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Psychological determinants of the cortisol stress response: the role of anticipatory cognitive appraisal

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Summary Psychosocial stress is a potent activator of the hypothalamus-pituitary-adrenal (HPA) axis. While the physiological mechanisms of HPA axis responses to stress as well as its short and long-term consequences have been extensively examined, less is known why someone elicits an acute neuroendocrine stress response, i.e. what are the psychological processes involved and how are they related to the acute neuroendocrine stress response.

To examine this question, a questionnaire to assess anticipatory cognitive appraisal processes was developed and administered to 81 male healthy subjects in a standardized psychosocial stress situation (Trier social stress test). Cortisol stress responses were assessed with repeated measurement of salivary free cortisol.

Hierarchical regression analyses show that anticipatory cognitive appraisal, in contrast to general personality factors and retrospective stress appraisal is an important determinant of the cortisol stress response, explaining up to 35% of the variance of the salivary cortisol response.

The reported results emphasize the importance of psychological stress processing for the understanding of psychobiological stress responses. Since stress and its biological consequences have been shown to be associated with the onset and the maintenance of somatic illnesses and psychiatric disorders, psychological processes are prime targets for prevention and intervention.

1. Introduction

In humans, psychosocial stress leads to the activation of the hypothalamus-pituitary-adrenal (HPA) axis. The permissive, stimulatory, suppressive, and preparative effects of HPA axis hormones released in response to stress are believed to

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ensure the maintenance of homeostasis through activation and coordination of various psychological and physiological processes, such as memory consolidation, immune functioning, cardiovascular activation, glucose metabolism, and emotional processing (Schulkin et al., 1994; Sapolsky et al., 2000). Besides these adaptive short- and medium-term consequences of acute stress-induced HPA axis responses, chronic dysregulation and/or enduring excessive secretion of its hormones corticotropin-releasing hormone (CRH), adrenocorticotropin hormone (ACTH), and cortisol have been shown to exert detrimental long-term effects on both somatic and mental well-being (Seeman et al., 2001; Raison and Miller, 2003).

In the majority of human psychoneuroendocrinological and -immunological research, psychosocial stress has been operationalized using experimental and natural situations deemed to be stressful, e.g. parachute jumping, mental arithmetic, fake job interviews, performance tasks, loud noise, academic exams, etc. (Ehlert and Straub, 1998). These situations were validated as stressful by their potency to elicit a psychobiological stress response. From a psychological perspective, these 'stimulus-and-response' definitions of stress have limited utility for the understanding of an individual stress response, and have therefore been abandoned in favor of a transactional definition of stress as 'a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being' (Lazarus and Folkman, 1984). According to this definition, stress in a given situation is understood as the result of a cognitive appraisal process resulting in an emotional, physiological, and behavioral stress response.

With regard to the activation of an HPA axis response through psychological stress, it should be noted that there are large differences among subjects and studies. This response heterogeneity speaks against a simple stimulus–response association or non-specific activation, respectively (Dickerson and Kemeny, 2004). Although the influence of physiological factors on the acute psychoneuroendocrine stress response has been extensively examined (e.g. glucocorticoid receptor polymorphism: Wust et al., 2004, gender: Kirschbaum et al., 1992b, endogenous and exogenous hormones: Kirschbaum et al., 1996, 1999; Heinrichs et al., 2001, age: Kudielka et al., 2004, glucose levels: Kirschbaum et al., 1997, and smoking: Kirschbaum et al., 1992c, 1994), the role and importance of psychological factors in general and cognitive appraisal processes in particular has received relatively little attention and is therefore not clearly delineated (Ursin, 1998; Dickerson and Kemeny, 2004). Research on factors influencing cortisol responses to acute stress can be distinguished into studies that examine the influence of pre-existing or experimentally modified psychological factors on HPA axis responses, and those that assess the association between endocrine stress responses and perceived stressfulness after the stressor has occurred.

With regard to the former, it has been shown that subjects with persistently high cortisol responses to repeated standardized psychosocial stress (Trier Social Stress Test (TSST), Kirschbaum et al., 1993) show a personality profile characterized by low self-esteem and a negative self-concept (Kirschbaum et al., 1995). In addition, increasing correlations between personality traits and cortisol stress responses were obtained by data that aggregated cortisol responses to five consecutive stress situations (Pruessner et al., 1997). However, significant associations between personality traits and acute HPA axis responses to a single psychosocial stressor have not been found (Kirschbaum et al., 1992a; Schommer et al., 1999). This latter finding underscores the importance of having comparable conceptual levels when examining psychoneuroendocrine interactions, i.e. general personality traits are associated to general (=trait), but not to single (=state) HPA axis stress responses. To the best of our knowledge, only one study explicitly examined the influence of cognitive appraisal processes on cortisol responses to acute psychosocial stress (Rohrmann et al., 1999). Using experimenter feedback designed to arouse or reassure subjects during an anticipation period before the stressor was applied, higher cortisol responses in both manipulative conditions in comparison to a control condition were observed. However, it should be noted that in this study, cognitive appraisal processes were an experimentally induced independent variable and were not directly measured in subjects. In addition, a number of studies examined the relationship between uncontrollability and cortisol responses, usually by experimental manipulation of the stress situation. However, results have been inconclusive (Dickerson and Kemeny, 2004).

The majority of studies assessed the retrospective appraisal of the previous stress situation. While this approach allows the validation of the respective situation as being subjectively and retrospectively stressful, it enables few conclusions to be drawn about the relationship between the retrospective evaluation and the extent of the associated HPA axis response. To illustrate this, studies investigating differences in HPA axis responses to a standardized psychosocial stress test between healthy controls and patients with atopic dermatitis (Buske-Kirschbaum et al., 2002), and between younger and older subjects (Kudielka et al., 2000, 2004) found significant differences in the HPA axis responses, but not in the retrospective perception of the previous situation, thus validating the assumption of a physiological basis of the observed HPA axis response differences. Theoretically, this should only hold true if the retrospective perception is indeed associated with the neuroendocrine stress responses. However, these associations have not yet been tested (Kudielka et al., 2000, 2004) or were found to be non-significant (Buske-Kirschbaum et al., 2002).

In order to investigate whether anticipatory and retrospective cognitive appraisal processes are related to HPA axis responses to acute stress, the present study set out to develop a questionnaire to assess anticipatory cognitive appraisal processes, and determine the association between anticipatory and retrospective appraisal processes as well as general personality factors and the cortisol response to a standardized stress paradigm.

2. Methods

2.1. Subjects

Subjects were recruited for the study through an email sent to all students of the Swiss Federal Institute of Technology, Zürich and the University of Zürich, Switzerland. The email contained a link to an Internet site, which briefly described the study. Interested subjects were able to enroll online. Upon enrollment, they received a screening questionnaire containing exclusion criteria designed to exclude factors or characteristics that have been shown to affect the physiological dependent measures under study. The following exclusion criteria were selected: female gender (Kirschbaum et al., 1999) and smoking (Kirschbaum et al., 1992c). In addition, subjects were excluded if they reported any acute or chronic somatic or psychiatric disorder in the screening questionnaire and in a subsequent 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 (2 min). They then returned to a different room, where they were given 10 min to prepare and to complete a questionnaire designed to assess cognitive appraisal processes (Primary Appraisal Secondary Appraisal scale, PASA, see below) regarding the stress situation described below. Afterwards, subjects were taken back into the TSST room, where they took part in a simulated job interview (5 min) followed by a mental arithmetic task (5 min) 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 min after the TSST to assess salivary free cortisol. The TSST was performed between 14.00 and 18.00 h. The TSST protocol employed differs from the protocol used in other TSST studies in terms of the 10 min of preparation time before the TSST (and after the introduction), where subjects in the current study completed the PASA.

2.3. Development of the transactional stress questionnaire (PASA)

During the development of the questionnaire, items were theoretically derived to assess each of the four cognitive appraisal processes relevant for the TSST: primary stress appraisal: 'Threat' and 'Challenge', as well as secondary appraisal: 'Self-Concept of Own Abilities', 'Control Expectancy'. The items for the primary appraisal scales ('Threat' and 'Challenge') we generated to fit in with the respective description of the theoretical constructs proposed by Lazarus and Folkman (1984). As we set out to operationalize anticipatory stress processes, i.e. the TSST, and not the appraisal of past stressful events, we omitted the third stress appraisal 'Harm/Loss'. Secondary appraisal has been described as an evaluation of '*what might and can be done*' (cited from Lazarus and Folkman, 1984, p. 35). This definition corresponds to the distinction between 'Efficacy Expectation' and 'Outcome Expectancy' proposed by Bandura (1977). A more recent reformulation of these concepts led to the description of 'Self-Concept of Own Abilities' and 'Control Expectancy' and the development of the 'Questionnaire of Competence and Control' (Fragebogen zu Kompetenz- und Kontrollüberzeugungen, FKK, Krampen, 1989), which includes two scales intended to operationalize these two personality factors. As the FKK operationalizes these personality factors as *generalized* expectancies, we reformulated the respective items into situation-*specific* items accordingly (e.g. FKK item 23 'I can control much of what is happening in my life' into PASA item 12 'I can control much of what will happen in the job interview').

Each scale comprised eight items, on which subjects had to evaluate the extent to which the particular statement applied to themselves on a 6-point scale ranging from 'Strongly disagree' to 'Strongly agree'. All items were directly related to the anticipated stress situation. The items were presented in the order of 'Threat', 'Challenge', 'Self-Concept of Own Abilities', and 'Control Expectancies' in sets of four. Items from the primary stress appraisal scales were formulated both positively and negatively in order to prevent possible response-set tendencies. With the exception of four items of the scale 'Self-Concept of Own Abilities', all items of the secondary appraisal scales were formulated positively, because the original FKK scales from which these items were derived were not systematically controlled for possible response-set tendencies. The items of the PASA are listed in Appendix A. A full version of the PASA in English and German can be obtained from the corresponding author.

2.4. Measures

Sampling methods and biochemical analyses: saliva was collected by the subjects using Salivette (Sarstedt, Nümbrecht, Germany) collection devices and stored at room temperature until completion of the session. Samples were then stored at −20 °C until biochemical analysis. Salivettes were then centrifuged at 3000 rpm for 5 min, which resulted in a clear supernatant of low viscosity. Salivary free cortisol concentrations were measured using a commercially available chemi-luminescence-assay (CLIA) with high sensitivity of 0.16 ng/ml (IBL, Hamburg, Germany).

Additional psychometric measures:

- Competence and Control Orientation (FKK, Krampen, 1989): this 32-item questionnaire assesses the following personality traits: 'Self-Concept of Own Competence', 'Control Expectancy: Internality', 'Control Expectancy: Powerful Others Control' and 'Control Expectancy: Chance Control'. The four primary scales can be summarized in two secondary scales ('General Self-Efficacy' = ('Self-Concept of Own Competence' + 'Control Expectancy: Internality')/2 and 'General External Control Expectancy' = ('Control Expectancy: Powerful Others Control' and 'Control Expectancy: Chance Control')/2), and one tertiary scale ('Internality versus Externality' = 'General Self-Efficacy'-'General External Control Expectancy'). The FKK was completed before the subjects were introduced to the TSST.
- Visual Analogue Scales (VAS): four VAS were employed to assess perceived stress, challenge, self-concept, and perceived control after cessation of the TSST. The VAS employed is similar to instruments used in other TSST studies (e.g. Kirschbaum et al., 1999).

2.5. Statistical analysis

As an indicator for structural validity and reliability of the PASA, factor analyses (principal component factor analysis with direct oblimin oblique rotation) and Cronbach's alpha were calculated. One-sample *t*-tests were calculated to compare personality characteristics with normative data, when available. ANCOVAs and ANOVAs for repeated measures were computed to analyze cortisol responses, controlling for differences in cortisol baseline levels when indicated. All reported ANOVA results were corrected by the Greenhouse–Geisser procedure where appropriate (violation of sphericity assumption). To assess associations between psychological and cortisol parameters, bivariate (Pearson product-moment and partial correlations) and multivariate (hierarchical multiple regression analysis) methods were used. For cortisol parameters, areas under the response curve were calculated with respect to increase (AUCi) and with respect to ground (AUCg) using the trapezoidal method as an indicator for the integrated cortisol response in the TSST (Pruessner et al., 2003). Data were tested for normal distribution and homogeneity of variance using a Kolmogorov-Smirnov and a Levene's test before statistical procedures were applied. For all analyses, the significance level was $\alpha = 5\%$. The optimal total sample size of $N = 82$ to detect an expected effect size of $f^2 = 0.20$ (representing a medium to large effect size) with a power ≥ 0.90, $\alpha = 0.05$ and four predictors was calculated a priori with the statistical software G-Power (Buchner et al., 1997). Unless indicated, all results shown are means $\pm$ standard error of means (SEM).

3. Results

3.1. Sample characteristics

220 male students enrolled online and 105 of these returned the screening questionnaire 81 subjects agreed to participate and were included in

Table 1 Psychometric characteristics of all participants.

Questionnaire	Study participants[a]	Normative *T* score	Statistic
FKK			
Self-concept of own competence	51.23 (1.04)	50	$t_{80}=1.19$; $P=0.24$
Control expectancy: internality	50.54 (0.96)	50	$t_{80}=0.56$; $P=0.58$
Control expectancy: powerful others	48.07 (0.92)	50	$t_{80}=-2.11$; $P=0.04$
Control expectancy: chance	44.10 (1.0)	50	$t_{80}=-5.79$; $P=0.00$

[a] Mean (SEM).

the study. The mean age in years was 24.6 (SEM 0.39, range 20–36 years) and the mean body mass index was 22.68 kg/m^2 (SEM 0.25, range 18.25–28.40). Study participants did not differ significantly from age-related normative data with regard to 'Self-Concept of Own Competence' and 'Control Expectancy: Internality', but had significantly lower scores on the scales 'Control Expectancy: Powerful Others' and 'Control Expectancy: Chance' (Table 1).

3.2. Psychometric evaluation of the PASA

A principal component factor analysis with direct oblimin oblique rotation of the PASA items for the total sample ($N=81$) indicated that 16 items loaded on more than one factor and were therefore excluded from further calculations (data not shown). After the exclusion of these items, a second principal component factor analysis with direct oblimin oblique rotation was conducted on the remaining PASA items. Based on the Scree curve, a four-factor solution was considered optimal for the data set. The resulting four factors explained a total of 62.02% variance after rotation (explained variance: factor 1=27.88%, factor 2=14.52%, factor 3=12.92%, factor 4=6.70%). The factor loading component matrix confirmed the theoretical assumptions (data not shown). To test for internal consistency, Cronbach's alpha was calculated. The PASA scales show reasonable (>0.60) to good (>0.80) internal consistency ('Threat': $\alpha=0.83$; 'Challenge': $\alpha=0.63$; 'Self-Concept of Own Competence': $\alpha=0.81$; 'Control Expectancy': $\alpha=0.77$). The positive intercorrelations within the primary and secondary appraisal scales, and the negative intercorrelations between the primary and secondary appraisal scales demonstrated logical relationships (Table 2).

Based on the theoretical assumption of the transactional stress model, we conducted further principal component factor analysis with direct oblimin oblique rotation with a two-factor extraction on the basis of the primary scales 'Threat', 'Challenge', 'Self-Concept of Own Competence' and 'Control Expectancy'. The resulting two factors explained a total variance of 72.91% (explained variance in %: factor 1=43.62%, factor 2=29.29%) and comprised the primary scales 'Threat' and 'Challenge' (Factor 1) and 'Self-Competence of Own Competence' and 'Control Expectancy' (Factor 2). They were consequently labeled secondary scales 'Primary Appraisal' (PA) and 'Secondary Appraisal' (SA). Internal consistency

Table 2 Intercorrelations of PASA scales.

Scales	PASA: 'Threat'	PASA: 'Challenge'	PASA: 'Self Concept'	PASA: 'Control expectancy'	Primary appraisal	Secondary appraisal	Stress index
T	1.00						
C	0.38*	1.00					
SC	−0.47*	−0.14	1.000				
CE	−0.11	0.05	0.24*	1.00			
PA	0.91*	0.77*	−0.42*	−0.07	1.00		
SA	−0.44*	−0.03	0.88*	0.75*	−0.33*	1.00	
SI	0.85*	0.54*	−0.76*	−0.46*	0.86*	−0.77*	1.00

Correlation is significant at the 0.05 level (2-tailed).

Table 3 Correlations between general and situation-specific personality factors.

Scales	PASA: 'Threat'	PASA: 'Challenge'	PASA: 'Self Concept'	PASA: 'Control expectancy'	Primary appraisal	Secondary appraisal	Stress index
FKK: 'Self-Concept of Own Competence'	−0.411***	−0.169	0.429***	0.123	−0.376***	0.370***	−0.469***
FKK: 'Control expectancy: Internality'	−0.295U**	0.099	0.247*	0.339**	−0.166	0.352**	−0.314*
FKK: Control expectancy: Powerful Others Control	0.209*	0.042	−0.218*	−0.136	0.171	−0.226*	0.246*
FKK: Control expectancy: Chance Control	0.131	−0.058	−0.360***	−0.117	0.067	−0.317**	0.226*

Note: $P<0.05$; $P<0.01$; $P<0.001$.

for these secondary scales was good ('Primary Appraisal': $\alpha=0.80$) or reasonable ('Secondary Appraisal': $\alpha=0.74$), respectively.

Furthermore, a global scale (tertiary scale: 'Stress Index', SI), comprising the combination of both secondary scales, was constructed in order to obtain an integrated measure of transactional stress perception. Since Lazarus and Folkman (1984) stressed the mutual dependency of primary and secondary processes, the integrated tertiary scale represents this assumed interaction.

The intercorrelations between the primary, secondary, and tertiary scales demonstrated logical relationships, corresponding to the underlying theoretical assumptions (Table 3). The correlations between the FKK and PASA scales also demonstrated logical relationships (Table 3).

3.3. Associations between psychological parameters and endocrine stress responses

The TSST resulted in a significant salivary free cortisol response over time (time effect: F (2.63/210.11)=111.07; $P<0.001$, Fig. 1). The mean integrated salivary free cortisol response with respect to ground (AUCg) and with respect to increase (AUCi) was AUCg: 2180.47 nmol/l (SEM 90.63, minimum: 720.76, maximum: 4980.30) and AUCi: 970.51 nmol/l (SEM 80.22, minimum: −800.91, maximum: 3130.35).

To analyze the associations between the PASA scales and the endocrine stress responses, a hierarchical regression analysis was carried out with integrated salivary free cortisol responses AUCg and AUCi as dependent variables and primary PASA scales as independent variables. This statistical approach allows the determination of both the proportion of variance in the endocrine data accounted for by the PASA scales and the significance of the contribution of each PASA scale. The results revealed that the primary PASA scales accounted for 35% of the variance in the integrated cortisol response with respect to ground (AUCg: $R=0.62$, $R^2=0.39$, adjusted $R^2=0.35$; F (4/76)=11.97; $P=0.001$), and 22% of the cortisol response with respect to increase (AUCi: $R=0.52$, $R^2=0.27$, adjusted $R^2=0.22$; F (4/76)=6.90; $P=0.001$). However, the two scales differed in terms of their significance of contribution. While primary appraisal PASA scales ('Threat' and 'Challenge') were identified as significant predictors of both AUCg and AUCi, secondary appraisal PASA scales were not found to be significant predictors (Tables 4 and 5). The scatter plots between the 'Stress Index' and both AUCs are depicted in Fig. 2.

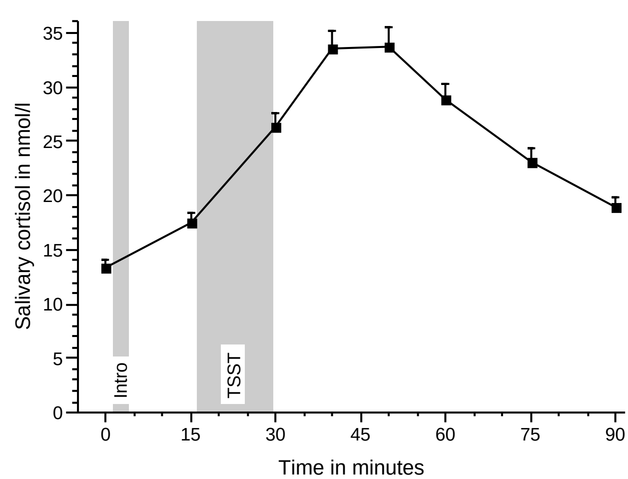

Figure 1 Salivary cortisol responses in the TSST.

Table 4 Results of regression analysis between AUCg of endocrine stress response (criterion) and PASA scales (predictors).

Variables	Partial correlations with AUCg	β	T	P	R^2 change
T	0.34	0.35	3.16	0.002	0.286
C	0.34	0.31	3.1	0.003	0.06
SC	−0.15	−0.15	−1.4	0.18	0.016
CE	−0.10	−0.09	−0.9	0.37	0.002
PA	0.55	0.56	6.02	0.000	0.38
SA	−0.17	−0.21	−1.85	0.07	0.016
SI	0.59	0.59	6.49	0.000	0.35

Table 5 Results of regression analysis between AUCi of endocrine stress response (criterion) and PASA scales (predictors).

Variables	Partial correlations with AUCi	β	T	P	R^2 change
T	0.33	0.35	3.1	0.003	0.22
C	0.21	0.31	2.1	0.04	0.04
SC	−0.01	−0.15	−0.1	0.90	0.00
CE	−0.08	−0.09	−0.7	0.50	0.005
PA	0.48	0.49	4.87	0.00	0.26
SA	−0.08	−0.07	−0.73	0.47	0.005
SI	0.47	0.47	4.66	0.000	0.22

These results were confirmed by further regression analyses including the secondary PASA scales 'Primary Appraisal' and 'Secondary Appraisal' as independent variables (AUCg: $R=0.62$, $R^2=0.38$, adjusted $R^2=0.37$, Table 4; F (2/78)$=$24.32; $P<0.001$; AUCi: $R=0.51$, $R^2=0.26$, adjusted $R^2=0.25$; F (2/78)$=$14.00; $P<0.001$, Table 5). In addition, the tertiary scale 'Stress Index' accounted for 34% of the total variance of the AUCg and 21% of the AUCi (AUCg: $R=0.59$, $R^2=0.35$, adjusted $R^2=0.34$; F (1/79)$=$42.15; $P<0.001$, Table 4; AUCi: $R=0.47$, $R^2=0.22$, adjusted $R^2=0.21$; F (1/79)$=$21.75; $P<0.001$, Table 5).

The correlations between single PASA scales and both AUCs of the salivary free cortisol response were significant for 'Threat' (AUCg: $r=0.54$, $P<0.001$;

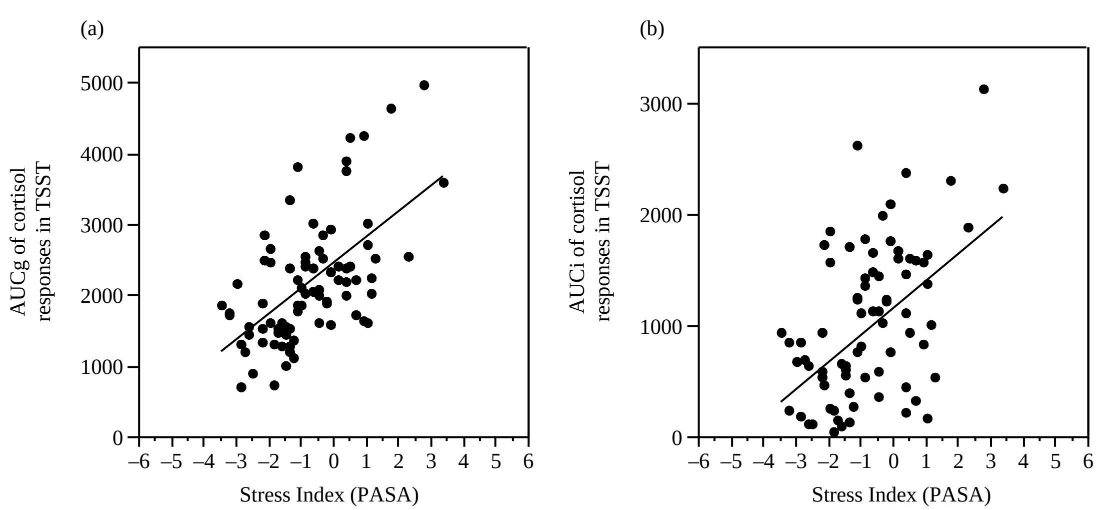

Figure 2 Associations between tertiary PASA scale and AUCg and AUCi of endocrine stress responses.

AUCi: $r=0.47$, $P<0.001$), 'Challenge' (AUCg: $r=0.44$, $P<0.001$; AUCi: $r=0.36$, $P=0.001$), and 'Self-Concept of Own Competence' (AUCg: $r=-0.35$, $P=0.001$; AUCi: -0.23, $P=0.02$), but not for 'Control Expectancies' (AUCg: $r=-0.12$, $P=0.15$; AUCi: $r=-0.08$, $P=0.25$). Both secondary PASA scales were significantly associated with both AUCs ('Primary Appraisal'-AUCg: $r=0.60$, $P<0.001$ and-AUCi: $r=0.51$, $P<0.001$; 'Secondary Appraisal'-AUCg: $r=-0.31$, $P=0.002$ and-AUCi: $r=-0.21$, $P=0.04$). In addition, the tertiary scale 'Stress Index' was significantly correlated with integrated salivary free cortisol responses (AUCg: $r=0.59$, $P<0.001$; AUCi: $r=0.47$, $P<0.001$).

With regard to the retrospective perception of the TSST, two general VAS scales (retrospective primary appraisal, VAS-PA (=(VAS 1+VAS 2)/2); retrospective secondary appraisal, VAS-PA=(VAS 3+VAS 4)/2)) were identified by means of factor analyses, accounting for 59.7% of the total variance (Internal consistency: VAS-PA: $\alpha=0.63$; VAS-PA: $\alpha=0.71$). No significant correlation between the two VAS scales and the two AUCs were detectable (VAS-PA-AUCg: $r=0.10$, -AUCi: $r=0.10$; VAS-SA-AUCg: $r=-0.11$, AUCi: $r=-0.07$; all n.s.). Furthermore, regression analysis did not show a significant impact of VAS scales on the integrated cortisol responses (AUCg: $R=0.15$, $R^2=0.02$, adjusted $R^2=0.001$; F (2/78)=0.94; $P=0.39$; AUCi: $R=0.13$, $R^2=0.02$, adjusted $R^2=0.009$; F (2/78)=0.63; $P=0.53$). However, VAS scales significantly correlated with PASA scales (VAS-PA-PASA-PA: $r=0.22$, $P=0.02$; VAS-SA-PASA-SA: $r=0.29$, $P=0.004$).

To examine the influence of general personality factors on cortisol stress responses, hierarchical regression analyses with the two AUCs as the dependent variable and the FKK scales ('Self-Concept of Own Competence', 'Control Expectancy: Internality', 'Control Expectancy: Powerful Others Control' and 'Control Expectancy: Chance Control') as independent variable were performed. The results revealed that the FKK scales accounted for 8 and 2% of the variance in the integrated salivary free cortisol response (AUCg: $R=0.36$, $R^2=0.13$, adjusted $R^2=0.08$; F (4/76)=2.80; $P=0.03$; AUCi: $R=0.27$, $R^2=0.07$, adjusted $R^2=0.02$; F (4/76)=1.43; $P=0.23$). In addition, two FKK scales correlated significantly with the integrated cortisol responses ('Self-Concept of Own Competence'-AUCg: $r=-0.32$, $P=0.002$ and-AUCi: $r=-0.19$, $P=0.04$; 'Control Expectancy: Internality'-AUCg: $r=-0.26$, $P=0.01$ and -AUCi: $r=0.22$, $P=0.02$; 'Control Expectancy: Powerful Others Control'-AUCg: $r=0.14$, $P=0.11$ and-AUCi: $r=0.07$, $P=0.27$; 'Control Expectancy: Chance Control'-AUCg: $r=0.17$, $P=0.07$ and-AUCi: $r=0.04$, $P=0.37$).

To determine whether the observed effects of these general personality factors on the AUCg were mediated through situation-specific cognitive appraisal processes (i.e. tertiary PASA scale 'Stress Stress Index'), a regression analysis with stepwise exclusion (Criteria: Probability-of-F-to-enter$<=0.050$, Probability-of-F-to-remove$>=0.100$) was performed. The resulting final regression model with the highest adjusted R^2 only consisted of the tertiary PASA scale, the changes between the different regression models in adjusted R^2 were minimal (first regression model (including all FKK scales and tertiary PASA scale 'Stress Index'): $R=0.60$, $R^2=0.36$, adjusted $R^2=0.32$; F (5/75)=8.37; $P<0.001$; final regression model (including only the tertiary PASA scale 'Stress Index') $R=0.59$, $R^2=0.35$, adjusted $R^2=0.34$;F(1/79)=42.15; $P<0.001$; adjusted R^2 change due to the exclusion of FKK scales: $=-0.1$).

In addition, calculating partial correlations between AUCg of the endocrine response in the TSST and general (i.e. tertiary) FKK scales and situation-specific (i.e. PASA) scales, personality factors, revealed that the inclusion of situation-specific appraisal processes, i.e. PASA scales, altered the associations between general personality factors, i.e. FKK scales, but not vice versa (Table 6).

Table 6 Correlations and partial correlations between general and situation-specific personality factors and AUCg of the endocrine stress response.

Correlation between	r	p	Controlling for	r	p
AUCg of cortisol response in TSST×'stress index' (tertiary PASA scale)	0.59	<0.000	Tertiary FKK scale	0.57	<0.000
AUC of cortisol response in TSST× tertiary FKK scale (tertiary PASA scale)	−0.21	0.03	'Stress Index'	−0.10	0.18

4. Discussion

The study set out to determine the impact of general and situation-specific psychological parameters on the neuroendocrine stress response in an acute stress situation. In order to achieve this, a situation-specific transactional stress questionnaire to assess anticipatory cognitive appraisal processes was developed and applied to healthy male subjects in an acute stress situation.

The development and statistical evaluation of the questionnaire led to the PASA, a short psychometric instrument comprising four primary scales, two secondary scales, and one tertiary scale, which validly and reliably assesses anticipatory cognitive appraisal processes according to the transactional stress theory. The PASA scales explained 35% of the variance of the total and 22% of the baseline-corrected cortisol responses to the TSST. PASA scales differed with respect to their significance and the size of their associations to the cortisol stress response. Interestingly, secondary appraisal processes were not significant determinants of the cortisol response.

General personality factors (FKK scales) were only weakly associated with the salivary cortisol stress response, explaining 8% (AUCg) and 2% (AUCi) of the total variance, respectively. Accordingly, results of regression analysis and partial correlations indicated that the influence of general personality factors on cortisol responses is mediated through situation-specific appraisal, but not vice versa. Interestingly, retrospective perception (VAS) of the TSST was not associated with the cortisol response to the TSST.

These results confirm previous observations of non-significant and/or low associations between general personality factors and acute HPA axis responses to psychosocial stress (Kirschbaum et al., 1992a; Pruessner et al., 1997; Schommer et al., 1999). They also shed new light upon these findings. Although general (FKK) and specific (PASA) personality scales are significantly correlated, this association is only modest. Thus an individual does not necessarily appraise a given situation in the same way in which it appraises situations in general. Under the assumption of a psychobiological stress response, i.e. that the magnitude of a biological response is determined by psychological factors, our results support the assumption that the influence of situation-specific factors is stronger than the influence of general personality factors on a given biological response.

With respect to situation-specific processes, our results indicate that the retrospective perception of a situation is not an adequate candidate to explain cortisol responses to the respective situation. The observed lack of criterion validity of retrospective perception on cortisol responses to stress could have important implications, since our results, as well as those from previous studies (e.g. Smyth et al., 1998; Kudielka et al., 2000, 2004; Buske-Kirschbaum et al., 2002), do not support the assumption that a retrospective perception of stress is a valid indicator that the subject also elicited a corresponding cortisol stress response. On the one hand, this could be a consequence of the temporal delay of the retrospective perception, meaning that it is based not only on the appraisal of the situation, but also on the appraisal of the outcome of the situation. The finding of low correlations between PASA and VAS scores supports this assumption. On the other hand, it should be noted that the HPA axis itself has a strong anticipatory component. In addition to fast and non-genomic actions (for example in negative feedback processes: Hinz and Hirschelmann, 2000), glucocorticoids have genomic actions, and thus the consequences of an HPA activation are exerted until about 1 h after the stressor has occurred. It therefore follows that HPA activation is more strongly associated with anticipatory, e.g. 'what will happen' stress appraisal, rather than retrospective, e.g. 'what has happened' stress appraisal. Further studies are clearly needed to elucidate whether retrospective assessment of perceived stress is associated with the cortisol response and if so, to what extent and under what circumstances.

Our study has several shortcomings. First, we only investigated healthy, young, nonsmoking males. The exclusion of possible confounding variables enhanced the internal validity at the expense of the external validity. A number of factors, such as gender, age, smoking, oral contraceptives, and menstrual cycle phase influence the activity and reactivity of the HPA axis on different levels through different mechanisms. Therefore, further studies with more liberal inclusion criteria are needed before general conclusions can be made.

Second, we employed a standardized and potent laboratory stress paradigm. Cortisol responses to the TSST showed an average increase with regard to baseline of 20 nmol/l. However, comparable cortisol responses are rarely found in natural situations. For example, Smyth et al. (1998) reported an average increase of cortisol between 1.18 nmol/l (in response to one current problem) and

1.67 nmol/l (after three stressors reported) to naturally occurring daily stressors. It is therefore possible that our results could not be easily transferred into real-life situations.

Third, we only measured salivary free cortisol as an indicator of the HPA axis response to stress. While salivary free cortisol has been shown to be a valid and reliable endocrine marker of HPA axis activity and reactivity (Kirschbaum and Hellhammer, 1994), and ACTH and cortisol stress responses have been shown to be tightly linked in healthy subjects (Dickerson and Kemeny, 2004), it remains to be shown whether and how other customary endocrine parameters, such as plasma cortisol, ACTH, and plasma catecholamines are related to psychological factors and processes examined in this study.

Fourth, we did not use identical psychometric instruments to compare associations between pre- (PASA) and poststress (VAS) stress appraisal and cortisol responses. We refrained from doing so in order to reproduce findings from other studies, showing nonsignificant associations between the VAS and cortisol responses in the TSST.

How can our results be explained? From a morphological perspective, the central control of the HPA axis is governed by the hypothalamic paraventricular nucleus (PVN). The PVN receives input from stress-excitatory and -inhibitory circuits, which can differentiated with respect to the central nervous system structures involved (limbic-insensitive vs. limbic-sensitive), the processing of sensory information (systemic vs. processive), or the type of perceived homeostatic disruption (reactive vs. anticipatory), respectively (Herman and Cullinan, 1997; Lopez et al., 1999; Herman et al., 2003). In this understanding, psychosocial stress activates the HPA axis on a hypothalamic level through processive stress pathways, involving inhibitory (mediated through indirect input from the ventral subiculum and the medial prefrontal cortex) and excitatory (mediated through indirect input from the amygdala) limbic-sensitive structures. The purpose of these processive pathways is to 'weigh the importance of a stimulus to survival, and to use the resulting information to tune an appropriate hormonal response' (cited from: Herman et al., 2003, page 170–171). Interestingly, the assumed purpose of these regulatory inputs in the PVN, i.e. the emotional processing of motivationally relevant stimuli in the amygdala and the integration of perceptual, attentional, and mnemonic functions in the frontal cortex and hippocampus (LeDoux, 2000; Compton, 2003), bear a resemblance to the cognitive appraisal processes involved in the subjective experience of stress (Lazarus, 1999).

This psychobiological framework promotes the understanding of why anticipatory but not retrospective perception of stress is related to the neuroendocrine stress response. With the exception of permissive effects, which are mediated by basal concentrations (De Kloet et al., 1998), secretion and physiological effects of HPA axis hormones are generally delayed, the latter reflecting the molecular mechanisms underlying the actions of cortisol. The physiological role of GCs have thus been described as being like 'preventing water damage rather than putting out the fire' (Sapolsky et al., 2000). Furthermore, in this light it becomes understandable why primary appraisal, but not secondary processes are predictors of the cortisol responses. The two appraisal processes are not independent of one another, and thus primary appraisal is not only the antecedent of secondary appraisal, but also its consequence. Therefore, although secondary processes are not directly involved in the activation of the HPA axis, they indirectly influence the perception of threat and challenge. From a biological perspective, the perception of threat would be the principal stimulus to induce HPA axis responses, while being strongly influenced by the perception of controllability.

Our findings support the conclusions of Dickerson and Kenemy (2004), who conducted a comprehensive meta-analysis of stress-induced cortisol responses in humans. However, in contrast to their approach of searching for situational stressor characteristics in order to explain the substantial variability in cortisol responses found between studies, we attempted to explain the variability found within studies, thus looking for psychological and not situational variables to account for cortisol responses.

Also, our results are congruent with reports of cortisol fluctuations with increases and decreases of negative affect (Buchanan et al., 1999). Although we did not assess changes in affect during the TSST, we assume that possible changes in affect are related to cognitive appraisal processes. However, the question whether and how affect influences cognitive appraisal was not addressed in our study.

The possible implications of our results should be discussed with respect to psychobiological models linking stress and mental and somatic health. In a reformulation of the historical homeostasis theory, the concept of 'allostatic load', defined as the 'wear and tear of stress on the body', has been proposed (McEwen, 1998) and operationalized by a set of physiological parameters, with cortisol as a primary mediator (Seeman et al., 2001). In this model, 'the perception of stress is influenced by one's experiences, genetics, and behavior. When the brain perceives an experience as stressful, physiologic and behavioral responses are initiated, leading to allostasis and adaptation. Over time, allostatic load can accumulate, and the overexposure to mediators of neural, endocrine, and immune stress can have adverse effects on various organ systems, leading to disease' (cited from McEwen, 1998). From this point of view, it is of crucial importance to gain an understanding of when and why an individual perceives a given situation as stressful and how this relates to the biological stress response. In other words, 'it appears that the modulation of anticipatory pathways may form a critical neuroendocrine effector component of these human disease processes' (cited from Herman et al., 2003). Therefore, the knowledge of psychological processes in the activation of the HPA axis could help to develop and employ preventive and therapeutic interventions in order to reduce physiological mechanisms of allostatic load (Ursin and Eriksen, 2004). We have previously shown that the modulation of cognitive appraisal processes through cognitive behavioral stress management training (CBSM) results in a reduction of cortisol responses (Gaab et al., 2003) and that these effects persist over a period of 4 months (Hammerfald et al., 2004).

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Appendix A

PASA items

I do not feel threatened by the situation
The situation is important to me.
In this situation I know what I can do.
It mainly depends on me whether the experts judge me positively.
I find this situation very unpleasant.
I do not care about this situation.
I have no idea what I should do now.
I can best protect myself against failure in this interview through my behavior.
I do not feel worried because the situation does not represent any threat for me.
The situation is not a challenge for me.
In this situation I can think of lots of action alternatives.
I am able to determine a great deal of what happens in this interview myself.
This situation scares me.
This task challenges me.
I can think of lots of solutions for solving this task.
If the experts judge me positively it will be a consequence of my effort and personal commitment.

VAS items

The past situation was stressful for me.
I found the past situation to be a challenge.
I knew what I had to do to influence the past situation.
I was able to do something to influence the course of the previous situation.

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