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Workplace Re-organization and Changes in Physiological Stress Markers

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Abstract

The aim of this study was to investigate changes in physiological stress markers as a consequence of workplace reorganization. Moreover, we aimed to investigate changes in the psychosocial work environment (job strain, effort-reward imbalance (ERI), in psychological distress (stress symptoms, perceived stress) and the mediating effect of these factors on changes in physiological stress markers.

We used data from a longitudinal study that studied the health consequences of a major reorganization of non-state public offices executed in Denmark on 1 January 2007. Collection of clinical and questionnaire data was in 2006 and 2008, and in this sub-study we included 359 participants. To reflect stress reactions of the autonomic nervous system, the endocrine system and the immune system, we included 13 physiological markers.

We observed significant change in several physiological stress markers. Moreover stress symptoms and perceived stress increased significantly but did not explain the physiological changes. ERI and job strain did not change significantly and adjustment for these factors did not change the results.

In this study, we found a significant association between workplace reorganization and changes in several physiological stress markers. However, these changes could not be explained by a significant change in psychological distress.

Keywords: Psychosocial work conditions; Longitudinal study; Autonomic nervous system; Endocrine system; Immune system

Introduction

It is well documented that impaired psychosocial work environment increases the risk of developing cardiovascular disease [1,2] and depression [3,4]. Moreover, other diseases, such as allergy, asthma and various autonomic conditions, were aggravated [5-7]. The pathological mechanisms linking impaired psychosocial work environment and disease may be prolonged physiological stress reactions.

The catabolic stress reactions of acute stress are well known, and it is probable that the same mechanisms are involved in long-term stress [8]. Acute and chronic stress responses promote adaptation via responses of the autonomic nervous system, the endocrine system and the immune system [9](figure 1).

Several studies have investigated the link between psychosocial work environment and physiological stress markers. In relation to the autonomic nervous system, a recent review concluded evidence pointing to a relationship between psychosocial work environment and hypertension although there also was a focus on the problematic aspects of the subject as different models for measuring and assessing effect, varying time spans and outcome variables [10]. This association corresponds to other studies [11,12]. The clinical relevance of heart rate variability (HRV) is the association with cardiovascular disease [13]. A low HRV may be associated with increased cardiovascular disease-

The autonomic nervous system
- Systolic blood pressure (mmHg) (SBP) ↑
- Diastolic blood pressure (mmHg) (DBP) ↑
- Heart rate variability, total power, work (ms^2) (TPw) ↓
- Heart rate variability, total power, sleep (ms^2) (TPs) ↓
- Heart rate variability, low frequency/high frequency, work (ratio) (LF/HFw) ↑
- Heart rate variability, low frequency/high frequency, sleep (ratio) (LF/HFs) ↑

The endocrine system
- Cortisol at awakening (nmol/l) (S0) ↑
- Awakening cortisol response (nmol/l) (ACR) ↑
- Glycated haemoglobine (mmol/l) (HBA1C) ↑
- High density lipoprotein cholesterol (mmol/l) (HDL) ↓
- Total cholesterol (mmol/l) (TCHOL) ↑

The immune system
- C-reactive protein (mg/l) (CRP) ↑
- Interleukin 6 (µmol/l) (IL6) ↑
- Fibrinogen (µmol/l) (FIBR) ↑

Figure 1: Physiological stress systems, stress markers and expected stress reactions.

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related morbidity and mortality [14]. In relation to psychosocial work environment, one study found association between low HRV and both high job strain and low decision latitude [15] and another study observed association between low HRV and high ERI in women [16]. Moreover, HRV might link to cardiovascular disease through factors related to the metabolic syndrome [17].

The metabolic syndrome is defined by various physiological changes, of which insulin resistance is the primary metabolic defect. In addition, the syndrome includes abdominal obesity, dyslipidaemia and hypertension. In a prospective follow-up study from 2005 using data from the Whitehall II study, there was a significant association between high job strain and metabolic syndrome [18]. Of the specific physiological markers related to the endocrine system and included in metabolic syndrome (glycated haemoglobine (HBA1C), high density lipoprotein cholesterol (HDL), and total cholesterol (TCHOL)), only HBA1C has a significant association with impaired psychosocial work environment [19].The association between psychosocial work environment and cortisol is inconsistent across studies [20]. In a recent review of 147 eligible studies, Chida et al. found positive association between an increase of awakening cortisol response (ACR) and job stress [21].

Aggravation of chronic diseases caused by psychological strain might link to inflammation and activation of the immune system. A review by Glaser from 2005 noted an association between long-term stress and an increased risk of infectious disease. Moreover, delayed wound healing and the risk of reactivation of latent infections such as herpes virus increased [22]. Different studies found positive association between psychological distress and the physiological markers c-reactive protein (CRP) and interleukin 6 (IL6) [23,24]. Moreover, a recent review stated that increased fibrinogen (FIBR) was a potential candidate for a physiological effect associated with adverse psychosocial work environment [19].

To investigate the association between psychosocial work environment and physiological stress markers, we used workplace reorganization shown to cause impaired psychosocial work environment and have negative health consequences [25,26]. The term "workplace reorganization" includes different factors such as workplace expansion and downsizing, where the latter may involve job insecurity. Ferrie et al. investigated job insecurity and found that those exposed to chronic job insecurity had the highest self-reported morbidity [27]. Another study found a higher relative risk for psychological distress between employees with self-reported increase in job insecurity compared with employees who did not report increase in job insecurity [28]. Different studies investigated downsizing and found negative health consequences in the form of increased absence due to sickness [29,30]. In a study by Westerlund, they reported a relationship between workplace expansion and an increased risk of long-term absence due to sickness and hospital admissions. The strongest association was among women in the public sector [31].

Karaseks and Theorell´s job demand-control model (job strain) [32] and Siegriest´s effort-reward imbalance model (ERI) [33] are the most used and tested models to describe the perceived psychosocial work environment. We therefore used these models to describe the effect of workplace reorganization on perceived psychosocial work environment in the form of job strain and ERI. Moreover, we wanted to describe the effect of workplace reorganization on psychological distress based on research about how psychosocial work environment relates to psychological distress [34]. We used validated questions about stress symptoms [35,36] and perceived stress.

A major reorganization of non-state public offices took place in Denmark on 1 January 2007. The non-state public sector in Denmark had two levels of administration: the counties and the municipalities. During the reorganization, the former 14 counties merged into five regions, and the 275 municipalities merged into 98. Typically, 2-4 units merged, but 25 municipalities remained unmerged and one county experienced only minor changes compared to the rest.

In contrast to earlier research on psychosocial work environment and physiological stress markers primary based on investigation of single physiological markers and cross sectional design, we used this workplace reorganization as a naturally occurring experiment to investigate changes in physiological stress markers. Moreover, we aimed to investigate changes in the psychosocial work environment (job strain, ERI), in psychological distress (stress symptoms, perceived stress) and the mediating effect of these factors on changes in physiological stress markers.

We expected workplace reorganization to affect changes in physiological stress markers according to expected stress reactions(figure1). Moreover, we hypothesized workplace reorganization to affect psychosocial work environment in the form of increased job strain and ERI and affect psychological distress in the direction of increased stress symptoms and perceived stress. We expected changes in perceived psychosocial work environment and psychological distress to have a mediating effect on physiological changes. More specific, we expected an increase in measures of psychosocial work environment and perceived distress to mediate changes in the physiological markers according to expected stress reactions.

Methods

In this sub-study, we used data from the study Organizational change, Stress and Health (OSH) [37].

The OSH study originates from The Clinic of Occupational Medicine at Hilleroed Hospital in collaboration with Statistics Denmark, The Danish Institute of Governmental Research and The National Research Centre for the Working Environment.

The regional ethics committee approved the study. All participants gave written, informed consent before entering the study, and all participants received the results of their clinical examinations.

Population

In November 2004, Statistics Denmark identified 2,030 potential participants from data regarding place of employment and salary code. The reason for identifying potential participants already in 2004 was to include only participants who had been employed for a longer period before the reorganization. The selection included white-collar employees in the administration of five municipalities and two counties and was based on our knowledge of the impending mergers. Four municipalities and one county merged with others, while one municipal and one county remained unmerged with only minor changes in tasks.

In spring 2006, the potential participants received a questionnaire and after two reminders, 1,379 employees completed it (response rate 68%). According to the answers from the questionnaires, 261 persons left the labour market or got another job between November 2004 and April 2006. Thus, 1,118 participants were included in the study.

In autumn 2006, we offered the 1,118 participants a clinical examination, and 502 agreed. We found no statistically significant difference between the 616 non-participants and the 502 participants

regarding demographic characteristics, although we observed a tendency for more perceived stress among non-participants (p=0.10).

In autumn 2008, we offered the 502 participants a follow-up clinical examination but only 391 completed. We compared the 111 participants who did not complete the follow-up with the 391 participants using data from autumn 2006 and found significant differences in the form of a higher age in the group of participants ($p<0.01$), more sick days among the 111 non-participants ($p<0.05$) and a significant higher IL6 ($p<0.01$) and ACR ($p<0.01$) among the non-participants compared with the participants.

To characterize the psychosocial work environment, psychological distress and covariates, we used data from the questionnaires in autumn 2006 and 2008. A criterion was employment in the period 2006-2008. Therefore, we excluded four persons who lost their job in this period and 28 persons who retired. To investigate changes in the physiological stress markers from 2006-2008, we included data only from persons with follow-up clinical examination of at least one physiological stress marker.

The result was 359 participants, 265 women and 94 men.

Physiological stress markers

The clinical examinations took place in autumn 2006 and 2008 at the workplace during working hours or at the Clinic of Occupational Medicine at Hilleroed Hospital.

The day before the examination, the participants received a questionnaire to complete and bring to the examination. The investigating physician reviewed the completed questionnaire and discussed issues or deficiencies, if any.

We measured weight, height, waist/hip circumference and casual blood pressure (systolic blood pressure (SBP) and diastolic blood pressure (DBP)) at the clinical examination and took blood samples (for HBA1C, HDL, TCHOL, CRP, IL6 and FIBR) that were analysed and stored afterwards in a laboratory at Hilleroed Hospital or at the National Research Centre for the Working Environment, Denmark.

For the determination of IL6, we used an enzyme-linked immune assay (R&D Systems, Minneapolis, USA). We used Westgard control charts to document that the analytical method remained under analytical and statistical control; in other words, that the trueness and precision of the analytical methods remained stable [38]. As a control, we used material from NIBSC Code No 89/548 (NIBSC, Hertfordshire, England.

We analysed the remaining blood samples following standard procedures at the hospital laboratory.

Cortisol, we measured in the saliva with a Salivette kit containing two cotton tampons (Saarstedt). The participants received the instructions to collect the first sample immediately after awakening, while still in bed, and another sample 30 minutes after awakening, at the examination together with the equipment to take home. They returned the samples to the physicians on the next day. The National Research Centre for the Working Environment analysed and kept the samples frozen at minus 20 degrees Celsius until analysis. We used cortisol at awakening (S0) and ACR, the difference between cortisol 30 minutes after awakening and S0, as variables.

We carried out the determination of cortisol in the saliva samples with a competitive radioimmunoassay (RIA) designed for quantitative in vitro measurement of cortisol in serum, plasma, urine, and saliva (Spectria Cortisol Coated Tube RIA, purchased from Orion Diagnostica, Espoo, Finland), according to the manufacturer's specifications. By inter-laboratory comparison schemes, we evaluated the method and validated the performance [39].

Only some of the participants completed the measurement of HRV (110 women, 45 men). We made this selection randomly and for practical reasons and limited equipment. HRV is the accepted term used to describe the variations of heart rate caused by a complex interaction between sympathetic and parasympathetic efferent impulse activity. We measured ambulatory ECGs in relation to HRV, and recorded the data using a 3-lead LifeCard CF Holter monitor (Delmar Reynolds Medical Inc., Irvine, CA, USA). We measured ECG over approximately 18 hours. We derived frequency domain HRV by spectral analysis of 15 min ECG during work and sleep after visual inspection and filtering for possible outliers and artefacts (ectopic beats, falsely detected beats, etc.), as previously described. In brief, we re-sampled the RR-intervals with a frequency of 4 Hz and the time series linearly detrended. We estimated the spectral components of the HRV by Welch's averaged, modified period gram method (Hamming window size 256 points, 50% overlap). We expressed HRV as the total power (TP) defined as the area under the spectral power density function in the range 0.003-0.4 Hz [16]. We also calculated the ratio between power in the low frequency range (LF, 0.04-0.15 Hz) and power in high frequency range (HF, 0.15-0.4 Hz). This ratio, low frequency/high frequency (LF/HF), has been used in a large number of studies as an indicator of the autonomic balance because an increase in LF/HF reflect changes in autonomic modulation of cardiac rhythm in the direction of more sympathetic activity relative to parasympathetic activity. We averaged spectral analysis values taken during work and sleep (3 times 5 minutes, total 15 minutes).

For calculating HRV, we used the variables heart rate variability, total power, work (TPw), heart rate variability, total power, sleep (TPs) and heart rate variability, low frequency/high frequency, work (LF/HFw), heart rate variability, low frequency/high frequency, sleep (LF/HFs). TP is the spectral power band between 0-0.4 Hz covering the spectral band of LF between 0.04-0.15 Hz and of HF between 0.15-0.4 Hz. Whereas TP is an indicator of parasympathetic activity, LF/HF reflects the sympathetic activity. For the determination of HRV, we included only recordings of the sinus rhythm. Artefacts and non-normal beats in the ECG segments we auto detected by commercial software and verified by visual inspection. Before calculating the HRV metrics, we filtered the RR-intervals for possible outliers (ectopic beats, falsely detected beats, and missed beats) using the algorithm published by Eller et al. [40], re-sampled at a frequency of 4 Hz and linearly detrended.

Perceived psychosocial work environment

Job strain: We constructed the dimensions of demand and control from a 17-item questionnaire partially derived from the job content questionnaire (JCQ) as described by Karasek et al. [32]. Eight questions measured demands: "My job requires working very fast", "My job requires working very hard", "I am asked to do an excessive amount of work", "My job is mentally demanding", "I have enough time to get the job done", "My work is done at a very high pace", "I am constantly behind with my work", "Sometimes my tasks are too difficult" (Cronbach`s alpha = 0.72), whereas nine questions measured control: "My job allows me to make a lot of decisions on my own", "On my job, I have very little freedom to decide how I do my work", "I have a lot of say about what happens on my job", "My job requires me to be creative", "My job requires that I learn new things", "My job involves a lot of repetitive work", "My job requires a high level of skill", I get to do a variety of different things on my job", "I have the opportunity to develop my own

special abilities" (Cronbach´s alpha=0.68). We categorised the answers on a 5-point Likert scale: "completely agree", "partially agree", "neither agree nor disagree", "partially disagree", or "completely disagree". The answers scored each 1-5 point, with 5 points corresponding to the highest level of demand or control. We summed up points for the two dimensions, and constructed job strain as demand/(control x 8/9). As the two dimensions did not include the same number of questions, we corrected demands by a factor 8/9.

ERI: By use of the questionnaire of Siegrist et al. [33] we measured the dimensions of effort and reward. Four questions evaluated effort (time pressure due to a heavy work load, interruptions, experiencing a more demanding work over years and pressure to work overtime) (Cronbach´s alpha = 0.75) and seven questions measured reward: Two statements considering esteem (respect from superiors and at work in general), three statements considering job promotion (promotion and work prospects, wage) and two statements considering job security (experiencing and undesirable change and risk of being laid off) (Cronbach´s alpha=0.82). The answer categories were on a 5-point scale: "disagree", "agree and I am not at all distressed", "agree and I am somewhat distressed", "agree and I am distressed" or "agree and I am very distressed". The answers scored each 1-5 point, with 5 points corresponding to the highest level of effort or reward. We summed up the points for the two dimensions, and calculated the effort/reward model as effort/ (reward x 4/7). Because the two dimensions did not include the same number of questions and no further questions were in the questionnaire, we included the correction factor 4/7 [41].

Psychological distress

Stress symptoms: We derived the variables of stress symptoms from the COPSOQ questionnaire [35] and included 10 items reflecting physiological symptoms (heart beating, headache, dizziness, stomach ache, pain in the body), cognitive symptoms (difficulty with remembering, difficulty in taking decisions, difficult to think clearly), and psychological symptoms (been irritable, felt sad). We asked the participants about symptoms during the previous 4 weeks, and the answer categories were on a 4-point scale with 4 corresponding to the highest level of symptoms and the answers categories were: "not at all", "occasionally", "often", or "daily". We summed the points of the 10 items to calculate the total score.

Perceived stress: We measured perceived stress by one question: "Stress means a situation in which a person feels tense, restless, nervous or anxious or is unable to sleep at night because his/her mind is troubled all the time. Do you feel this kind of stress these days?" [36]. The answer categories were on a 5-point Likert scale varying from "not at all" to "very much" and 5 corresponding to the highest level of perceived stress.

Co-variates: We used the following co-variates from the autumn 2006 questionnaire: Gender, age, occupation (technician, academic, clerk, consultant, other), physical activity in leisure time (less or more than 4 hours per week), and body mass index (BMI).

Moreover, we adjusted for reorganization groups according to the original design of OSH. From the information given in the questionnaire about the workplace in spring 2006 and in autumn 2008, we divided the participants into three groups: merger, new job, and control.

Of the 359 participants, 201 persons employed in the four municipalities and one county that merged with other units on 1 January 2007 formed the merger group. The new job group consisted of 113 participants who took new jobs outside the organisation during the follow-up. The control group consisted of 45 participants employed in the one municipality and one county that did not merge with another unit; these participants also stated that they had the same job tasks before and after the reform.

Statistical methods: We carried out the statistical analysis using the Statistical Package for the Social Sciences (SPSS), versions 11 and 19 (SPSS Inc., Chicago, IL, USA).

We used the t-test to compare the continuous variables for the participants and non-participants and general linear models to compare the discrete variables.

To describe demographic characteristics at baseline, we used descriptive statistics. We used Pearson Correlation to describe the correlation between physiological and psychological markers.

The analysis of changes in both the physiological and the psychological markers during the period 2006 to 2008, we examined in hierarchical linear regression analyses with explaining variables and potential confounders as covariates by use of mixed models. We analysed both the psychological and physiological markers as continuous variables.

In the analysis of the physiological stress markers model 1 was unadjusted and model 1A adjusted for gender, age (continuous variable), occupation (5 levels classification), physical activity in leisure time (2 levels classification) and reorganization groups (3 levels classification).

In the analysis of the psychological stress markers model 2 was unadjusted and model 2A adjusted for gender, age (continuous variable), occupation (5 levels classification), physical activity in leisure time (2 levels classification) and reorganization groups (3 levels classification).

To investigate the mediating effect of the psychological markers on the physiological changes, we also used mixed models; model 3 unadjusted, model 3A adjusted for job strain, model 3B adjusted for ERI, model 3C adjusted for stress symptoms and model 3D adjusted for perceived stress. Furthermore and not described in Table 5, we adjusted for BMI to observe the mediating effect of change in BMI on changes in physiological stress markers.

Results

Table 1 illustrates the demographic characteristics at baseline

Variable	
Women (%)	73.8
Age (mean) (SE)	49.4 (0.4)
Occupation (%)	
- Technician	26.6
- Academic	12.1
- Clerk	32.1
- Consultant	12.1
- Others	17.1
Smoker (%)	15.6
Physical activity (%)	
– more than 4 h weekly	52.5
Heart medicine (%)	10.6
Alcohol (mean, drinks per week) (SE)	7.3 (0.4)
BMI (mean) (SE)	25.7 (0.2)
Sickness absence (%)	
- 0-1	25.8
- 2-10	63.2
- 11-365	11.0

All values are given from questionnaire autumn 2006.

Table 1: Demographic characteristics at baseline in 2006 (N=359).

in 2006 and Table 2 the correlation between both physiological and psychological stress markers. Many of the physiological markers were significantly correlated. Markers of the same systems (e.g. blood pressure, HRV or markers of the immune system) had relatively strong correlation (0.37-0.78), whereas other correlations were more moderate (<0.37). Among the psychological markers, we observed correlation between job strain and perceived stress (p<0.05), ERI and stress symptoms (p<0.001), ERI and perceived stress (p<0.001), and stress symptoms and perceived stress (p<0.001). Stress symptoms correlated to SBP (p<0.01) and DBP (p<0.01) and perceived stress to SBP (p<0.001), DBP (p<0.001) and FIBR (p<0.001).

First, we investigated the association between workplace reorganization and changes in the physiological stress markers during the period 2006-2008 illustrated in Table 3. We observed significant changes in the expected directions of several physiological markers presented in model 2: SBP (3.2, SE (0.9), p<0.01), S0 (1.6, SE (0.4),

	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1.SBP	**0.78*** **	-0.15	-0.05	0.09	0.08	-0.01	0.02	0.07	0.00	**0.20*** **	0.15	0.18	0.22	0.05	-0.05	**-0.14** **	**0.17*** **
2.DBP	1	**-0.16***	-0.04	0.10	0.01	0.01	-0.03	0.01	-0.09	**0.18*** **	0.13	**0.18*** **	**0.21*** **	0.08	-0.05	**-0.14** **	**0.14** **
3.TPw		1	**0.53*** **	-0.13	-0.12	0.07	0.06	-0.18	0.03	-0.06	-0.08	**-0.22***	**-0.16***	-0.06	-0.03	0.07	-0.07
4. TPs			1	-0.11	-0.05	0.07	0.08	-0.15	-0.02	-0.08	-0.06	-0.08	-0.15	-0.05	-0.03	-0.02	0.01
5.LF/HFw				1	**0.50*** **	0.10	-0.02	0.03	-0.09	0.09	-0.05	0.10	-0.10	0.07	-0.01	-0.02	-0.07
6.LF/HFs					1	0.00	0.08	0.08	0.02	-0.02	-0.09	-0.04	**-0.18***	0.09	-0.06	-0.05	-0.02
7.S0						1	**-0.44*** **	-0.10	0.01	-0.05	0.06	**0.30*** **	0.06	0.27	-0.09	-0.05	-0.02
8.ACR							1	0.00	0.03	-0.04	-0.06	**-0.22*** **	**-0.13***	-0.03	0.04	-0.02	0.02
9.HBA1C								1	0.01	0.08	0.07	0.06	**0.13***	-0.01	0.09	0.04	0.07
10.HDL									1	**0.14***	**-0.14***	**-0.12***	**-0.15** **	0.02	0.01	-0.07	0.05
11.TCHOL										1	0.00	0.05	**0.19*** **	-0.09	-0.04	-0.11	0.04
12.CRP											1	**0.37*** **	**0.49*** **	0.03	0.10	0.07	-0.01
13.IL6												1	**0.40*** **	0.05	0.00	0.05	0.02
14.FIBR													1	0.03	0.06	**0.13***	**0.10***
15.JS														1	0.09	-0.01	**0.11***
16.ERI															1	0.31	0.22
17.SS																1	**0.29*** **
18.PS																	1

P-values *=<0.05, **=<0.01, ***=<0.001

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; Tpw: Heart Rate Variability, Total Power At Work; Tps: Heart Rate Variability, Total Power At Sleep; LF/Hfw: Heart Rate Variability, Low Frequency/High Frequency at Work; LF/Hfs: Heart Rate Variability, Low Frequency/High Frequency At Sleep, S0: Cortisol At Awakening; ACR:Awakening Cortisol Response; HBA1C: Glycated Haemoglobine; HDL: High Density Lipoprotein Cholesterol; TCHOL: Total Cholesterol; CRP: C-Reactive Protein; IL6: Interleukin 6; FIBR: Fibrinogen; JS: Job Strain; ERI: Effort-Reward Imbalance; SS: Stress Symptoms; PS: Perceived Stress

Table 2: Pearsson Correlation between physiological and psychological stress markers.

	N	2006	N	2006-2008 Model 1	p-value	2006-2008 Model 1A	p-value
SBP (mmHg)	358	136.9 (1.1)	346	3.2 (0.8)	**<0.01**	3.3 (0.9)	**<0.01**
DBP (mmHg)	358	83.3 (0.6)	346	0.2 (0.5)	0.61	0.2 (0.5)	0.69
TPw (ms^2)	158	2908.9 (1869.8)	142	-97.4 (180.4)	0.59	-104.6(185.1)	0.57
TPs (ms^2)	156	2794.8 (2405.5)	143	-153.6 (179.4)	0.39	-148.5(181.9)	0.42
LF/HFw	158	5.9 (4.0)	141	-0.07 (0.3)	0.83	-0.06 (0.3)	0.85
LF/HFs	156	3.4 (3.0)	143	-0.09 (0.2)	0.68	-0.07 (0.2)	0.78
S0 (nmol/l)	351	9.3 (0.3)	338	1.6 (0.4)	**<0.01**	1.6 (0.4)	**<0.01**
ACR (nmol/l)	351	6.4 (0.4)	335	1.3 (0.5)	**0.01**	1.4 (0.5)	**0.01**
HBA1C (mmol/l)	358	5.4 (0.02)	357	0.07 (0.01)	**<0.01**	0.07 (0.01)	**<0.01**
HDL (mmol/l)	357	1.7 (0.02)	357	-0.07 (0.01)	**<0.01**	-0.07 (0.01)	**<0.01**
TCHOL (mmol/l)	357	5.3 (0.05)	357	0.2 (0.04)	**<0.01**	0.2 (0.04)	**<0.01**
CRP (mg/l)	290	1.9 (2.2)	289	0.3 (0.1)	**0.04**	0.2 (0.1)	**0.05**
IL6 (µmol/l)	294	1.2 (0.9)	291	1.1 (0.06)	0.07	0.1 (0.06)	0.07
FIBR (µmol/l)	357	9.7 (0.1)	254	1.1 (0.08)	0.15	0.1 (0.08)	0.20

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; Tpw: Heart Rate Variability, Total Power At Work; Tps: Heart Rate Variability, Total Power At Sleep; LF/Hfw:Heart Rate Variability, Low Frequency/High Frequency At Work; LF/Hfs:Heart Rate Variability, Low Frequency/High Frequency At Sleep, S0:Cortisol At Awakening; ACR: Awakening Cortisol Response; HBA1C: Glycated Haemoglobine; HDL: High Density Lipoprotein Cholesterol; TCHOL: Total Cholesterol; CRP: C-Reactive Protein; IL6: Interleukin 6; FIBR: Fibrinogen

Model 1: Changes in physiological markers during workplace reorganization unadjusted

Model 1A: Changes in physiological markers during workplace reorganization adjusted for gender, age (continous), occupation (5 levels), physical activity in leisure time (2 levels) and reorganization groups (3 levels)

Table 3: Mean (SE) of physiological stress markers at baseline (2006) and changes during workplace reorganization (2006-2008).

p<0.01), ACR (1.3, SE (0.5), p=0.01), HBA1C (0.07, SE (0.01), p<0.01), TCHOL (0.2, SE (0.04), p<0.01) and CRP (0.3, SE (0.1), p=0.04) increased, whereas HDL (-0.07, SE (0.01), p<0.01) decreased. These results did not change after adjustment for gender, age, occupation, physical activity in leisure time and reorganization groups shown in model 3. The remaining markers all changed insignificantly in the expected directions except from TPw and TPs.

Next, we investigated the association between workplace reorganization and changes in psychosocial work environment and psychological distress illustrated in Table 4. We observed no change in job strain (-0.05, SE 0.07, p=0.47) and ERI (-0.01, SE 0.02, p=0.77) and a significant increase of stress symptoms (0.5, SE 0.2, p=0.01) and perceived stress (0.3, SE 0.07, p<0.01) illustrated in model 2. Adjustment for gender, age, occupation, physical activity in leisure time and exposure groups in model 3 did not influence the results.

Finally, Table 5 illustrates the mediating effect of changes in the psychological stress markers on changes in the physiological stress markers. We found only perceived stress to have significant influence (p=0.03) on change in SBP during reorganization but still the change was significant (2.7, SE (0.9), p=0.03) after adjustment. Neither job strain, ERI or stress symptoms had significant influence on the physiological changes. Furthermore, we investigated the mediating effect of BMI on changes in physiological stress markers. These results are not shown in Table 5, but we found BMI to have a significant influence on changes in SBP, HBA1C, HDL, TCHOL and CRP. However, the changes were still significant after adjustment.

Discussion

We studied the relationship between a major reorganization of non-state public offices in Denmark and changes in physiological and psychological stress markers. Supporting the hypothesis, we confirmed an effect on many of the physiological and the psychological stress markers during the reorganization. We observed significant changes in several physiological markers: SBP, S0, ACR, HBA1C, TCHOL and CRP increased, whereas HDL decreased. All the physiological changes correspond to the expected physiological stress reactions [8,42]. Furthermore, stress symptoms and perceived stress increased significantly but could not explain the physiological changes.

	N	**2006**	N	**2006-2008 Model 2**	p-value	**2006-2008 Model 2A**	p-value
Psychosocial work environment							
Job strain	359	2.4 (0.06)	349	-0.05 (0.07)	0.47	-0.06 (0.07)	0.40
ERI	359	0.8 (0.02)	349	-0.01 (0.02)	0.77	-0.01 (0.02)	0.81
Psychological distress							
Stress symptoms	359	17.1 (0.2)	348	0.5 (0.2)	0.01	0.5 (0.2)	0.01
Perceived stress	350	1.9 (0.05)	342	0.3 (0.07)	<0.01	0.2 (0.08)	<0.01

Model 2: Changes in psychological stress markers during workplace reorganization unadjusted
Model 2A: Changes in psychological stress markers during workplace reorganization adjusted for gender, age (continous), occupation (5 levels), physical activity in leisure time (2 levels) and reorganization groups (3 levels)

Table 4. Mean (SE) of psychological stress markers at baseline (2006) and changes during workplace reorganization (2006-2008).

	Model 3		**Model 3A**		**Model 3B**		**Model 3C**		**Model 3D**	
	Estimate	p-value	Estimate	p-value	Estimate	p-value	Estimate	p-value	Estimate	p-value
SBP	3.2 (0.8)	**<0.01**	2.9 (0.8)	**<0.01**	2.9 (0.8)	**0.01**	3.6 (0.9)	**<0.01**	2.7 (0.9)	**0.03**
DBP	0.2 (0.5)	0.61	0.2 (0.5)	0.69	0.1 (0.5)	0.80	0.4 (0.5)	0.38	-0.04 (0.5)	0.93
TPw	-97.4 (180.4)	0.59	-64.5 (181.6)	0.72	-67.5 (181.1)	0.71	-93.5 (183.7)	0.61	-94.2 (191.1)	0.62
TPs	-153.6 (179.4)	0.39	-132.7 (181.7)	0.47	-138.1 (181.0)	0.45	-129.2 (181.8)	0.48	-104.1 (190.2)	0.59
LF/HFw	-0.07 (0.3)	0.83	-0.06 (0.3)	0.86	-0.06 (0.3)	0.85	-0.06 (0.3)	0.86	-0.03 (0.3)	0.94
LF/HFs	-0.09 (0.2)	0.68	-0.07 (0.2)	0.74	-0.07 (0.2)	0.73	-0.07 (0.2)	0.73	-0.02 (0.2)	0.94
S0	1.6 (0.4)	**<0.01**	1.6 (0.4)	**<0.01**	1.6 (0.4)	**<0.01**	1.6 (0.4)	**<0.01**	1.6 (0.4)	**<0.01**
ACR	1.3 (0.5)	**0.01**	1.3 (0.5)	**0.01**	1.3 (0.5)	**0.01**	1.3 (0.5)	**0.01**	1.1 (0.5)	**0.05**
HBA1C	0.07 (0.01)	**<0.01**	0.07 (0.01)	**<0.01**	0.07 (0.01)	**<0.01**	0.07 (0.01)	**<0.01**	0.08 (0.01)	**<0.01**
HDL	-0.07 (0.01)	**<0.01**	-0.07 (0.01)	**<0.01**	-0.07 (0.01)	**<0.01**	-0.07 (0.01)	**<0.01**	-0.07 (0.01)	**<0.01**
TCHOL	0.2 (0.04)	**<0.01**	0.2 (0.04)	**<0.01**	0.2 (0.04)	**<0.01**	0.2 (0.04)	**<0.01**	0.2 (0.04)	**<0.01**
CRP	0.3 (0.1)	**0.04**	0.3 (0.1)	**0.02**	0.3 (0.1)	**0.02**	0.2 (0.1)	**0.05**	0.2 (0.1)	**0.05**
IL6	1.1 (0.06)	0.07	0.08 (0.06)	0.15	0.08 (0.06)	0.14	0.08 (0.06)	0.16	0.1 (0.06)	0.07
FIBR	1.1 (0.08)	0.15	0.1 (0.08)	0.11	0.1 (0.08)	0.12	0.1 (0.08)	0.20	0.1 (0.08)	0.16

Model 3: Changes in physiological markers during workplace reorganization unadjusted
Model 3A: Changes in physiological markers during workplace reorganization adjusted for job strain
Model 3B: Changes in physiological markers during workplace reorganization adjusted for ERI
Model 3C: Changes in physiological markers during workplace reorganization adjusted for stress symptoms
Model 3D: Changes in physiological markers during workplace reorganization adjusted for perceived stress
SBP:systolic blood pressure; **DBP**:diastolic blood pressure; **TPw**:heart rate variability, total power at work; **TPs**: heart rate variability, total power at sleep; **LF/HFw**:heart rate variability, low frequency/high frequency at work; **LF/HFs**:heart rate variability, low frequency/high frequency at sleep, **S0**:cortisol at awakening; **ACR**:awakening cortisol response; **HBA1C**:glycated haemoglobine; **HDL**: high density lipoprotein cholesterol; **TCHOL**:total cholesterol; **CRP**:c-reactive protein; **IL6**:interleukin 6; **FIBR**:fibrinogen

Table 5. Mean (SE) of changes in psychological markers during workplace reorganization (2006-2008) and the mediating effect of psychological markers.

The association between workplace reorganization and changes in physiological markers correspond with earlier studies investigating the effect of downsizing [43] and job insecurity [44,27]. One could argue that the physiological changes do no harm and can be seen as normal fluctuations caused by different life events. However, according to the theory of allostatic load, several episodes of strain on the body produced by repeated ups and downs of physiologic responses can predispose the organism to disease [45]. Several physiological markers correlated significantly, but the strongest correlation was among markers of the same physiological systems. Therefore, the use of many physiological markers reflecting same system only confirms the results.

In relation to the results of psychological stress markers, we only found an increase of psychological distress in the form of increased stress symptoms and perceived stress but no effect on the perceived psychosocial work environment reflected by job strain and ERI. The explanation of this could be that the reorganization did not affect the investigated factors of the psychosocial work environment but only the experience of being a part of a major reorganization. The significant association between workplace reorganization and psychological distress correspond to the findings of other studies [28,46].

We investigated the original design of both mergers and controls by adjusting for exposure groups in the analyses and found no influence of this variable. This result could indicate either that the exposure groups were incorrectly defined in the design of the study or that all employees involved in the reorganization were affected whether they were merging or not. Unfortunately, we did not have the information to describe the more specific and individual type of change. Moreover, the finding corresponds to an earlier study on downsizing, where the results also included the survivors of downsizing and suggested that "layoff survivor sickness", a negative reaction among survivors instead of relief, was the typical experience [47]. Reorganization probably involves the same mechanisms.

We expected to explain part of the physiological changes through a more subjective perspective by investigating the mediating effect of the psychological stress markers. However, we found no effect and a possible explanation to this might be the difference in individual reactions to stress being either physiological or psychological. Another explanation could be the construction of the questions used to measure stress symptoms and perceived stress. To determine stress symptoms, we asked about stress symptoms during the previous 4 weeks; to define perceived stress, we asked about stress at that moment. Because we do not know the exact time perspective of physiological reactions in relation to a stress exposure, a mismatch between these factors could be of importance.

Another relevant perspective is that the observed changes of physiological markers are caused by factors other than stress, for example, increased weight during the reorganization. We observed significant changes of physiological stress markers especially related to the metabolic system confirming this perspective. However, we investigated the mediating effect of BMI on changes in physiological stress markers and found BMI to have a significant influence on the changes in SBP, HBA1C, HDL, TCHOL and CRP but the changes were still significant after adjustment. Further, stress is thought to influence human eating behaviour, and stress-induced eating may be one factor contributing to the development of obesity.

The main strength of this study is the repeated measurements of physiological and psychological stress markers during major workplace reorganization that allows for prospective analyses. Moreover, the study covers a wide range of physiological markers including important physiological systems in relation to stress [9] (McEwen 2008).

The main weakness of this study is the limited number of participants. To compensate for this problem, we analysed men and women together and also the unequal distribution of men and women (94 men and 265 women) should be taken into account when drawing conclusions from the results. Moreover, the homogenous population should be taken into account. The same social and racial background minimizes confounders and confirms the results. However, it may also be a limitation due to generalizability.

One inclusion criterion was two measurements of at least one physiological marker, and 111 participants did not complete the follow-up. The 111 non-participants reported poorer health, more stress and higher sickness absence at baseline. The dropout part of these baseline participants with more signs of poor health is as an indication of selection bias that may cause an underestimation of the true effect. Moreover, perceived regular support and communication among the participants could have an impact on better outcomes. Among physiological markers, only ACR was significantly higher among the non-participants.

Another perspective is the timing of measuring both physiological and psychological markers according to the study design. Perhaps the measurements in autumn 2006 do not reflect the participants' true baseline but instead a physiological and psychological stress condition caused by knowledge about the reorganization to come and negative expectations. In addition, perhaps the measurements in autumn 2008 were too late and did not reflect the actually stress condition. This problem may influence the observed results, but more important, it illustrates the difficulties and uncertainties about the time perspective of the both physiological and psychological reactions of long-term stress in relation to exposure as mentioned above.

In conclusion, we found workplace reorganization to be associated with significant changes in several physiological stress markers according to known physiological stress reactions and significant changes in psychological stress markers in the form of stress symptoms and perceived stress. However, the physiological changes could not be explained by changes in psychological stress markers during this workplace reorganization. Further investigation is needed to confirm and explain these results. The use of a larger population or repeated measurements of shorter intervals to explain the natural fluctuations of both physiological and psychological markers could be of particular interest.

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