Stress Management at the Worksite
Reversal of Symptoms Profile and Cardiovascular Dysregulation

Daniela Lucini, Silvano Riva, Paolo Pizzinelli, Massimo Pagani

Abstract—Work stress may increase cardiovascular risk either indirectly, by inducing unhealthy life styles, or directly, by affecting the autonomic nervous system and arterial pressure. We hypothesized that, before any apparent sign of disease, work-related stress is already accompanied by alterations of RR variability profile and that a simple onsite stress management program based on cognitive restructuring and relaxation training could reduce the level of stress symptoms, revert stress-related autonomic nervous system dysregulation, and lower arterial pressure. We compared 91 white-collar workers, enrolled at a time of work downsizing (hence, in a stress condition), with 79 healthy control subjects. Psychological profiles were assessed by questionnaires and autonomic nervous system regulation by spectral analysis of RR variability. We also tested a simple onsite stress management program (cognitive restructuring and relaxation training) in a subgroup of workers compared with a sham subgroup (sham program). Workers presented an elevated level of stress-related symptoms and an altered variability profile as compared with control subjects (low-frequency component of RR variability was, respectively, 65.2 ± 2 versus 55.3 ± 2 normalized units; $P<0.001$; opposite changes were observed for the high-frequency component). These alterations were largely reverted (low-frequency component of RR variability from 63.6 ± 3.9 to 49.3 ± 3 normalized units; $P<0.001$) by the stress management program, which also slightly lowered systolic arterial pressure. No changes were observed in the sham program group. This noninvasive study indicates that work stress is associated with unpleasant symptoms and with an altered autonomic profile and suggests that a stress management program could be implemented at the worksite, with possible preventive advantages for hypertension. **(*Hypertension*. 2007;49:291-297.)**

Key Words: lifestyle ■ hypertension ■ nervous system ■ autonomic ■ prevention ■ stress

Recent epidemiological evidence compellingly indicates that psychosocial factors have a profound influence on cardiovascular mortality and morbidity, predisposing to acute myocardial infarction.[1,2] In this context, work-related stress seems to play a critical role,[3] in view of its ubiquitous nature and long-term impact; however, an accurate assessment may be elusive because of the dependence of stress on the subjective perception of work-related demands and on individual genetic–behavioral characteristics.[4,5]

According to the job strain model proposed by Karasek et al,[6] downsizing,[7,8] changing organization,[9] and, in general, low job and career control, are recognized conditions of work stress that eventually become associated with sickness, absenteeism,[10] and cardiovascular diseases.[1,2,4]

Mechanisms linking chronic stress to the increased cardiovascular risk are complex and multifarious. In humans, stress may act indirectly by inducing unhealthy lifestyles like smoking, reduced physical activity, and increased calorie intake, thus worsening cardiovascular risk.[4,5,11] Stress may also act directly[1,4,12] by affecting major regulatory systems, in particular, the hypothalamic–pituitary–adrenal axis[4,13] and the autonomic nervous system (ANS),[14–18] leading to abnormal catecholamine release impairing vascular performance,[19] inappropriately elevated sympathetic drive, and, thus, contributing to increase arterial pressure.[20]

In view of the intrinsic dynamic nature of autonomic regulation, to capture more easily the effects of work related stress, it may be useful to plan studies at the worksite instead of in the more usual clinical laboratory, where environmental factors may act differently. Obviously, this design imposes technical constraints, suggesting the use of simple, noninvasive methodologies, such as spectral analysis of RR variability. This technique provides quantitative markers of autonomic regulation[21–24] capable of distinguishing between different autonomic profiles as related to posture,[25] psychological stress,[18,26,27] or various grades of hypertension.[24] Notably, RR variability may be assessed onsite with very simple telemedicine techniques, providing results highly consistent with those obtained in the clinical laboratory.[28]

The main goal of this field investigation on healthy white-collar workers was to test the hypothesis that, before any apparent sign of disease, work-related stress is already

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From the Department of Clinical Sciences "L. Sacco" (D.L., P.P., M.P.), University of Milan, Milan, Italy; and DuPont De Nemours Italiana (S.R.), Milan, Italy.

Correspondence to Massimo Pagani, Centro Terapia Neurovegetativa, Università di Milano, Ospedale "L. Sacco," Via G.B. Grassi 74, 20157 Milan, Italy. E-mail mp@ctnv.unimi.it

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accompanied by alterations of the RR variability profile, suggesting ANS dysregulation. As secondary goals, we tested the possibility of implementing an onsite stress management program (SMP), based on cognitive restructuring and relaxation training,[29] and tested the additional hypothesis that such a program could reduce the level of stress symptoms, revert stress-related ANS dysregulation, and lower arterial pressure.

Methods

Study Population

This study considered 170 subjects divided into 2 groups. The first group consisted of all white-collar employees of the Italian subsidiary of a multinational US company (workers: n=91; age: 40.1±1.0 years; body mass index: 23.6±0.3 kg/m^2; men: n=59; women: n=32), who volunteered to participate in a work-related multiparametric stress assessment at a time of substantial (≈10%) work downsizing conducted by the central headquarters. Following the job strain model of Karasek et al,[6] because of the realistic fear of losing their jobs, absence of communication with the headquarters, and low control on this critical process, these workers were considered to be exposed to work-related stress. The second group consisted of 79 healthy volunteers (control subjects), randomly enrolled outside the considered company, who did not complain of any work-related problem. These volunteers served as the reference group (age: 38.4±1.6 years; body mass index: 23.2±0.4 kg/m^2; men: n=52; women: n=27).

As in previous studies,[18,27] the absence of clinically manifest disease and traditional risk factors in all of the subjects was determined by history, physical examination, laboratory, and routine tests. None of the subjects included in the study smoked, were on any medication, or admitted abuse of alcohol or use of recreational drugs.

Protocol

Subjects were asked to avoid alcohol and caffeinated beverages for the 12 hours preceding the recording session and to abstain from heavy physical activity the day before the session. All of the subjects were instructed about the study procedure and gave their informed consent. Our institution ethics committee approved the protocol of the study.

Stress Evaluation

All of the subjects were assessed by a clinical psychologist through semistructured interviews to establish the possible presence of chronic psychosocial stress and stress-related symptoms and to exclude patients with psychiatric diseases (with particular attention to depression and somatoform disorders) following *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* criteria.[30]

As in a previous study on the autonomic effects of acute and chronic stress,[18,27] all of the subjects filled out a self-administered questionnaire providing nominal self-rated scales that focus on overall stress, tiredness perception, and stress-related symptoms. The overall stress and tiredness perception scale[18,27] uses Likert linear analogue scales from 0 ("no perception") to 10 ("strong perception") to approximate the perceived overall stress and tiredness levels. The Subjective Stress-Related Somatic Symptoms Questionnaire (4S-Q)[18,27] inquires about 18 somatic symptoms accounting for the majority of somatic complaints. For scoring purpose, responses are coded from 0 ("no feeling") to 10 ("a strong feeling"); thus, the total score ranges from 0 to 180.

Autonomic Evaluation

After a 10-minute rest, a single lead ECG was also continuously recorded in all of the subjects for a period of 5 to 10 minutes while subjects were recumbent. Subsequently, an additional 5-minute recording was performed while the subjects were standing up, unaided. Standard sphygmomanometric pressures were obtained in both conditions (rest and stand).

Workers were studied at the worksite, in an office that had been prepared and shielded from the usual work environment noise to minimize ambient influence. ECG was recorded with a microminiature (20-g weight) single-channel transtelephonic ECG recorder (Card Guard-Sport Model).[28] Fifty-four control subjects were recorded using the same technique at their home, whereas 25 of them were recorded in our clinic laboratory using an ECG radiotelemetry recording (Marazza[18]) that provides similar results.[28] Spectral analysis of RR interval variability was used to obtain noninvasive markers of ANS regulation. According to the sympatho-vagal model, as applied in our laboratory, and on the basis of a strong coherence between similar oscillations in the variability of the RR interval and of muscle sympathetic efferent activity,[31] the low-frequency component ([LF] in normalized units) represents a marker of oscillatory sympathetic modulation of the senoatrial node, whereas the high-frequency component ([HF] nu) is a marker of vagal oscillatory modulation.[21–28]

SMP

Investing in health at work can reduce sickness rates and accidents and improve performance, productivity, and competitiveness. The work environment can offer benefits, such as positive peer pressure and peer support, and establish channels of communication that can be used to publicize programs, encourage participation, and provide feedback: critical aspects when dealing with the sensitive issue of cardiovascular prevention at work.

DuPont has pioneered the implementation of comprehensive health promotion programs,[32] inclusive of stress management. Taking advantage of this opportunity, the Italian subsidiary offered to all of its workers the possibility to participate in a structured onsite stress management program.

On the basis of self-selection, a first subgroup (n=26; age: 43.5±1.6 years; body mass index: 22.7±0.5 kg/m^2) elected to participate in an active SMP of 1 year of duration, whereas a second subgroup of subjects (n=25; age: 42.7±1.8 years; body mass index: 23.7±0.6 kg/m^2) chose to participate in a sham program (SP). Both groups underwent ANS and psychological assessment twice, at the beginning and at the end of the year of intervention. Gender ratio was unbalanced, because SMP was composed of more women (8 men and 18 women), whereas the SP contained more men (18 men and 7 women). This inequality most likely reflects the usually lighter routine of the female workforce, allowing women to accept the more demanding commitment[33] of following the more rigorous SMP as compared with men, who have a more frequent travel program and, hence, may be forced to skip scheduled encounters.

SMP consisted of two parts. First, it included weekly onsite encounters of 1 hour duration during which all of the participants learned mental relaxation techniques.[34] To minimize any impact on work routine, thanks to the presence of a flexible work schedule, these encounters were arranged, in agreement with the company's management, during the lunch break in a 5×8-m^2 relaxation room conveniently located in the office building, close to the medical department quarters. The encounters, organized in groups (8 to 10 people), were conducted by an experienced trainer and focused on respiration, muscle relaxation, and guided imagery. Second, cognitive restructuring, addressing in particular possible life stressors (including job stress), coping strategies, physiological responses, personal skills, and company resources to manage stress was designed and delivered by a clinical psychologist.

The SP consisted of a scheduled yearly onsite informatory encounter and short articles published in the house magazine and in e-mail messages sent approximately every month. Subjects were also invited to maintain a healthy lifestyle and urged to contact the medical department regularly and whenever they wanted, also from afar using the telephone or e-mail.

Statistics

Data in the text, figure, and tables are presented as mean±SE. Significance of groups differences were assessed with parametric or nonparametric tests (Mann–Whitney), with the Monte Carlo procedure, as appropriate. Simple nonparametric correlation (Spearman) was used to assess the statistical link between stress scores and indices of autonomic cardiovascular regulation. Discriminant analy-

TABLE 1. Stress Perception, Tiredness Perception, and 4S-Q Scores in Control Subjects and Workers

Variables	Stress Perception	Tiredness Perception	4S-Q
Control subjects	2.94±0.25	3.27±0.30	20.55±3.02
Workers	5.20±0.27*	5.28±0.26*	43.14±2.89*

*Significant differences, $P<0.001$.

sis was used to assess the integrated capacity of several psychometric and autonomic variables to correctly classify subjects as control subjects or workers. Significant interactions (group×time) were assessed on ANS and psychological variables before testing for individual effects in the stress management subsection. Mediation analysis was performed following MacKinnon et al.[35] A $P<0.05$ was considered significant. All of the computations were performed with a commercial statistical package (SPSS version 13).

Results

Workers Versus Controls

Stress Evaluation

As expected, whereas most of the workers reported stress, mainly because of work problems (possibility of losing job, lack of control over their future, personal relationships with managers or other employees, dissatisfaction with their role or salary, lack of social support, etc) and also personal problems (family, friends, relatives, etc), none of the control subjects reported any particular source of stress in their life, as per enrollment criteria.

Overall Stress and Tiredness Perception Scale

Workers showed a significantly higher perception of stress and tiredness as compared with controls (5.20±0.27 versus 2.94±0.25 for stress and 5.28±0.26 versus 3.27±0.30 for tiredness, respectively; $P\ll0.001$; Table 1). The total 4S-Q score was significantly higher in workers as compared with control subjects (43.14±2.89 versus 20.55±3.02, respectively; $P\ll0.001$; Table 1).

As expected, a significant correlation was found between scores of the stress perception scale and the 4S-Q ($r=0.52$; $P\ll0.001$), between scores of the stress perception scale and scores of the tiredness perception scale ($r=0.80$; $P\ll0.001$), and between scores of the tiredness perception scale and the 4S-Q ($r=0.47$; $P\ll0.001$).

Autonomic Evaluation

RR interval, RR interval variance, and systolic and diastolic arterial pressure were similar in the 2 groups (Tables 2 and 3 and Figure). Conversely, the LF component of RR interval variability (LF_{RR}) expressed in normalized units (marker of sympathetic oscillatory modulation to the senoatrial node) was higher in workers ($P<0.001$; Table 2). As a corollary, the HF component of RR interval variability (HF_{RR}) expressed in normalized units (marker of vagal oscillatory modulation to the senoatrial node) was lower ($P<0.001$; Table 2). Conversely, absolute power of both LF and HF components were not significantly different between the 2 groups. The LF/HF ratio (a marker of sympatho-vagal balance) was also significantly higher in workers.

Standing induced changes (Table 3) in the RR interval were reduced in workers, but no significant difference was observed in changes of RR variance or in the absolute values of spectral components between groups. Attendant increases in normalized LF and, specularly, reductions in HF (normalized units), were smaller in workers as compared with control subjects ($P\ll0.001$).

Correlations

Stress perception scores correlated significantly (Table 4) with LF_{RR} normalized unit, HF_{RR} normalized unit, and with LF/HF at rest and with the stand-induced changes in LF_{RR} normalized unit ($r=-0.0195$; $P<0.017$). Tiredness perception scores correlated significantly with LF_{RR} normalized unit, HF_{RR} normalized unit, and LF/HF at rest (Table 4) and with the stand-induced changes in LF_{RR} normalized unit ($r=-0.0173$; $P<0.035$). 4S-Q scores correlated with diastolic arterial pressure and LF_{RR} normalized unit at rest (Table 4).

To assess the integrated capacity of used indices to correctly categorize the study subjects into either workers or control subjects, discriminant analysis was also performed. Although the combination of both psychological and autonomic variables provided a correct classification in >80% of cases, the separate use of all psychometric or all autonomic variables reduced correct classification to ≈70%. Notably, progressively restricting the number of all variables to the top ranking 10, and subsequently 5, determined a trivial loss of classification capacity. When only the 3 top ranking variables (rest-stand difference of LF_{RR} in normalized units, stress perception, and 4S-Q scores) were used, the correct classification was still ≈80%.

SMP

Stress Evaluation

Workers who elected to follow SMP, starting from a more elevated baseline, showed at the end of the program a significantly lower perception of stress (6.65±0.54 before versus 5.14±0.51 after) and tiredness (6.05±0.66 before versus 5.14±0.60 after). Also, the 4S-Q score was significantly lower

TABLE 2. Descriptive Statistics of Resting Values of RR Interval Variability in Control Subjects and Workers

Variables	RR, ms	VAR_{RR}, ms^2	LF ms^2	LF nu	HF ms^2	HF nu	LF/HF	Respiratory Frequency, Hz	SAP, mm Hg	DAP, mm Hg
Control subjects	904±14	2537±322	775±125	55.3±2.0	526±86	35.7±1.9	2.9±0.4	0.27±0.01	117±2	75±1
Workers	892±16	3400±455	732±89	65.2±2.0*	518±82	26.3±1.8*	5.1±0.6*	0.26±0.01	119±2	76±1

RR indicates RR interval; VAR_{RR}, RR variance; LF, low-frequency component; HF, high-frequency component; LF/HF, ratio between low- and high-frequency components; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; nu, normalized units.

*Significant differences at $P\ll0.001$.

TABLE 3. Stand-Induced Changes: Descriptive Statistics of RR Interval Variability in Control Subjects and Workers

			LF		HF		
Variables	RR, ms	VAR_{RR}, ms^2	ms^2	nu	ms^2	nu	LF/HF
Control subjects	−152±9	−620±266	21±104	26.4±1.9	−433±84	−22.3±1.9	9.8±1.5
workers	−83±9*	−447±253	−8±72	11.3±1.7*	−367±74	−9.7±1.7*	4.4±0.9*

RR indicates RR interval; VAR_{RR}, RR variance; LF, low-frequency component; HF, high-frequency component; LF/HF, ratio between low- and high-frequency components; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; nu, normalized units.

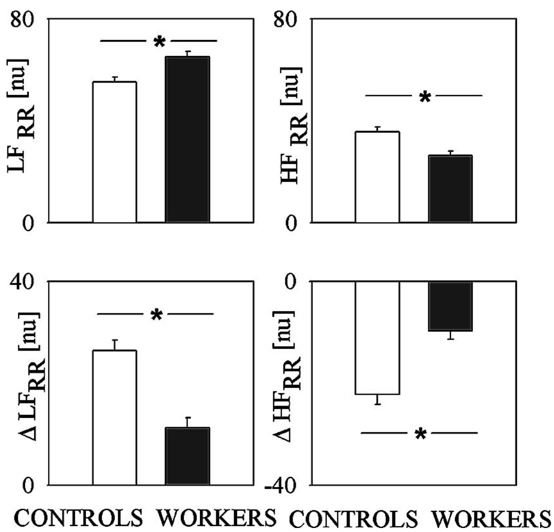
*Significant differences at $P \ll 0.001$.

after SMP (60.55±5.89 before versus 46.40±5.46 after). Conversely, subjects belonging to the sham subgroup presented similar values at the entry and at the end of the considered period (stress: 4.70±0.53 before versus 5.09±0.43 after; tiredness: 4.39±0.48 before versus 5.48±0.39 after; 4S-Q: 37.33±5.59 before versus 42.04±4.83 after; *P* value not significant).

Autonomic Evaluation

From a similar baseline in the 2 groups, SMP induced a significant, small reduction in systolic arterial pressure and clear changes in spectral indices of RR variability (Table 5). Notably, LF_{RR} normalized unit and LF/HF at rest were reduced, and HF_{RR} normalized unit was increased. No significant changes were apparent in the SP subgroup.

To see whether the improvement in stress perception scores accounted for the improvement in autonomic indices in the SMP group, we performed a mediation analysis,[35] considering the relative differences of LF (providing an index of autonomic effects) and stress perception between values obtained at entry and at end of the program. Tiredness and symptom scores were considered as mediators. Results show a significant overall effect of stress on autonomic parameters (regression coefficient=0.542; P=0.014). Introduction of tiredness and symptom scores increased the stress regression coefficient, suggesting a suppression effect of the first 2 variables.



Average value (and SEM) of LF_{RR} (left top) and HF_{RR} (right top) at rest and of standing-induced changes of low (ΔLF_{RR}, left bottom) and high (ΔHF_{RR}, right bottom) frequency in control subjects (□) as compared with workers (■). nu indicates normalized units. *$P \ll 0.001$.

Discussion

This field study shows that, in otherwise healthy workers, work-related stress is associated to an elevated level of subjective symptoms simultaneously to an altered autonomic profile. These alterations can be largely reverted by an onsite behavioral SMP, which also leads to a slight reduction of systolic arterial pressure.

Work Stress

Market globalization in a rapidly changing world renders stress at work a virtually obligate experience, suggesting that stress management, rather than stress elimination,[10] could represent a more realistic goal. Several methodologic issues must be considered when dealing clinically with stress, particularly in a field investigation, as in the present study. The majority of traditional studies on work stress deal with organizational issues,[6,8–10] use questionnaires and self-reports, and signal the broad intention of improving the working environment and conditions. More recently, large epidemiological investigations have highlighted the importance of stress as a major cardiovascular risk factor,[1,2,36] suggesting that individual psychophysiological responses to stressors could represent a target for diagnosis, clinical interventions, and preventive strategies.[37] However, relatively few studies have thus far addressed the relationship between real-life stress and clinical applications, probably because of methodologic and technical reasons.

Stress, in fact, consists of several (inter)related elements, and its (patho)physiological effects are characterized by pronounced interindividual variability.[4,5] Responses to stress may be difficult to assess even in the controlled laboratory

TABLE 4. Simple Nonparametric Correlations Between Stress Perception Scores and Autonomic Indices at Rest

	Stress Perception		Tiredness Perception		4SQ	
ANS	*r*	*P*	*r*	*P*	*r*	*P*
RR	0.086	ns	−0.084	ns	−0.007	ns
RR var	0.008	ns	−0.079	ns	0.002	ns
LF abs	−0.091	ns	−0.0119	ns	−0.069	ns
LF nu	0.225	0.005	0.266	0.001	0.167	0.042
HF abs	−0.105	ns	−0.0169	0.038	−0.081	ns
HF nu	−0.191	0.019	−0.0246	0.002	−0.144	ns
LF/HF	0.206	0.011	0.258	0.001	0.154	ns

RR indicates RR interval; var, variance; LF, low-frequency power; abs, absolute units (milliseconds squared); nu, normalized units; HF, high-frequency power; LF/HF, ratio between low- and high-frequency power.

TABLE 5. Descriptive Statistics of Resting Values of RR Interval Variability in SPM and SP Groups

Group	RR, ms	VAR_{RR}, ms^2	LF ms^2	LF nu*	HF ms^2	HF nu*	LF/HF*	Respiratory Frequency, Hz	SAP, mm Hg*	DAP, mm Hg
SMP										
Before	924±36	2480±369	869±151	63.6±3.9	398±83	30.1±3.4	4.7±1.5	0.26±0.02	121.7±4.1	78.5±2.2
After	947±26	2177±235	592±89	49.3±3.1†	484±78	38.9±3.0†	1.8±0.4†	0.23±0.01	114.1±3.3†	76.7±2.1
SP										
Before	879±36	2871±948	799±237	61.6±3.3	387±135	28.3±3.1	3.4±0.6	0.26±0.01	118.3±3.8	77.0±2.4
After	898±23	2226±289	767±153	58.9±4.9	324±77	33.9±4.7	4.0±0.8	0.28±0.01	125.3±4.2	78.0±2.7

RR indicates RR interval; VAR_{RR}, RR variance; LF, low-frequency component; HF, high-frequency component; LF/HF, ratio between low- and high-frequency components; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; nu, normalized units.

*Significant interaction.

†Significant differences at $P \ll 0.001$.

environment. To partly overcome these problems, we developed and tested a noninvasive, nonintrusive methodology to simultaneously study multiple dimensions of stress in the clinical laboratory, addressing both autonomic changes and symptoms profiles.[18,27]

Autonomic Dysregulation

In previous studies we showed that, in otherwise healthy humans, lamenting various levels of stress related symptoms, indices of autonomic cardiac and vascular regulation were concomitantly altered.[18] We showed, in addition, that autonomic markers were significantly correlated with stress perception scores and were capable of discriminating between control subjects and patients with a high degree of accuracy.

In the present field study, we used a simplified technique, limiting recorded variables to a single transtelephonic ECG trace. We had already shown the capacity of this telemedicine technique to furnish consistent data from various settings (from the physician's office[28] to the training field of top-level Olympic athletes[38]) and that it can be combined with a psychological assessment, still maintaining the time and technical requirements to a minimum compatible with a demanding working environment.

Considering that confounding factors, such as chronic psychiatric conditions or drugs, and behaviors affecting symptoms profiles or cardiovascular regulation were carefully avoided, we feel that the greater values of stress and fatigue perception, together with higher values of somatic symptoms and altered RR variability profile, support the notion that greater stress levels in workers are accompanied by signs of autonomic cardiac dysregulation. It must be noted that such an autonomic imbalance was limited to oscillatory properties of RR variability, whereas time domain measures (RR interval and RR variance), as well as arterial pressure, were not different between the 2 groups of workers. Under the general hypothesis that autonomic alterations might frequently follow a continuum,[39] we might argue that behaviorally induced changes in oscillatory indices might represent, in susceptible individuals, the first step leading subsequently to the occurrence of symptoms and, eventually, also of hemodynamic alterations, as in prehypertension.[24] Accordingly, in this group of workers, none of which spontaneously referred stress-related problems, the relatively recent work downsizing[7,8] was associated with still-unrecognized symptoms of stress and signs of autonomic dysregulation. It may, thus, be argued that work stress acting for longer periods or with greater intensity might be required to induce long-lasting hypertension,[40] as is sometimes shown with behavioral experiments in animals.[41]

SMP

The outcomes of SMPs, such as the well-known relaxation response,[42] have been long described and include an improved autonomic and hormonal regulation.[34,37,43–45] SMPs offered to patients recovering from acute cardiovascular events are usually a component of multidimensional hospital-based programs, including, particularly, aerobic exercise training.[1,44] Accordingly, it may be difficult to recognize the cardiac and autonomic effects of SMP, per se. The possibility that SMP might improve baseline blood pressure control[46,47] or pressure responses to stressful conditions, such as at the worksite, is also debated.[43,48]

The present investigation shows that an SMP was not only possible within the constraints of a normal working environment but that it was also successful. Indeed, in the limited population that was tested, both stress-related symptoms and signs of autonomic dysregulation were reduced in the active intervention group. It should also be noted that the workers who signed up for the SMP followed the program for the full year, and many are still actively enrolled. From a practical point of view, the company health promotion policy facilitated the organization and planning of the SMP, and group encounters did not interfere with working activities, because they were scheduled during the lunch breaks. The sham group showed a somewhat lower baseline value of stress symptoms, suggesting a potential self-selection bias, which, however, does not undermine the observation that active intervention improved the autonomic profile. Additional elements of self-selection are suggested by the different gender representation in the SMP and SP.

Notably, SMP, although not modifying mean RR interval, was associated with a small, but significant, reduction in resting systolic arterial pressure, as compared with the SP group. The attendant simultaneous reduction in the profile of symptoms and in indices of oscillatory sympathetic modulation suggests that the hypotensive effect is part of a more general beneficial effect of SMP.

Limitations

By design, because of local constraints, we limited our autonomic assessment to transtelephonic ECG recordings and spectral analysis of RR variability. Thus, we have no information on other important autonomic parameters, such as baroreflex gain and efferent sympathetic nerve activity.

Moreover, this real-life, observational study had to comply with Italian work health legislation, and with the company's policies. Thus, a balance had to be struck between strict randomization and observation,[49] accepting elements of self-selection that could be avoided only with randomized, controlled trials. In a previous study on patients recovering from acute coronary events,[44] we noticed that, indeed, patients who elected to participate in an active rehabilitation program tended to be older and with lower levels of high-density lipoprotein.

Furthermore, given the difficulty of objectively assessing the stressful effects of work downsizing,[8] in spite of some circularity of the argument, we decided to approximate it from subjective measures, an approach that had proved valuable both in small-[18] and large-scale[2] studies. Therefore, these findings should not be considered definitive, but only hypothesis generating, until larger, more robust studies are performed.

Finally, at variance with studies performed in clinical settings, we did not address hormonal, molecular, or genetic aspects of chronic stress. Nonetheless, data show marked differences between the 2 study groups and, moreover, suggest beneficial SMP-induced changes. From a practical point of view, we would like to emphasize the strong capacity of only a few variables to discriminate between workers and control subjects, provided both autonomic and psychological variables were simultaneously considered.

Perspectives

Stress is a fundamental experience of modern work,[10] and several models have been used to provide a formal description of their relationship[6] in an attempt to design company-wide programs of intervention capable of minimizing the impact of stress on organizational, economic, and health outcomes.[10,48] The present investigation provides a potential model for the assessment of work-related stress at an individual level; in addition, it suggests that SMPs can be implemented at the worksite, with a capacity to reduce the stress symptoms level, revert stress-related ANS dysregulation, and lower resting arterial pressure. The practical long-term impact of this approach on symptoms, well being, and health of interested workers requires specific longitudinal studies on large populations.

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Disclosures

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References

1. Rozanski A, Blumenthal JA, Saab PG, Davidson KW, Kubzanski L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioural cardiology. *J Am Coll Cardiol*. 2005;45:637–651.
2. Rosengren A, Hawken S, Ôunpuu S, Sliwa K, Zubaid M, Almahmeed WA, Blackett KN, Chitr Sitthi-amorn, Sato H, Yusuf S. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 case and 13648 controls from 52 countries (The INTERHEART study): case control study. *Lancet*. 2004;364:953–962.
3. Kivimäki M, Leino-Arjas P, Luukkonen R. Riihimäki H, Vahtera J, Kirjonen J. Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. *BMJ*. 2002;325:857–861.
4. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med*. 1998;338:171–179.
5. Everly GS, Lating JM Jr. *A Clinical Guide to the Treatment of the Human Stress Response*. 2nd ed. New York, Boston, Dordrecht, London, Moscow: Plenum Publishers; 2002.
6. Karasek R, Baker D, Marxer D, Ahlbom A, Theorell T. Job decision latitude, job demands, and cardiovascular disease: a prospective study of Swedish men. *Am J Public Health*. 1981;71:694–705.
7. Westerlund H, Ferrie J, Hagberg J, Jeding K, Oxenstierna G, Heorell T. Workplace expansion, long-term sickness absence, and hospital admission. *Lancet*. 2004;363:1193–1197.
8. Kivimäki, Vahtera J, Pentti J, Ferrie J. Factors underlying the effect of organizational downsizing on health of employees: longitudinal cohort study. *BMJ*. 2000;320:971–975.
9. Landsbergis PA. The changing organization of work and the safety and health of working people: a commentary. *J Occup Environ Med*. 2003;45:61–72.
10. European Agency for Safety and Health at Work. Research on work-related stress 2002. Available at: http://osha.eu.int. Accessed October 31, 2006.
11. Berkman L. Tracking social and biological experiences - the social etiology of cardiovascular disease. *Circulation*. 2005;111:3022–3024.
12. Hjemdahl P. Stress and the metabolic syndrome. An interesting but enigmatic association. *Circulation*. 2002;106:2634–2636.
13. Steptoe A, Siegrist J, Kirschbaum C, Marmot M. Effort-reward imbalance, overcommitment, and measures of cortisol and blood pressure over the working day. *Psychomat Med*. 2004;66:323–329.
14. Horsten M, Ericson M, Perski A, Wamala SP. Schenck-Gustafsson K. Psychosocial factors and heart rate variability in healthy women. *Psychomat Med*. 1999;61:49–57.
15. Vrijkotte TGM, van Doornen LJP, de Geus EJC. Overcommitment to work is associated with changes in cardiac sympathetic regulation. *Psychomat Med*. 2004;66:656–663.
16. Hemingway H, Shipley MJ, Runner EJ, Britton A, Malik M, Marmot M. Does autonomic function link social position to coronary risk? - the Whitehall II study. *Circulation*. 2005;111:3071–3077.
17. Vrijkotte TGM, van Doornen LJP, Geus EJC. Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. *Hypertension*. 2000;35:880–886.
18. Lucini D, Di Fede G, Parati G, Pagani M. Impact of chronic psychosocial stress on autonomic cardiovascular regulation in otherwise healthy subjects. *Hypertension*. 2005;46:1201–1206.
19. Ghiandoni L, Donald DE, Cropley M, Mullen JM, Oakley G, Taylor M, O'Connor G, Betterridge J, Klein N, Steptoe A, Deanfield JE. Mental stress induces transient endothelial dysfunction in humans. *Circulation*. 2000;102:2473–2478.
20. Julius S. Sympathetic hyperactivity and coronary risk in hypertension. *Hypertension*. 1993;21:886–893.
21. Pagani M, Lombardi F, Guzzetti S, Rimoldi O, Furlan, Pizzinelli P, Sandrone G, Malfatto G, Dell'Orto S, Piccaluga E, Turiel M, Baselli G, Cerutti S, Malliani A. Power spectral analysis of heart rate and arterial

pressure variabilities as a marker of sympathovagal interaction in man and conscious dog. *Circ Res*. 1986;58:178–193.
22. Malliani A, Pagani M, Lombardi F, Cerutti S. Cardiovascular neural regulation explored in the frequency domain. *Circulation*. 1991;84:482–492.
23. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Circulation.* 1996;93:1043–1065.
24. Lucini D, Mela GS, Mailliani A, Pagani M. Impairment in cardiac autonomic regulation preceding arterial hypertension in humans. Insights from spectral analysis of beat-by-beat cardiovascular variability. *Circulation*. 2002;106:2673–2679.
25. Malliani A, Pagani M, Furlan R, Guzzetti S, Lucini D, Montano N, Cerutti S, Mela GS. Individual recognition by heart rate variability of two different autonomic profiles related to posture. *Circulation*. 1997;96:4143–4145.
26. Pagani M, Mazzuero G, Ferrari A, Liberati D, Cerutti S, Vaitl D, Tavazzi L, Malliani A. Sympathovagal interaction during mental stress. A study using spectral analysis of heart rate variability in healthy control subjects and patients with prior myocardial infarction. *Circulation.* 1991;83:II-43–II-51.
27. Lucini D, Norbiato G, Clerici M, Pagani M. Hemodynamic and autonomic adjustments to real life stress conditions in humans. *Hypertension*. 2002;39:184–188.
28. Lucini D, Porta A, Pagani M. Assessing autonomic disturbances of hypertension in the general practitioner's office: a transtelephonic approach to spectral analysis of heart rate variability. *J Hypertens*. 2003;21:755–760.
29. Esch T, Fricchione GL, Stefano GB. The terapeutic use of relaxation response in stress-related diseases. *Med Sci Mont.* 2003;9:RA23–RA34.
30. *Diagnostic and Statistical Manual of Mental Disorders IV (DSMIV)*. Washington, DC: American Psychiatric Society; 1994.
31. Pagani M, Montano N, Porta A, Malliani A, Abboud FM, Birkett CL, Somers VK. Relationship between spectral components of cardiovascular variabilities and direct measures of muscle sympathetic nerve activity in humans. *Circulation*. 1997;45:1441–1448.
32. Pell S, Fayerweather WE. Trends in the incidence of myocardial infarction and in associated mortality and morbidity in a large employed population, 1957–1983. *N Engl J Med*. 1985;312:1005–1011.
33. Steinbrook R. Imposing personal responsability for health. *N Engl J Med*. 2006;355:753–756.
34. Lucini D, Covacci G, Milani R, Mela GS, Malliani A, Pagani M. A controlled study of the effects of mental relaxation on autonomic excitatory responses in healthy subjects. *Psychosomat Med*. 1997;59:541–552.
35. MacKinnon DP, Krull JL, Lockwood CM. Equivalence of the mediation, confounding and suppression effect. *Sci Prev*. 2000;1:173–181.
36. Chandola T, Brunner E, Marmot M. Chronic stress at work and the metabolic syndrome: prospective study. *BMJ*. 2006;doi:10.1136/bmj.38693.435301.80 (published 14 February 2006).
37. Rozanski A. Integrating psychologic approaches into the behavioral management of cardiac patients. *Psychosomat Med*. 2005;67:567–573.
38. Iellamo F, Pigozzi F, Spataro A, Malacarne M, Pagani M, Lucini D. Autonomic and psychological adaptation to Olympic Games training. A study employing a simple telemedicine approach on the Italian rowing team. *J Sport Med Phys Fitness.* In press.
39. Narkiewicz K, Somers VK. Chronic orthostatic intolerance-Part of a spectrum of dysfunction in orthostatic cardiovascular homeostatis. *Circulation*. 1998;98:2105–2107.
40. Schnall P, Schwarz JE, Landsbergis PA, Warren K, Pickering TG. A longitudinal study of job strain and ambulatory blood pressure: results from a three-year follow-up. *Psychomat Med*. 1998;60:697–706.
41. Manuck SB, Adams MR, McCaffery JM. Kaplan GA. Behaviorally elicited heart rate reactivity and atherosclerosis in ovarioctomized cynomolgus monkeys (Macaca fascicularis). *Arterioscler Thromb Vasc Biol*. 1997;17:1774–1779.
42. Benson H. Systemic hypertension and the relaxation response. *N Engl J Med*. 1977;296:1152–1156.
43. Rahe RH, Taylor CB, Tolles RL, Newhall LM, Veach TL, Bryson S. A novel stress and coping workplace program reduces illness and healthcare utilization. *Psychomat Med*. 2002;64:278–286.
44. Lucini D, Milani RV, Costantino G, Lavie CJ, Porta A, Pagani M. Effects of cardiac rehabilitation and exercise training on autonomic regulation in patients with coronary artery disease. *Am Heart J*. 2002;143:977–983.
45. Nolan RP, Kamath MV, Floras JS, Stanley J, Pang C, Picton P, Young QR. Heart rate variability biofeedback as a behavioral neurocardiac intervention to enhance vagal heart rate control. *Am Heart J*. 2005;149:1137 e1–1137 e7.
46. Dickinson HO, Mason JM, Nicolson DJ, Campbell F, Beyer FR, Cook JV, Williams B, Ford GA. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. *J Hypertens*. 2006;24:215–233.
47. Parati G, Steptoe A. Stress reduction and blood pressure control in hypertension: a role for transcendental meditation? *J Hypertens*. 2004;22:2057–2060.
48. Michie S. Causes and management of stress at work. *Occup Environ Med*. 2002;59:67–72.
49. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research design. *N Engl J Med*. 2000;342:1887–1892.