) wave of the Copenhagen City Heart Study according to level of stress as well as amongst women and men who were lost to follow-up between the two waves

	Participants in both the 2nd and 3rd waves (n = 7066)	Stress			Participants who were lost to follow-up between the two waves (n = 5428)
		Low (n = 3275)	Medium (n = 3285)	High (n = 506)	
Age at baseline (year); mean ± SD	53 ± 12	55 ± 12	52 ± 11	55 ± 10	60 ± 12
Women; %	58	53	61	72	52
Education <8 year; %	40	43	36	48	53
Married; %	66	68	67	54	58
Current smoker; %	55	53	56	62	62
Physically inactive; %	13	12	13	26	22
Alcohol above sensible drinking limits; %	13	12	13	17	12
Overweight; %	46	50	44	42	51
Total cholesterol (mmol/L); mean ± SD	5.9 ± 1.2	5.9 ± 1.2	5.8 ± 1.2	5.9 ± 1.2	6.0 ± 1.2
HDL cholesterol (mmol/L); mean ± SD	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	1.1 ± 0.3
Systolic blood pressure (mmHg); mean ± SD	137 ± 20	138 ± 20	136 ± 20	137 ± 20	146 ± 23
Diastolic blood pressure (mmHg); mean ± SD	84 ± 12	84 ± 12	84 ± 12	85 ± 11	86 ± 13
Antihypertensive treatment; %	13	10	14	19	23
Diabetes; %	1	1	1	1	4

1.09–1.60), and stressed individuals who drank above the limits at baseline were less likely to stop drinking above the limits during follow-up (0.43; 0.24–0.79). Stressed women were slightly less likely to be overweight at baseline compared with women with low stress (OR = 0.74, 95% CI: 0.62–0.88), but they were on the other hand more likely to become overweight during follow-up (1.55, 1.12–2.15). There were no differences in the proportion of men who were overweight at baseline or who changed weight during follow-up according to stress. The *P*-value for effect modification between sex and stress with regard to becoming overweight was 0.14.

Stress and cardiac risk profile

Stress was not associated with total cholesterol, HDL cholesterol or high blood pressure at baseline or during follow-up (Table 3). Compared with those with low stress, women and men with high stress were about two times more likely to use antihypertensive medication at baseline and they were also more likely to start using antihypertensive medication during follow-up (OR = 1.39; 95% CI: 1.05–1.84). Stress was not associated with diabetes at baseline, but stressed men were more than twice as likely to develop diabetes during follow-up as men with low stress (OR = 2.36; 95% CI: 1.22–4.59). The *P*-value for effect modification between sex and stress regarding development of diabetes was 0.10.

Discussion

In this longitudinal study where more than 7000 men and women were followed for a decade, high stress was associated with adverse health behaviour, use of antihypertensive medication and development of diabetes. We have previously found stress to be a modest risk factor for ischaemic heart disease in the Copenhagen City Heart Study, and in line with the findings of this study, we found the risk estimates to attenuate after adjustment for measures of smoking, physical activity, alcohol consumption and body mass index at baseline [4]. According to this study, we might have

Table 2 Associations of stress with health behaviours at baseline (1981–1983) and changes in health behaviours during follow-up (1991–1993) amongst participants in the Copenhagen City Heart Study

	Study population	Low stress		Medium stress		High stress	
	N	%	OR[a] (95% CI)	%	OR[a] (95% CI)	%	OR[a] (95% CI)
Smoking							
Baseline	11,964	56	1 (ref)	59	1.13 (1.05; 1.22)	67	1.59 (1.38; 1.84)
Start smoking[b]	3161	5	1 (ref)	6	1.23 (0.89; 1.71)	6	1.54 (0.81; 2.91)
Quit smoking[c]	3879	21	1 (ref)	19	0.88 (0.75; 1.05)	12	0.58 (0.41; 0.83)
Physical inactivity							
Baseline	11,960	15	1 (ref)	16	1.19 (1.07; 1.32)	32	2.63 (2.25; 3.08)
Become inactive[b]	6058	11	1 (ref)	9	0.97 (0.81; 1.16)	19	1.90 (1.41; 2.55)
Become active[c]	929	69	1 (ref)	67	0.84 (0.62; 1.14)	63	0.74 (0.48; 1.14)
Alcohol above sensible drinking limits							
Baseline	11,916	12	1 (ref)	13	1.22 (1.08; 1.38)	17	1.87 (1.53; 2.27)
Start drinking above limits[b]	6081	7	1 (ref)	9	1.32 (1.09; 1.60)	6	1.00 (0.64; 1.54)
Stop drinking above limits[c]	887	46	1 (ref)	41	1.03 (0.68; 1.55)	40	0.43 (0.24; 0.79)
Overweight (women)							
Baseline	6671	44	1 (ref)	38	0.87 (0.78; 0.96)	38	0.74 (0.62; 0.88)
Become overweight[b]	2406	22	1 (ref)	25	1.15 (0.94; 1.41)	32	1.55 (1.12; 2.15)
Become normal weight[c]	1507	10	1 (ref)	11	1.21 (0.85; 1.72)	13	1.39 (0.76; 2.54)
Overweight (men)							
Baseline	5228	60	1 (ref)	54	0.93 (0.83; 1.05)	55	0.86 (0.68; 1.10)
Become overweight[b]	1244	27	1 (ref)	26	0.87 (0.67; 1.13)	25	0.87 (0.47; 1.62)
Become normal weight[c]	1612	10	1 (ref)	9	1.12 (0.78; 1.62)	5	0.59 (0.21; 1.69)

[a]Adjusted for sex, age, education, marital status. [b]Amongst those who do not have the adverse health behaviour in question at baseline. [c]Amongst those who have the adverse health behaviour in question at baseline.

expected even more of the association between stress and ischaemic heart disease to be explained by these factors, if we had also taken changes in health behaviour and cardiac profile during follow-up into account. This is in line with recent results from the Whitehall II study, which reports work-related stress to be an important determinant of coronary heart disease amongst civil servants in London, a link most likely mediated through effects on both health behaviour and neuroendocrine stress pathways [9].

The human body is in a state of dynamic equilibrium, also known as allostasis [13]. The stress response is initiated when external or internal forces, the stressors, challenge this allostasis. The sympathetic nervous system and the HPA axis are the main mediators of the stress response, and changes in health behaviour and neuroendocrine changes may be important in gaining the energy required to re-establish allostasis. Most allostatic mediators have a biphasic role with protective effects in the short run and damaging effects under chronic stress. Long-term stress is therefore hypothesized to play a role both in the development and in the progression of disease.

Smoking may increase the risk cardiovascular disease through a range of biological mechanisms. Amongst other things, nicotine can increase fibrinogen and promote thrombosis, increase myocardial work, activate release of catecholamines and thereby promote the forming of atherosclerotic plaque [14]. Most previous studies on stress and smoking have been cross-sectional making it difficult to tell cause from effect [15]. An exception is a small study including 189

Table 3 Associations of stress with cardiac risk profile at baseline (1981–1983) and changes in cardiac risk profile during follow-up (1991–1993) amongst participants in the Copenhagen City Heart Study

	Study population	Low stress		Medium stress		High stress	
	N	%	OR[a] (95% CI)	%	OR[a] (95% CI)	%	OR[a] (95% CI)
Total cholesterol ≥6.22 mmol/L							
Baseline	11,775	36	1 (ref)	35	1.05 (0.96; 1.14)	38	1.04 (0.90; 1.20)
Normal → high cholesterol[b]	4478	34	1 (ref)	34	1.00 (0.88; 1.14)	34	0.88 (0.68; 1.15)
High → normal cholesterol[c]	2390	18	1 (ref)	17	1.03 (0.82; 1.29)	21	1.44 (0.97; 2.12)
HDL cholesterol ≤1.16 mmol/L							
Baseline	11,759	59	1 (ref)	54	0.91 (0.83; 0.98)	53	0.94 (0.81; 1.09)
Normal → low HDL[b]	3082	4	1 (ref)	5	1.39 (0.95; 2.04)	1	0.34 (0.10; 1.10)
Low → normal HDL[c]	3769	69	1 (ref)	70	0.97 (0.84; 1.13)	71	0.96 (0.70; 1.30)
High blood pressure							
Baseline	11,946	57	1 (ref)	51	1.06 (0.98; 1.15)	54	0.99 (0.85; 1.14)
Normal → high BP[b]	3677	45	1 (ref)	39	0.94 (0.81; 1.10)	43	0.94 (0.71; 1.23)
High → normal BP[c]	3314	16	1 (ref)	20	1.24 (1.03; 1.50)	22	1.36 (0.96; 1.91)
Antihypertensive medication							
Baseline	11,966	14	1 (ref)	17	1.43 (1.28; 1.59)	24	1.94 (1.63; 2.30)
Start using[b]	6109	14	1 (ref)	15	1.20 (1.03; 1.40)	19	1.39 (1.05; 1.84)
Stop using[c]	877	29	1 (ref)	29	0.86 (0.62; 1.20)	39	1.24 (0.75; 2.04)
Diabetes (women)							
Baseline	6679	1	1 (ref)	2	1.29 (0.86; 1.95)	1	0.70 (0.31; 1.56)
Develop diabetes[b]	4043	2	1 (ref)	2	1.03 (0.65; 1.64)	2	0.80 (0.33; 1.91)
Diabetes (men)							
Baseline	5206	3	1 (ref)	3	1.33 (0.95; 1.89)	4	1.32 (0.69; 2.52)
Develop diabetes[b]	2867	4	1 (ref)	4	1.08 (0.72; 1.61)	9	2.36 (1.22; 4.59)

[a]Adjusted for sex, age, education, marital status. [b]Amongst those who do not have unfavourable levels of the risk factor in question at baseline. [c]Amongst those who have unfavourable levels of the risk factor in question at baseline.

male workers followed prospectively for 3 years, in which they found increasing decision latitude to be associated with a decrease in cigarette smoking [16]. This is in line with the results from this study where we found men and women with high stress to smoke more at baseline and to also be less likely to quit smoking during follow-up.

Physical activity reduces the incidence of cardiovascular disease most likely by lowering established atherosclerotic risk factors, including elevated blood pressure, insulin resistance and glucose intolerance, elevated triglyceride concentrations and obesity [17]. Stress could affect the risk of cardiovascular disease by reducing the time and energy required to engage in physical activity. On the other hand, there is a general consensus that exercise has an alleviating effect on anxiety and mood states [18]. So, individuals who engage in regular physical activity may perceive their life as less stressful than individuals who do not. Women and men with high levels of stress were two times less likely to engage in physical activity in their leisure time at baseline compared with those who were not stressed, and we also found stressed men and women to be more likely to stop exercising during follow-up, indicating that stress may be an actual risk factor for lack of physical activity.

A J-shaped relation between alcohol consumption and cardiovascular disease has been reported in many

observational studies [19]. Both experimental and human research support that stress may lead to higher alcohol intake, especially in men [20, 21]. In line with this, we found stress to be associated with drinking above the sensible drinking limits at baseline, and that stressed individuals were less likely to stop drinking above these limits during follow-up.

Stress may also affect the risk of cardiovascular disease by inducing changes in frequency, amount and type of food consumed. We did not have information on diet in this study, but weight changes may be used as an indicator of dietary changes and we found stressed women to be more likely to become overweight during follow-up. It is difficult to disentangle the effect of stress on dietary patterns because of the complex range of other factors that also influence the process of choosing food. In a summary of the literature, Wardle and Gibson [22] reported inconsistent findings on stress-induced changes in diet; some people tend to over-eat in stressful situations, whilst others eat less. However, some evidence indicates that during stress, individuals tend to eat smaller, but more frequent, amounts of energy dense, fatty and sweet foods [22–24].

Experimental studies have found acute stress to lead to pathophysiological changes in cardiac risk profile and thereby more directly explain a link to cardiovascular disease [6].We found a more chronic measure of stress to affect some – but not all – factors in the cardiac risk profile in this study. Although we found no associations between stress and hypertension, both men and women with high stress used more antihypertensive medication. Elevated blood pressure is assumed to be a key mechanism through which stress increases the risk of heart disease, but the empirical evidence has been conflicting [25, 26]. In line with our results, recent findings from the Whitehall II Study showed no mediation effect of hypertension for the relation between job strain and coronary heart disease [27]. More interestingly, men with high levels of stress compared with those with low levels of stress were more than two times as likely to develop diabetes during follow-up in this study, which may be an important mediating pathway between stress and cardiovascular disease.

Strengths and weaknesses

To our knowledge, this is the first large-scale study to address longitudinal changes in both health behaviour and cardiac risk profile. The prospective design of the Copenhagen City Heart Study ensured temporality between stress and changes in health behaviour and cardiac risk profile, and the large sample size ensured sufficient statistical power to prospectively assess changes in health behaviour and cardiac risk profile.

Two questions on stress intensity and frequency were used to assess perceived stress. As these two questions are not validated against a more extensive scale, such as the Perceived Stress Scale [28], we cannot fully determine the magnitude of the misclassification. By using only two questions on stress instead of a more extensive scale, a stronger relation between stress and changes in health behaviour and cardiac risk profile may have been blurred. However, in a recent study, two single-item measures on stress were found to be reliable at measuring stress with a validity similar to three longer multi-item measures on perceived stress [29]. This may provide some assurance that the two-item measurements used in this study provided a reasonable measure of stress. Also, the same measure of stress has previously been found to be predictive of morbidity and mortality in the same cohort [4, 30, 31]. In the questionnaire, stress was exemplified as impatience, anxiety and sleeplessness. We cannot fully exclude that we have also partly measured the effects of depressive symptoms or personality traits, which may be closely related to stress as it is measured in this study.

Slightly less than half of those who participated in the second wave of the Copenhagen City Heart Study did not participate in the third wave either because they died between the two waves (21%) or because they chose not to participate (22%). Those who did not participate were older and had a more adverse risk factor profile and one may be concerned that differential dropout could have affected our results. By only including those who participated in both surveys (which was the only way to get information on changes in health behaviour and cardiac risk profile),

we might have created an artificial association between stress and the risk factors. For example, we assessed the association between stress and smoking cessation amongst individuals who smoked at baseline (i.e. amongst those who were at risk of quitting smoking). As both stress and smoking cessation can affect survival, knowing that a person survived and was stressed at baseline would make it more likely that he or she had quit smoking during follow-up. So, even if stress and smoking cessation were independent, conditioning on survival may have created a positive association between stress and smoking cessation. This is opposite to the negative association we observed between stress and smoking cessation in this study and if anything that this type of bias may have resulted in attenuated effect estimates.

There may be some concern that personal traits could cause some individuals to report negatively on both stress and health behaviour and thereby create a spurious association between the two. This is a potential problem with the baseline associations, whilst we find it unlikely to explain the changes in health behaviour over time. Assessments of body mass index, blood lipids and blood pressure were performed independently of individual reportings of stress and are therefore not expected to be affected by this type of bias.

In conclusion, perceived stress is associated with unfavourable changes in health behaviour and cardiac risk profile, which support a causal relation between stress and cardiovascular diseases mediated by these pathways.

Conflict of interest statement

There are no conflicts of interests.

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