Randomized controlled evaluation of the effects of cognitive–behavioral stress management on cortisol responses to acute stress in healthy subjects

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Abstract

Psychosocial stress is a potent activator of the hypothalamus–pituitary–adrenal (HPA) axis. While neuroendocrine stress responses are essential for the maintenance of homeostasis, evidence suggests that excessive activation of the HPA axis constitutes a risk for disease and psychopathology. The purpose of the present study was to assess the effect of cognitive–behavioral stress management training on endocrine stress responses and cognitive appraisal under acute psychosocial stress among healthy young subjects. Forty-eight healthy, non-smoking male students without acute or chronic medical or psychiatric disorder on self report were randomly assigned to receive group-based cognitive–behavioral stress management training either before or after a standardized psychosocial stress test (Trier Social Stress Test, TSST). Endocrine and psychological stress responses were assessed with salivary free cortisol response and cognitive appraisal processes to the TSST. In comparison with the control group, subjects in the treatment group showed an attenuated endocrine response ($F (2.55/117.41) = 3.81; P = 0.02$; effect size $f^2 = 0.35$) to the TSST. In addition, subjects in the SIT group had lower stress appraisal and higher control expectancies ($F (2/45) = 6.56; P = 0.003$, effect size $f^2 = 0.29$) compared to controls. Short group-based cognitive–behavioral stress management training reduces the neuroendocrine stress response to an acute stressor in healthy subjects. Therefore, stress management training may prove useful in preventing detrimental effects of stress-induced neuroendocrine activation

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1. Introduction

Psychosocial stress leads to the activation of several physiological stress responses, which in the short term are essential for the maintenance of homeostasis. Being the principal endocrine component of the stress response, the hypothalamus–pituitary–adrenal (HPA) axis mediates a multitude of adaptive physiological and psychological processes. It influences cardiovascular function, fluid volume and hemorrhage, immunity and inflammation, metabolism, neurobiology, and reproductive physiology (Sapolsky et al., 2000). Besides physiological influences (Kirschbaum et al., 1999), the induction of a HPA axis response is regulated by psychological factors. For example, individuals with low self-esteem and negative self-concept failed to habituate to a repeated standardized stressor (Kirschbaum et al., 1995). Furthermore, experimental variation of verbal comments prior to an experimental stressor significantly influenced the subsequent cortisol responses (Rohrmann et al., 1999). Thus, personality factors and cognitive appraisal processes not only play an important part in determining what is stressful (Lazarus and Folkman, 1984), but also modulate the extent and the habituation of the HPA axis response to stress. With regard to possible underlying central nervous system stress circuits involved in the neuroendocrine stress responses, the distinction between ‘systemic’ and ‘processive’ stress pathways has been proposed (Herman and Cullinan, 1997). In contrast to ‘systemic’ stress pathways, which are activated during direct threat of survival, such as hemorrhage and hypoglycemia, and thus do not require integrative processing of higher-order brain structures, psychosocial stressors usually involve the processing of multiple sensory inputs on cortical and limbic levels, including the cerebral cortex, hippocampus, and amygdala. These regions are known to be involved in the cognitive and emotional processing of potentially threatening stimuli and are most likely the primary integrators of the anticipatory stress response, leading to the modulation of neuroendocrine paraventricular output on the hypothalamic level (Herman et al., 2002). The psychological equivalent of these processes could be seen in the stress appraisal processes proposed by Lazarus and Folkman (1984). Consequently, stress-reducing psychosocial interventions aimed at modifying cognitive appraisal are a possible means of influencing HPA axis activity under stress.

A number of studies have demonstrated the effectiveness of cognitive–behavioral stress management in influencing psychological and physiological parameters and health outcomes in health and disease. For example, in symptomatic HIV-positive gay men, ten-week long, group-based cognitive–behavioral stress management training has been shown to reduce symptoms of distress and urinary free cortisol output (Antoni et al., 2000) and to prevent increases in the cortisol/dehydroepiandrosterone-sulfate ratio (Cruess et al., 1999). In women with breast cancer, similar cognitive–
behavioral stress management training after surgery led to a reduction in evening serum cortisol levels (Cruess et al., 2000).

Given that cognitive–behavioral stress management interventions have been shown to influence stress-relevant physiological parameters, we evaluated the effects of short-term, group-based cognitive–behavioral stress management training on endocrine responses and cognitive appraisal under acute stress in a population of healthy young male students.

2. Methods

2.1. Subjects

Subjects were recruited for a study of stress management through an email to all students of the Swiss Federal Institute of Technology, Zurich. The email contained a link to an Internet site, which briefly described the study. Interested subjects had the opportunity to enroll online. They then received a screening questionnaire, containing exclusion criteria designed to reduce confounding factors that have been shown to affect physiological dependent measures. The following exclusion criteria were selected: female gender (Kirschbaum et al., 1999) and smoking (Kirschbaum et al., 1992). Also, subjects were excluded when they reported any acute or chronic somatic or psychiatric disorder in the screening questionnaire and in a telephone interview. After the subjects were provided with complete written and oral descriptions of the study, written informed consent was obtained.

2.2. Procedures

Psychosocial stress test: The Trier Social Stress Test (TSST) has repeatedly been found to induce profound endocrine and cardiovascular responses in 70–80% of the subjects tested (Kirschbaum et al., 1993). After a basal sample of salivary free cortisol was taken, subjects were introduced to the TSST (two minutes). They were then returned to a different room, where they had ten minutes to prepare and to complete a questionnaire designed to assess cognitive appraisal processes (PASA, see below) regarding the anticipated stress situation. Afterwards, subjects were taken back into the TSST room, where they took part in a simulated job interview (five minutes) followed by a mental arithmetic task (five minutes) in front of an audience of two people. A saliva sample was taken immediately before and after the TSST, with further samples taken at 10, 20, 30, 45, and 60 minutes to assess salivary free cortisol. The TSST was performed from 1400 to 1800 h. The employed TSST protocol differs from the protocol used in other TSST studies regarding the ten-minutes preparation time before the TSST, where subjects completed the PASA.

Stress management training: All subjects attended group-based cognitive–behavioral stress management training following the principles of stress inoculation training developed by Meichenbaum (Meichenbaum, 1985), referred to as the stress inoculation training (SIT). Four groups attended group therapy sessions. Groups 1
and 2 met separately on two alternate Saturdays and Groups 3 and 4 met separately on two alternate Sundays. Each group consisted of 12 people and each session lasted from 1000 hours to 1700 hours.

Groups were led by a postdoctoral psychotherapist in training (JG), according to a training manual, and were assisted on each training day by two psychology students. The intervention focused on the four cognitive–behavioral stress-reducing techniques, including stress management (cognitive restructuring, problem-solving, self-instruction) and relaxation training modules (progressive muscle relaxation). Group therapy session 1 consisted of a theoretical introduction and a group discussion about the transactional stress concept (2 h). After a lunch break (1 h), each SIT module was introduced and practiced in groups of four (4 x 1 h). At the end of group therapy session 1, participants received a training manual containing a summary of the transactional stress concept and of all stress-reducing techniques that had been introduced. The manual included a set of flash cards, which briefly described each technique. For homework, all participants were encouraged to assess stress-relevant cognitions, to permanently carry and use the flash cards, and to apply the techniques in the interval between group therapy sessions 1 and 2. Group therapy session 2 began with a review of homework (2 h). After a lunch break (1 h) each technique was again discussed and practiced. Experiential exercises and role-plays used in the group therapy sessions did not resemble the situation used in the TSST.

2.3. Protocol

Upon return of all screening questionnaires, all subjects fulfilling the selection criteria were randomly assigned to four groups by drawing numbers out of an envelope. Because the a priori power calculation resulted in an optimal sample size of N = 48 (see below), only 48 subjects were randomized. The remaining subjects were excluded. After randomization but before the group treatment or waiting condition, all participants were given a set of questionnaires in order to obtain comprehensive descriptions of relevant personality and stress factors (TICS, MESA, FKK). Groups 1 and 2 underwent the TSST after completing the SIT while Groups 3 and 4 received the TSST before the SIT. Thus, Groups 1 and 2 served as treatment groups, while Groups 3 and 4 formed the waiting control condition. The TSST committee did not know whether or not the respective participant had performed the SIT beforehand. The TSST was performed in different rooms from the SIT.

2.4. Measures

Sampling methods and biochemical analyses: Saliva was collected by the subjects using Salivette (Sarstedt, Rommelsdorf, Germany) collection devices and stored at room temperature until completion of the session. Samples were then stored at −20 °C until biochemical analysis took place. The free cortisol concentration in saliva was determined using a time-resolved immunoassay with fluorometric detection, as described in detail elsewhere (Dressendorfer et al., 1992). Inter- and intra-assay coefficients of variance were below 10% for all analytes.
Psychometric measures: To allow comparison of relevant parameters between the randomized groups, the following questionnaires were used:

- Trier Inventory of Chronic Stress (TICS): Perceived chronic stress was assessed with this recently developed measure. Subjects are required to indicate how often the described stressful situations were experienced during the past year. The TICS comprises six subscales, namely ‘work overload’, ‘work discontent’, ‘social stress’, ‘lack of social recognition’, ‘worries’ and ‘intrusive memories’ (Schulz and Schlotz, 1999).
- Competence and Control Orientation (FKK): This 32-item questionnaire assesses the following personality traits: ‘Self-Concept of Own Competence’, ‘Internality’, ‘Powerful Others Control’ and ‘Chance Control’ (Krampen, 1989).
- Stress susceptibility (MESA): This recently developed 36-item questionnaire assesses stress susceptibility on six different subscales (Schulz and Schlotz, unpublished questionnaire).

Psychometric pre–post evaluation of the SIT and the control-waiting condition was performed with the following questionnaire:

- Perceived Stress Scale (PSS): A German translation of the Perceived Stress Scale was used to assess the degree to which situations in life experienced during the previous month are perceived as stressful. Items in the PSS were designed to assess how predictable, uncontrollable, and overloading participants find their lives (Cohen et al., 1983).

Anticipatory cognitive appraisal processes in the TSST were assessed with the following questionnaire:

- Primary Appraisal Secondary Appraisal Scale (PASA): This instrument was specifically constructed to assess cognitive appraisal processes in the TSST according to the transactional stress theory (Gaab et al., unpublished data; Lazarus and Folkman, 1984). The PASA is composed of four situation-specific subscales assessing ‘Challenge’ and ‘Perceived Threat’ (primary appraisal) as well as ‘Self-Concept of Own Competence’ and ‘Control Expectancy’ (secondary appraisal). To be able to assess anticipatory cognitive appraisals, the PASA is administered between the introduction and the actual TSST. The reliability Cronbach’s $\alpha$ in this sample ranges between 0.64 and 0.85. To control for group differences in the perception of ‘Novelty’, we also included 10 items assessing this important situational characteristic (Cronbach’s $\alpha = 0.84$).

2.5. Statistical analysis

ANCOVAs and ANOVAs for repeated measures were computed to analyze endocrine responses between groups, controlling for differences in endocrine baseline levels when indicated. All reported results were corrected by the Greenhouse–Geisser
procedure where appropriate (violation of sphericity assumption). Correlations were computed as Pearson product–moment correlations. For all endocrine parameters, areas under the total response curve (AUC), expressed as area under all samples, were calculated using the trapezoidal method. Data were tested for normal distribution and homogeneity of variance using a Kolmogorov–Smirnov and Levene’s test before statistical procedures were applied. The optimal total sample size of \( N = 48 \) to detect an expected large effect size of \( f^2 = 0.35 \) (representing a large effect size) with a power \( \geq 0.85 \) and \( \alpha = 0.05 \) was calculated a priori with the statistical software G-Power (Buchner et al., 1997). For all analyses, significance level was \( \alpha = 5\% \). Unless indicated, all results shown are means ± standard error of means (SEM).

3. Results

3.1. Sample characteristics

One-hundred-and-fifteen students enrolled online and 68 returned the screening questionnaire. Randomization resulted in 4 groups of 12, so that 24 participants underwent the SIT before the TSST and 24 participants received the SIT after they performed the TSST. Since treatment groups 1 and 2 and waiting control groups 3 and 4 did not differ significantly in any of the assessed demographic, psychometric, and endocrine variables, the respective groups were joined to form a treatment and a control group (data not shown).

Groups did not differ significantly in mean age in years (SIT group: 24.17 vs. control group: 24.54, \( F (1/46) = 0.22; P = 0.64 \)), body mass index (SIT group: 22.74 kg/m\(^2\) vs. control group: 22.50 kg/m\(^2\), \( F (1/46) = 0.11; P = 0.74 \)) or any of the descriptive and pre-treatment psychometric questionnaires (Table 1). Questionnaires employed in the TSST were evaluated according to their psychometric properties using principal component analysis with varimax rotation, showing satisfactory factorial validity (data not shown).

3.2. Endocrine stress responses

The TSST resulted in a significant salivary free cortisol response (time effect: \( F (2.52/117.41) = 62.32; P < 0.000 \)). ANCOVA (first saliva cortisol sample as covariate) showed that baseline differences between the groups did not significantly influence endocrine stress response (time effect: \( F (2.56/115.12) = 1.67; P = 0.19 \)). Groups differed significantly in their salivary free cortisol stress response over time (group by time interaction effect: \( F (2.55/117.41) = 3.81; P = 0.02 \); effect size \( f^2 = 0.35 \); Fig. 1), with subjects in the SIT group showing an attenuated salivary free cortisol response. Groups did not differ in the number of non-responders in the TSST, defined by a 25% increase regarding the baseline (SIT-group: 3 out of 24; control group: 2 out of 24; \( \chi^2 = 0.233; P = 0.637 \)).

In addition, subjects in the SIT group had a significantly lower integrated salivary free cortisol response (group effect: AUC: SIT group mean, 193.41; 95% CI 153.13–
Table 1
Psychometric characteristics of all participants

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>SIT group(^{1})</th>
<th>Control group(^{1})</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>FKK</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-Concept of Own Competence</td>
<td>52.08 (1.64)</td>
<td>50.58 (2.25)</td>
<td>F (3/44) = 0.14; P = 0.94</td>
</tr>
<tr>
<td>Internality</td>
<td>50.88 (1.51)</td>
<td>50.00 (1.71)</td>
<td>F (1/46) = 0.15; P = 0.70</td>
</tr>
<tr>
<td>Powerful Others</td>
<td>47.79 (1.44)</td>
<td>47.88 (1.85)</td>
<td>F (1/46) = 0.001; P = 0.97</td>
</tr>
<tr>
<td>MESA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity to failure</td>
<td>13.96 (0.50)</td>
<td>13.87 (0.52)</td>
<td>F (1/46) = 0.01; P = 0.91</td>
</tr>
<tr>
<td>Tolerance to work overload</td>
<td>11.79 (0.46)</td>
<td>10.88 (0.56)</td>
<td>F (1/46) = 0.161; P = 0.21</td>
</tr>
<tr>
<td>Tolerance to social conflict</td>
<td>11.25 (0.46)</td>
<td>11.88 (0.46)</td>
<td>F (1/46) = 0.93; P = 0.34</td>
</tr>
<tr>
<td>Sensitivity to criticism</td>
<td>11.46 (0.55)</td>
<td>11.83 (0.38)</td>
<td>F (1/46) = 0.34; P = 0.58</td>
</tr>
<tr>
<td>Tolerance to uncertainty</td>
<td>11.92 (0.48)</td>
<td>11.58 (0.51)</td>
<td>F (1/46) = 0.23; P = 0.64</td>
</tr>
<tr>
<td>Ability to relax</td>
<td>9.25 (0.53)</td>
<td>8.33 (0.35)</td>
<td>F (1/46) = 2.07; P = 0.16</td>
</tr>
<tr>
<td>TICS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Work overload</td>
<td>2.68 (0.13)</td>
<td>2.80 (0.15)</td>
<td>F (1/46) = 0.37; P = 0.54</td>
</tr>
<tr>
<td>Work discontent</td>
<td>2.40 (0.13)</td>
<td>2.43 (0.12)</td>
<td>F (1/46) = 0.02; P = 0.89</td>
</tr>
<tr>
<td>Social stress</td>
<td>2.11 (0.08)</td>
<td>2.06 (0.09)</td>
<td>F (1/46) = 0.18; P = 0.68</td>
</tr>
<tr>
<td>Lack of social recognition</td>
<td>2.12 (0.11)</td>
<td>2.28 (0.11)</td>
<td>F (1/46) = 1.20; P = 0.28</td>
</tr>
<tr>
<td>Worries</td>
<td>2.67 (0.16)</td>
<td>2.58 (0.17)</td>
<td>F (1/46) = 0.18; P = 0.68</td>
</tr>
<tr>
<td>Intrusive memories</td>
<td>2.42 (0.19)</td>
<td>2.46 (0.18)</td>
<td>F (1/46) = 0.17; P = 0.90</td>
</tr>
<tr>
<td>PSS (pre-treatment)</td>
<td>38.92 (1.41)</td>
<td>38.42 (1.22)</td>
<td>F (1/46) = 0.07; P = 0.79</td>
</tr>
</tbody>
</table>

\(^{1}\) mean (SEM)
233.69; control group mean, 266.84; 95% CI 226.56–307.14; F (1/46) = 6.73; P = 0.013; effect size f = 0.35). To assess whether group differences in cognitive appraisal of the TSST (see below) had an influence on the salivary free cortisol stress response, the PASA scales were included in the calculations as covariates. ANCOVA results indicated that primary stress appraisal had a significant influence on the salivary free cortisol stress response (time effect: F (2.78/124.97) = 4.12; P = 0.01; effect size f^2 = 0.19). The inclusion of this psychological factor eliminated the observed significant group differences in the salivary free cortisol response over time (group by time interaction effect: F (2.78/124.97) = 1.85; P = 0.15) and the integrated salivary free cortisol response (group effect: AUC: F (1/45) = 3.26; P = 0.08). The inclusion of the additional PASA subscale ‘Novelty’ (see below) did not influence the salivary free cortisol stress response (time effect: F (2.58/115.97) = 1.09; P = 0.35) nor did it change the group by time interaction and group effects (group by time interaction effect: F (2.57/363.93) = 2.91; P = 0.045; group effect: AUC: F (1/45) = 4.38; P = 0.042).

There was no significant association between the number of days between the SIT and the TSST (mean, 14.4 days, range 1–33 days) and the integrated salivary free cortisol response (AUC) in the TSST (r = −0.007, P = 0.98).

3.3. Psychometric measures

Groups differed significantly in their anticipatory cognitive appraisal of the TSST, assessed by the PASA (group effect: F (2/45) = 6.56; P = 0.003, effect size f^2 = 0.29). In comparison with controls, subjects in the SIT group had lower primary stress appraisal (secondary scale ‘primary appraisal’: F (1/46) = 4.81; P = 0.03; primary scales: ‘Challenge’: F (1/46) = 4.55; P = 0.03 and ‘Threat’: F (1/46) = 2.96;
P 0.09) and higher self efficacy appraisal (secondary scale ‘secondary appraisal’: F (1/46) = 11.25; P = 0.002; primary scales: ‘Control Expectancy’: F (1/46) = 2.43; P = 0.12 and ‘Self-Concept of Own Competence’: F (1/46) = 13.08; P = 0.001) (Fig. 2).

Groups did not differ significantly in their perception of ‘Novelty’ (SIT group mean, 2.80; 95% CI 2.35–3.21; control group mean, 3.30; 95% CI 2.88–3.74; F (1/46) = 3.06; P = 0.09). The SIT led to significant changes in the PSS (group by time interaction effect: F (1/46) = 5.27, P = 0.026, effect size f² = 0.11), with SIT participants showing a reduction in the level of perceived stress post treatment (Fig. 3).

4. Discussion

This study demonstrates that short, group-based, cognitive–behavioral stress management training reduces the salivary free cortisol stress response to an acute stressor in healthy male subjects. As indicated by analysis of covariance, these endocrine response differences were influenced by the observed differences in the cognitive appraisal of the situation. Subjects in the treatment group appraised the situation as less stressful and displayed more competence in coping with the situation. According to reported conventions, all reported effect sizes for significant endocrine and psychometric group differences in the TSST were large, whereas the pre–post changes in perceived stress were of medium effect size (Buchner et al., 1997).

To guarantee internal validity, we randomized subjects and controlled for stress-relevant physiological and psychological factors. A comparison of demographic and
psychometric parameters confirmed the randomization of subjects. Furthermore, since both groups had inconspicuous scores in the personality and stress scales, it is unlikely that participants were particularly stressed or stress prone. Thus, we assume that the reported results are not influenced by pre-existing differences between the groups or selection bias.

The salivary free cortisol responses observed in our sample is somewhat higher than those published by other groups using the TSST. This could be a consequence of the altered TSST protocol we used in order to obtain data concerning the anticipatory appraisal processes. However, this difference in the response magnitude does not seem to be a result of group differences, since groups did not differ significantly in the basal cortisol levels and the respective psychometric scales.

We excluded female subjects because their inclusion would have required the control for menstrual cycle phase and for the use of oral contraceptives (Kirschbaum et al., 1999). Although the exclusion of female subjects affects the external validity of the study, we have decided against the inclusion of women in order to enhance the internal validity. However, since gender differences of HPA axis stress responses seem to be mediated through differences in sex hormone levels and the observed response differences in our study were mediated through differences in the cognitive appraisal, we are confident that the stress inoculation training has similar neuroendocrine effects in women.

Because a repeated exposure to the TSST leads to a habituation of the neuroendocrine stress response in a majority of subjects (Kirschbaum et al., 1995; Pruessner et al., 1997), we have decided against a repeated, i.e., pre- and post-treatment/control condition assessment of neuroendocrine stress reactivity. The employed study design can not rule out that the HPA axis response differences observed could be a result of pre-existing group differences in stress reactivity, independent of the stress inoculation training. However, the results of the psychometric personality and stress scales,
both in pre- and in pre-post-training comparison between the groups, speak against this possibility.

Also, because the treatment group received their training before the TSST and thus could have been more acquainted with testing circumstances, it could have been possible that groups differed with regard to their perception of novelty in the testing situation, which could consequently influence the neuroendocrine stress response. However, groups did not differ significantly in their perception of novelty nor did this factor have a significant influence on the salivary free cortisol response.

With regard to the fact that the salivary free cortisol response differences between the treatment and control group were mediated through differences in the cognitive anticipatory appraisal processes, it seems appropriate to assume that the stress inoculation training exerted its effects through the modulation of ‘processive stress pathways’, thus influencing the cognitive and affective processing of stressful stimuli (Herman and Cullinan, 1997). From a psychotherapeutical perspective, a prerequisite of cognitive, emotional, and consequently behavioral changes induced by psychotherapy is the activation and self-awareness of relevant cognitive schemes and the alteration of dysfunctional aspects by ‘corrective emotional experience’ (Grawe, 2002). It is possible that through the use of experiential exercises, role-plays, and the encouragement to practice the stress-reducing techniques at home, these mediators of psychotherapeutical change were effectively employed by the stress inoculation training.

This is the first study to report that short, group-based, cognitive–behavioral stress management training attenuates the endocrine and psychological response to acute stress in healthy subjects. Alterations of HPA axis functioning have been linked to the development and maintenance of psychosomatic and psychiatric disorder (Ehlert et al., 2001) and somatic illness (McEwen, 1998). According to the concept of allostatic load, which represents a marker of cumulative biological burden exacted on the body through attempts to adapt to life’s demands, several conditions of how stress leads to alterations of the HPA axis can be distinguished. These include repeated activation during chronic stress and failure to habituate to repeated stressors (McEwen, 2000). With the observed attenuation of the neuroendocrine stress response and the changes in cognitive appraisal of the stress situation, it is possible that group-based, cognitive–behavioral stress management training could prove useful in preventing detrimental consequences of stress-induced neuroendocrine responses, such as the risk of developing hypertension (al’Absi and Arnett, 2000; al’Absi et al., 1998) and metabolic syndrome X (Bjorntorp and Rosmond, 1999). However, it is important to note that we have not assessed the effects of short, group-based, cognitive–behavioral stress management training on markers of allostatic load, but rather on mechanisms that have been discussed to lead to the development of allostatic load. There is consensus that the relation between HPA axis parameters and health is not linear, thus both too much and too little HPA axis activity and reactivity can be linked to disease and health complaints (McEwen, 1998). As a consequence, our finding of a reduced neuroendocrine stress response should not be considered to be protective per se, but rather with regard to its possible role in the development of stress-related health complaints. Since cortisol has been considered
a primary mediator in the development of allostatic load (Seeman et al., 2001), further studies are needed to evaluate possible long-term effects of the neuroendocrine response differences we observed.

Recently, increased pituitary sensitivity to psychosocial stress, possibly due to severe early life stress, has been described as a biological risk factor for psychopathological conditions in adulthood (Heim et al., 2000). As we have employed the identical psychosocial stress protocol, our findings indicate that similar cognitive–behavioral interventions could be a useful non-pharmacological approach for the prevention of psychopathological conditions related to early-life stress. However, before definite conclusions are drawn, it needs to be shown that the observed neuroendocrine effects persist over a longer period of time and generalize across different stress situations.

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References


