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Associations between fear-avoidance and endurance responses to pain and salivary cortisol in the context of experimental pain induction

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Summary Recent clinical studies in patients with lower back pain indicate that maladaptive fear-avoidance- and endurance-related pain responses (FAR and ER) have an influence on pain-induced physiological stress levels. The aim of the present study was to follow-up these results under well-controlled laboratory conditions. For this purpose, 30 healthy adults were asked to indicate their usual responses to pain, and were then confronted with an experimental pain stimulus (cold pressor test). Cortisol served as a measure of physiological stress. The results reveal positive associations between cortisol and FAR patterns, and negative associations between cortisol and behavioral ER. Conceivably, FAR contribute to long-lasting elevated stress levels in patients with stress-related musculoskeletal pain. In contrast, short-term, stress-lowering effects of ER might even be considered an advantage in coping with pain.

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1. Introduction

The activation of the hypothalamic—pituitary—adrenocortical (HPA) axis is an essential response to stressors such as acute pain, and is influenced by several factors, including stress-associated cognitions and coping behavior (Heim et al., 2000; Ursin and Eriksen, 2004). Clinical studies in patients with lower back pain have investigated the associations between cognitive, affective and behavioral pain responses and HPA axis activity as measured by salivary cortisol release (Sudhaus et al., 2009, 2012). These studies were based on the assumptions made by the Avoidance-Endurance Model (AEM) (Hasenbring and Verbunt, 2010). Concerning musculoskeletal pain, the AEM describes two time-stable maladaptive pain response patterns, both increasing the risk of pain chronification. The fear-avoidance-related (FAR) pattern, including pain responses such as depressive mood, helplessness/hopelessness, and avoidance of activities potentially causing pain, heightens the risk of chronification of musculoskeletal pain primarily via physical disuse. The endurance-related (ER) pattern (i.e. active coping strategies such as humor/distraction and pain persistence behavior) heightens the risk of chronification via an overload/overuse of physical structures, primarily due to long-lasting pain persistence behavior. Regarding the impact of FAR and ER responses on stress levels and HPA axis activity, the results of the above-mentioned studies suggest that FAR responses have a stress-increasing effect. In contrast, and although maladaptive in the long term, ER responses appear to have a short-term, stress-lowering effect (Sudhaus et al., 2009, 2012). The aim of the present study was to follow up these results under well-controlled laboratory conditions. For this purpose, 30 healthy adults were asked to indicate their usual responses to pain, and were then confronted with an experimental pain stimulus. Changes in salivary cortisol concentrations served as a neuroendocrine marker of stress. It was hypothesized that FAR responses would be positively, and ER responses would be negatively associated with cortisol.

2. Material and methods

2.1. Participants

Thirty healthy students participated in the study. Inclusion criteria allowed for students between the age of 18 and 35, and a body mass index between 18 and 27. Exclusion criteria were as follows: any acute or chronic somatic disease or psychiatric disorder; smoking and/or drug use; administration of corticosteroids within the preceding eight weeks; insufficient knowledge of the German language; shift work with night hours within a week before participation; current high emotional pressure (e.g. exam period); use of oral contraceptives; menses on the day of participation. To recruit participants, posters and flyers advertising the study were placed at different locations on the University campus. Interested students were informed about the procedure (pain induction) and checked for in- and exclusion criteria on the phone. Immediately after arriving at the laboratory, participants received more detailed information about the study and provided informed consent. All participants were compensated. The study was approved by the local Ethics Committee.

2.2. Procedure and measurements

2.2.1. Pain induction

Pain induction took place 30 min after the arrival of the subjects, using the Cold Pressor Test (CPT). This is a widely used, reliable and valid low-risk method used in research to expose participants to pain, and is known to induce robust and reliable stress responses (Smeets et al., 2008). Subjects were instructed to keep their non-dominant hand submerged in a basin with ice-cold water (0—3° C) up to the wrist and without moving their fingers for as long as they could tolerate it. CPT duration was limited to 180 s, but subjects did not know this.

2.2.2. Self-reported data

FAR and ER patterns were measured with the Avoidance-Endurance Questionnaire (AEQ; Hasenbring et al., 2009), an instrument that assesses the habitual frequency of several affective, cognitive and behavioral responses to pain. Higher scores indicate a higher frequency of self-reported responses. Based on former study results (Sudhaus et al., 2009), the ER pattern was represented by the AEQ scales Humor/Distraction and Pain Persistence, whereas the scales Helplessness/Hopelessness, Avoidance of Social Activities and Avoidance of Physical Activities represented the FAR pattern. To reduce the number of statistical tests, an overall behavioral avoidance scale was created by averaging together the two avoidance subscales ($\alpha = .89$) (Hasenbring et al., 1994). The Beck Depression Inventory (BDI; Beck et al., 1961) served to assess depressive mood, a potential consequence of long-term FAR coping in patients with musculoskeletal pain (Hasenbring and Verbunt, 2010). Higher scores indicate a more depressive mood. Both questionnaires were completed before pain induction. In order to control for potential effects of affect on cortisol, participants additionally filled out the Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988) before, immediately after and 25 min after cessation of the CPT. Pain intensity was measured with an 11-point numerical rating scale (0 = no pain, 10 = maximal imaginable pain). Subjects were asked to verbally rate the pain intensity at removal of their hand from the water as well as every 20 s leading up to 120 s after withdrawal. A stopwatch served to assess pain tolerance by measuring the time from submersion of the hand until withdrawal. Maximum pain tolerance time was 180 s.

2.2.3. Physiological data: salivary cortisol

Physiological stress levels were measured by means of salivary cortisol as an indicator of HPA axis activity (Dickerson and Kemeny, 2004). Participants were requested to refrain from strenuous exercise, alcohol, drugs and pain relievers 24 h before testing, and not to eat, drink (except tap water) or exercise during the hour before testing. Saliva samples were taken with Salivette collection devices (Sarstedt, Nuembrecht, Germany) five minutes before (baseline) and 3, 10, 25 and 45 min after submersion of the hand. Sampling took between two and three minutes, depending on the individual amount of saliva production. The saliva

samples were immediately stored at −20° C on collection. Free cortisol levels were determined by commercial immunoassays (CLIA; IBL International, Hamburg, Germany). Inter- and intra-assay variations were below 10%. To control for the diurnal rhythm of cortisol, all participants attended afternoon laboratory sessions (1:30—4:30 pm).

2.3. Data analysis

A repeated-measures analysis of variance (ANOVA) followed by Bonferroni-adjusted post hoc tests were used to assess cortisol level variation. For each participant, the degree of the cortisol response to the pain stimulus was calculated by means of delta increase, defined as cortisol levels 25 min after CPT minus baseline levels. Furthermore, delta decrease (cortisol levels 25 min minus levels 45 min) was calculated as an index for recovery. Potential associations between cortisol (baseline, increase, decrease), pain ratings, and psychological variables were examined by means of Pearson correlations.

3. Results

3.1. Demographic and self-reported data

Fourteen (46.7%) of the thirty participants were female. The mean age of the sample was 23.6 ± 3.1 years and the mean body mass index (BMI) was 22.6 ± 2.4. The mean pain tolerance of the sample as measured by time until withdrawal was 106.1 ± 72.8 s, while the mean pain intensity was highest at withdrawal (5.73 ± 2.1). It was positively correlated with the AEQ scale Helplessness/Hopelessness ($r = .358$, $p = .026$), and negatively with Pain Persistence ($r = -.422$, $p = .01$).

3.2. Salivary cortisol

Because the Salivettes obtained from one participant did not contain enough saliva, the presented results are based on the data of 29 participants. Mean cortisol concentrations ± SE (nmol/l) of the sample were 8.23 ± 0.66 at baseline, 7.87 ± 0.71 at 3 min, 8.57 ± 0.73 at 10 min, 11.36 ± 1.23 at 25 min, and 8.59 ± 0.89 at 45 min after submersion of the hand. The ANOVA yielded a significant effect of time on cortisol levels ($F(4,112) = 8.909$, $p = .000$). Post hoc tests revealed that pain induction lead to a significant increase from baseline, 3 and 10 min measurements to the measurement at 25 min (all $p < .05$), followed by a decrease from 25 to 45 min after submersion of the hand ($p < .01$) (Fig. 1).

3.3. Associations between cortisol and demographics and self-reported data

Age, sex and BMI were not associated with cortisol. Pain tolerance was positively correlated with cortisol increase ($r = .466$, $p = .011$), and depressive mood (BDI) was positively correlated with cortisol baseline ($r = .414$, $p = 026$). Regarding the AEQ scales, Helplessness/Hopelessness was positively correlated with cortisol baseline ($r = .395$, $p = .017$), and Avoidance of Activities correlated positively with both cortisol baseline (trend: $r = .253$, $p = .093$) and increase ($r = .387$, $p = .019$). In contrast, analyses revealed negative correlations between Humor/Distraction and cortisol baseline ($r = -.394$, $p = .017$) and decrease ($r = -.436$, $p = .009$), and between Pain Persistence and cortisol baseline (trend: $r = -.273$, $p = .076$) (Table 1). Cortisol was not associated with any of the PANAS measurements.

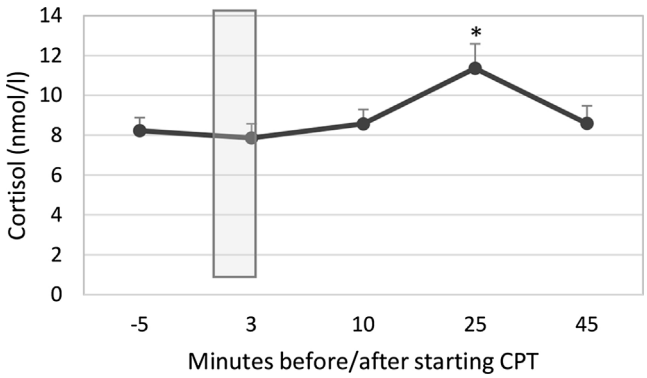

Figure 1 Salivary cortisol levels before (−5 min) and after starting CPT. Data are presented as group mean ± SE ($N = 29$). *Level different to level at −5, 3, 10, and 45 min ($p < .05$).

Table 1 Correlations (Pearson) between Cortisol and psychometric characteristics.

	Baseline	Increase[a]	Decrease[b]
FAR responses[c]			
Help-/Hopelessness	.395*	.125	.112
Avoidance of activities	.253***	.387*	.243
Depressive mood[d]	.414*	−.123	.068
ER responses[e]			
Humor/Distraction	−.394*	−.181	−.436**
Pain Persistence	−.273***	−.079	−.241

[a] Delta increase (cortisol concentration baseline minus concentration 25 min after immersion of hand).
[b] Delta decrease (cortisol concentration 25 min minus 45 min after immersion of hand).
[c] Fear-avoidance responses to pain (AEQ).
[d] BDI.
[e] Endurance responses to pain (AEQ).
* $p < .05$.
** $p < .01$.
*** $p < .1$.

4. Discussion

Clinical research suggests that maladaptive pain responses as described by the Avoidance-Endurance Model (Hasenbring and Verbunt, 2010) have an impact on pain-induced stress as reflected in basal HPA axis activity (Sudhaus et al., 2009, 2012). The present results support this assumption by demonstrating that discrete FAR responses have cortisol-increasing effects in healthy adults in anticipation of as well as after confrontation with pain, and that behavioral ER

responses have cortisol-decreasing effects during pain anticipation. Hence, the results reveal that, in the context of pain confrontation, the associations between FAR responses and cortisol on the one hand, and ER responses and cortisol on the other hand, must be regarded separately. This also holds true for different time points of cortisol measurement. Based on this effect, the hypotheses of the study could be partly, but not completely confirmed. Concerning FAR responses, the results point to an increasing effect on baseline cortisol levels already, which seems to be attributable in particular to an elevated depressive mood and cognitions of helplessness/hopelessness; in line with the present results, Pruessner and colleagues found higher basal cortisol levels in healthy adults with an elevated depressive mood. However, the causal relationship between depressive mood and cortisol remains to be determined (Pruessner et al., 2003). Regarding helplessness/hopelessness, negative expectations associated with the success of the chosen stress response might account for their effects on baseline cortisol levels (Ursin and Eriksen, 2004). This is conceivable because participants were made aware of the upcoming pain confrontation early on, even before entering the laboratory. Unfortunately, there was no measurement of anticipatory stress via self-report, and no measurement of basal cortisol on a different day without an upcoming stress exposure. The positive association between Avoidance of Activity and cortisol increase after pain stimulation suggests that the inclination toward avoidant behavior has a cortisol-increasing effect. This might be caused by the belief of not being able to avoid the pain stimulus in an experimental setting, unlike in everyday life. In line with this, avoidance of activities was not correlated with pain tolerance. In contrast to FAR responses, behavioral ER responses were negatively associated with cortisol baseline levels. This result suggests that strategies associated with ER responses lower perceived stress in anticipation of pain. Distraction from pain represents an organized and focused method of attentional diversion away from the pain stimulus (Hasenbring and Verbunt, 2010), and, like pain persistence, might be accompanied by the expectation of being able to successfully manage the situation despite of the pain (Sudhaus et al., 2009). However, ER responses did not influence the cortisol increase after pain stimulation, and the negative association between humor/distraction and cortisol decrease might indicate that this strategy prevents physiological recovery after pain confrontation. The calculation of the sample size was based on our previous work relating the cortisol awakening response to FAR and ER patterns. In these studies we found significant associations with sample sizes ranging between 19 and 24 (Sudhaus et al., 2009, 2012). A larger sample size would have been desirable nevertheless. Due to the small sample size, the lacking measurement of anticipatory stress via self-report as well as the moderate size of the observed correlations, and, of course, their non-causal nature, the present results need to be interpreted cautiously. More research is undoubtedly need in this area. Regarding the results in the context of stress-related pain conditions such as chronic lower back pain, the effects observed could be of clinical relevance. In patients with stress-related musculoskeletal pain, an FAR response pattern might contribute to long-lasting elevated stress levels. As a consequence of over-adjustment, they might then, in the long run, lead to a state of hypocortisolism, which itself may play a causal role in the development and maintenance of chronic pain syndromes in some patient groups (Heim et al., 2000; Fries et al., 2005). Longitudinal studies are needed in order to test this model empirically. In contrast, stress-lowering ER response effects could be considered an advantage of this response pattern in the short-term.

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Conflict of interest statement

We wish to confirm that there are no conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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