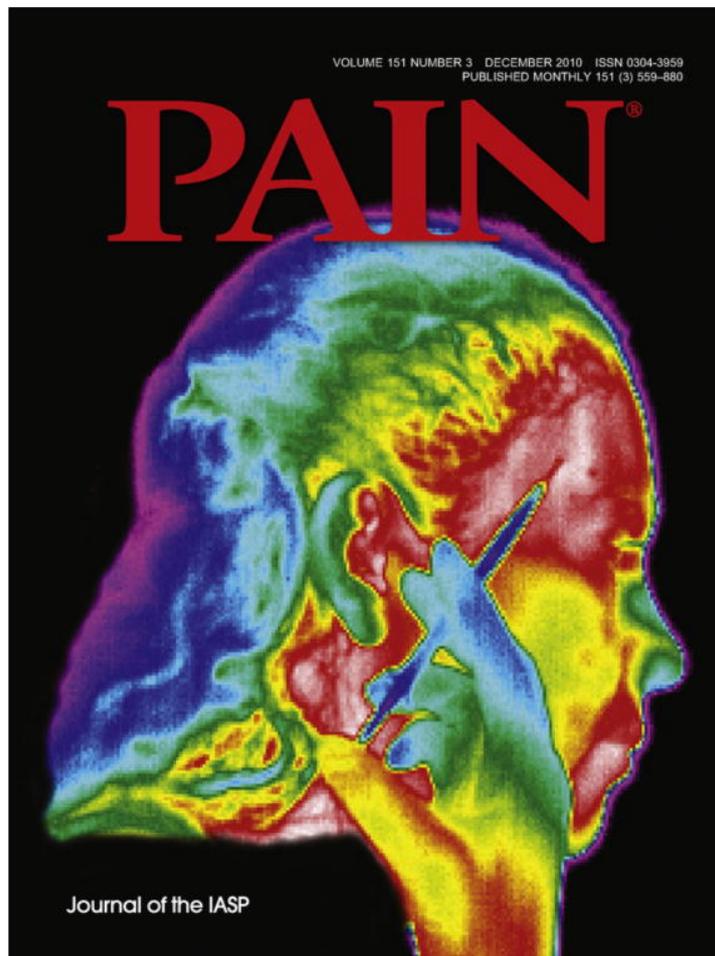


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Attentional and emotional mechanisms related to pain as predictors of chronic postoperative pain: A comparison with other psychological and physiological predictors

Stefan Lautenbacher^{a,*}, Claudia Huber^{a,b}, Dorothea Schöfer^{a,b}, Miriam Kunz^a, Andreas Parthum^{a,b}, Peter G. Weber^c, Carbon Roman^c, Norbert Griessinger^b, Reinhard Sittl^b

^aPhysiological Psychology, Otto-Friedrich University Bamberg, Germany

^bPain Center, Friedrich-Alexander University Erlangen, Germany

^cDepartment of Pediatric Surgery, Friedrich-Alexander University Erlangen, Germany

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ABSTRACT

The present prospective longitudinal study on chronic postoperative pain was conducted to assess the predictive power of attentional and emotional variables specifically assumed to augment pain, such as pain hypervigilance, pain-related anxiety, pain catastrophizing and attentional biases to pain. Their relevance was determined in comparison with other psychological and physiological predictors (depression, anxiety, somatization, cortisol reactivity, pain sensitivity). In 84 young male patients the predictor variables were assessed one day before surgery (correction of chest malformation). Postoperative outcome (subjective pain intensity and pain-related disability) was assessed three ($N = 84$) and six months ($N = 78$) after surgery. Patients were classified into good and poor outcome groups. Patients with high pain intensity three (25%) or six months (14%) after surgery, differed significantly from those low in pain with regard to their preoperative performance in the dot-probe task (high attentional bias towards positive words). A sizeable portion (54%) of patients still felt disabled due to pain after three months and a few patients after six months (13%). These patients were those with high preoperative ratings in the Pain Vigilance and Awareness Questionnaire. The few subjectively disabled patients after six months could be identified in addition by low pressure pain and high cold pain thresholds before surgery. An attentional bias towards positive stimuli prior to surgery may indicate a maladaptive coping style, which avoids necessary confrontation with pain and predisposes patients to chronic postoperative pain. Lasting subjectively felt pain-related disability occurs predominantly in patients with high levels of pain hypervigilance before surgery.

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1. Introduction

Persistent postoperative pain emerges in up to 50% of patients [41,53]. The exact reasons why some patients suffer from ongoing postoperative pain whereas others are pain-free shortly after surgery are largely unknown. The relevance of psychological factors as predictors of postoperative pain has been established [18,20,49]. Especially, depression, stress, state anxiety, specific anxieties, expectations relating to surgery and neuroticism have often been discussed as potent predictors of acute pain, however, with less clear findings for chronic postoperative pain. Accordingly,

there is still more unexplained variance in the last case, rendering it worthwhile to test new psychological factors.

Emotional and attentional mechanisms of pain processing, such as pain anxiety, pain catastrophizing and pain hypervigilance have recently attracted interest. These factors have been shown to be related to pain sensitivity and may play a role in the development as well as in the maintenance of clinical pain [26,33,60]. Furthermore, attentional bias for pain-related stimuli such as words and faces has been increasingly investigated, namely by use of the dot-probe task and emotional stroop test. These bias measures have demonstrated potency in identifying individuals with high pain sensitivity or strong vulnerability for clinical pain [2,23,24] and might also help to predict postoperative pain.

Pain catastrophizing has proven to be a successful predictor for acute postoperative pain in the majority of studies [13,15,28,40,44,54,55] but not in all [14,50]. The predictive power of pain anxiety and pain hypervigilance for postoperative pain has rarely been

* Corresponding author. Address: Physiological Psychology, University of Bamberg, Marktpl. 3, 96045 Bamberg, Germany. Tel.: +49 951 8631851; fax: +49 951 8631976.

E-mail address: stefan.lautenbacher@uni-bamberg.de (S. Lautenbacher).

tested so far [13,28]. It has been shown that an attentional bias for pain-related information – in the form of cognitive avoidance – increases the likelihood of acute postoperative pain [28,37]. However in spite of these partially promising results, it has hardly been investigated whether these variables can also predict chronic postoperative pain, with a few exceptions. For example, Forsythe et al. [11] presented data, suggesting that preoperative pain catastrophizing predicts chronic postoperative pain.

The aim of the present study was to test whether these attentional and emotional mechanisms of pain processing – specifically pain hypervigilance, pain catastrophizing, pain anxiety and attentional bias towards pain-related cues – help to predict postoperative pain three and six months after surgery. When determining the quality of prediction, it is not sufficient to only rely on statistical significance, but comparisons with other well-known predictors are required. For that purpose, we also assessed preoperatively affective and bodily distress (depression, state anxiety, somatization) as well as experimental pain sensitivity (heat, cold and pressure pain thresholds, temporal pain summation). Since failed back surgery was found to be associated with reduced cortisol secretion in the morning and enhanced feedback sensitivity of the HPA axis [12], we added cortisol reactivity as a predictor to our protocol.

A postoperative pain model with absent pain before surgery is ideal and was found in patients undergoing corrections of chest malformations [31,43,63]. The surgical correction is sufficiently extensive to potentially cause chronic postoperative pain. Since pain intensity and pain-related disability are critical but weakly related outcome measures [35], we assessed these two variables separately. A part of these patients were also participants of our study on acute postoperative pain [28].

2. Materials and methods

2.1. Subjects

84 Male patients with congenital malformations of thorax (mostly funnel chest) between the ages of 16 and 37 years (mean age 21.1 ± 4.5 years) participated in this study. Subjects were recruited amongst inpatients of the Department of Pediatric Surgery of the University of Erlangen. This department is specialized in the surgical correction of thorax malformations; patients from all over Germany are treated here. Weber and Huemmer [62] have described the surgical technique for correction of this thorax malformation, the so-called Erlangen technique of funnel chest correction, in detail. Therefore, only a brief description is given here. The lower part of the sternum is freed through an interior incision. Mobilization of the sternum begins with freeing of the xiphisternum. A spring balance is attached to the sternum with a hook; afterwards the sternum is moved into the desired position. The chest wall is then stabilized with a lightweight trans-sternal metal implant. After placing wound drains, the chest wall is closed. Patients are discharged from the hospital after 7–10 days post surgery. The metal plate is removed after 1 year.

Patients with chronic pain conditions, major surgeries in the past and psychological disorders (current or previous ones as being diagnosed by the Mini-DIPS for ICD-10 and DSM IV diagnoses) were excluded from the study. We also excluded patients, who have experienced strong levels of discomfort or even pain due to functional limitations associated with the chest malformations. Minor surgery earlier in life did not lead to exclusion. 170 patients were approached, of whom 114 did not meet any exclusion criterion and agreed to participate. In 22 patients the PCEA system could not be installed successfully. From the remaining 92 patients 8 dropped out and did not show up for the testing sessions three or six months after surgery.

The study protocol was approved by the ethics committee of the medical faculty of the University of Erlangen. All participants gave written informed consent. In case of not having attained full age, written informed consent was obtained from their parents and written assent was obtained from them. All subjects were paid for their participation six months after surgery.

2.2. Materials and procedure

There were three sessions. The first session took place one day prior to surgery in order to assess the predictor variables (questionnaires, dot-probe task, experimental pain sensitivity) except for cortisol reactivity (this predictor variable was assessed outside sessions as described below). The other sessions were scheduled for assessment of the criterion variables, namely postoperative outcome in terms of self-rated pain intensity and pain-related disability. These sessions took place approximately three months (session 2) and six months (session 3) after surgery. All patients participated in session 2 and 78 subjects in session 3. There was also a session one week after surgery for measurement of acute postoperative pain, the results of which were described by Lautenbacher et al. [28] and are not reported here.

The assessment of the predictor variables in session 1 took place between 4.00 p.m. and 8.00 p.m. This session, which lasted for approximately 2 h and 15 min, included in the following order, screening for psychological disorders by use of a standardized psychological interview (Mini-DIPS¹ [32]), running of the dot-probe task, self-rating of pain hypervigilance, pain-related anxiety and pain catastrophizing (questionnaires), assessment of experimental pain sensitivity (pressure and thermal pain) as well as assessment of affective and bodily distress (again questionnaires). Cortisol reactivity was determined prior to this session. Subjects were asked to collect morning salivary samples for two consecutive days prior to the admission to the hospital.

Postoperative outcome was assessed by two measures (criterion variables): self-rating of pain intensity and of pain-related disability. Table 1 gives an overview of all predictor and criterion variables assessed.

2.2.1. Assessment of the predictor variables

2.2.1.1. Pain-related questionnaires. Pain hypervigilance, pain-related anxiety and pain catastrophizing were assessed by questionnaires requiring self-ratings (German versions of the Pain Vigilance and Awareness Questionnaire (PVAQ [34]), Pain Anxiety Symptom Scale (PASS [33]), Pain Catastrophizing Scale (PCS [56])).

The PVAQ [34] was developed as a comprehensive measure of attention to pain and has been validated for use in chronic pain and non-clinical samples [35]. It consists of 16 items (e.g., “I am quick to notice changes in pain intensity.”) that are rated on a six-point scale and assess awareness, vigilance, preoccupation, and observation of pain. For further analyses we used the combined sum score of the PVAQ.

The PASS [33] is composed of four subscales; cognitive anxiety, escape/avoidance, fearful appraisal, and physiological anxiety and is designed to measure fear of pain across cognitive, behavioural and physiological domains. The items (e.g., “When I feel pain I am afraid that something terrible will happen.”) are rated on a six-point scale. For further analyses, we used the combined sum score (40 items) of the PASS.

The PCS [56] was developed as a measure of catastrophizing related to pain. It contains 13 items (e.g., “I worry all the time about

¹ The mini-DIPS is a structured interview according to DSM-IV and ICD-10 criteria for current (six months) psychological disorders and covers the following disorders: anxiety, affective, somatization, obsessive-compulsive, post-traumatic stress, acute stress, dissociative, eating disorders and schizophrenic psychoses.

Table 1
Descriptive statistics (mean \pm SD) of all predictor and criterion variables.

		Mean	SD
<i>Predictor variables</i>			
Dot-probe task	Pain-related words (index score)	−0.0024	0.0477
	Social threat words (index score)	−0.0037	0.0451
	Positive words (index score)	−0.0094	0.0502
Pain-related questionnaires	PCS (sum score)	16.68	6.49
	PASS (sum score)	72.56	25.58
	PVAQ (sum score)	33.40	12.42
Experimental pain sensitivity	Pressure pain threshold (kPa)	278.83	124.21
	Cold pain threshold (°C)	17.87	8.94
	Heat pain threshold (°C)	42.79	2.81
	Temporal summation (rating scale)	0.19	1.11
Affective and bodily distress	SOMS (somatization severity index)	9.81	7.71
	STAI-X1 (sum score)	44.31	9.69
	CES-D (sum score)	11.01	6.09
Cortisol reactivity	Morning cortisol (ng/ml min)	422.31	163.77
	Cortisol suppression (ng/ml min)	205.86	125.36
<i>Criterion variables</i>			
Pain intensity	NRS, three months post surgery	1.64	1.64
	NRS, six months post surgery	1.15	1.56
Pain disability	PDI (sum score), three months post surgery	12.61	11.91
	PDI (sum score), six months post surgery	3.86	6.12

PCS, Pain Catastrophizing Scale; PASS, Pain Anxiety Symptom Scale; PVAQ, Pain Vigilance and Awareness Questionnaire; SOMS, Screening for Somatoform Disorders; STAI-X1, State-Anxiety Inventory; CES-D, Center for Epidemiology Studies Depression; NRS, numerical rating scale; PDI, Pain Disability Index.

whether the pain will end.”) that can be divided into three subscales, namely rumination, magnification and helplessness. The items are rated on a five-point scale. For further analyses we used the combined sum score of the PCS.

With the exception of the PASS (which had been translated into German and validated by Walter et al. [61]) we had to translate the other two questionnaires into German, using a standard “forward-backward” procedure. Only if the resulting backward English version was very similar to the original version according to the evaluation of an English native speaker, translation accuracy was considered sufficient. The inter-correlations of the three German questionnaires ranged between $r = 0.502$ and $r = 0.741$, which is in accordance with inter-correlations reported in the literature for English and Dutch versions [4,36,47,48].

2.2.1.2. Dot-probe task. We used a dot-probe task based on the one described by Keogh et al. [23], as we have done previously [26]. It contains three emotional word categories: pain-related (e.g., *stechend (Ger.)/stinging*), social threat (e.g., *beschämt (Ger.)/ashamed*) and positive words (e.g., *glücklich (Ger.)/lucky*). These words are paired with neutral words (*Anstrich (Ger.)/paintwork*); neutral-neutral word pairs served as filler items. We translated the words of the original version by Keogh et al. [23] into German. Since not all words in German fulfilled the criteria of being similar in length and frequency of use, a series of words had to be replaced. In a pilot study it was tested whether each word of the new list (containing more items than necessary) was representative for the designated word category. If this was not the case, these words were excluded from the final use in the dot-probe task.

Following Keogh et al. [23] a fixation cross in the center of a computer screen was presented first for 500 ms. Following this, two words (a neutral one paired with an emotional one) were presented concurrently, one below and one above the center. After another 500 ms, words were removed and a dot appeared in the location of one of the words. Subjects were required to indicate via a key press as quickly as possible where the dot appeared

(below, above). A reaction time measurement was taken. After 20 practice trials, participants had to complete 128 test trials (32 trials per word-pair category), all of which were presented in a random order by the computer. Bias indices were calculated on the basis of reaction times to assess separately the attentional bias toward each emotional word category (for more details see Keogh et al. [23]). A positive score indicates an attentional preference for the location of the emotional word, which may suggest vigilance, whereas a negative score may suggest attentional avoidance.

Additionally, patients completed a wordcomprehension task (Intelligence-Structure-Test 2000 R Form A [1]) as well as a reading task (analogue to the dot-probe task, word pairs of real and nonsense words were presented on a computer screen for 500 ms and subjects had to indicate by key press where the real word appeared) to ensure the patient's capacity to read and understand words quickly enough. Patients with results poorer than 1.5 standard deviations below mean in the word comprehensive task would have been excluded from analysis as well as those with more than 15 missing or false values in the reading task. However, none of the 84 patients had to be excluded.

2.2.1.3. Experimental pain sensitivity. Experimental pain sensitivity was assessed through the measurement of pressure pain threshold, cold pain threshold, heat pain threshold and temporal summation of heat pain. All subjects were trained until they understood all procedures and were able to follow the instructions before testing. The assessments of pain thresholds and temporal summation were the same as described by Lautenbacher et al. [28].

2.2.1.3.1. Pressure pain threshold. The assessment of pressure pain threshold was performed using a hand-held pressure algometer (Somedic Sales AB, Algometer type II, Sweden) with a probe area of 1 cm². Site of stimulation was the volar site of the right forearm. The pressure was increased from 0 kPa at a rate of change of 50 kPa/s until the subject felt the first pain sensation and pressed a button. There were five trials and the threshold was determined as the average of these trials.

2.2.1.3.2. Cold and heat pain thresholds. Thermal stimuli were delivered by use of a Peltier-based, computerized thermal stimulator (Medoc TSA-2001; Medoc Ltd., Ramat Yishai, Israel) with a 3×3 cm² contact probe. Site of stimulation was the volar site of the left forearm, where the contact thermode was attached. For assessment of cold and heat pain thresholds, thermode temperature started from a baseline of 32 °C at a rate of 1 °C/s until the subjects felt the first pain sensation and responded by pressing a button; then the temperature returned to baseline temperature, which was held constant until the next trial. There were five trials each of heat and cold stimulation and the pain thresholds were determined as the average of the five trials. For further computations cold pain threshold scores were inversed in order that the meaning of high and low thresholds was similar to heat and pressure stimulation.

2.2.1.3.3. Temporal summation. For assessment of temporal summation, trains of 10 stimuli were applied with an inter-stimulus interval (ISIs) of 2.5 s (0.4 Hz) to the volar site of the left forearm. Temporal summation was tested by comparing the sensations evoked by single pulses (assessed first) to sensations evoked by trains of 10 pulses (only the last pulse was rated), which were delivered 60 s later. Subjects rated their sensation on a numerical rating scale (0–10, being labeled with verbal anchors “no pain” to “strongest pain imaginable”). The heat pain stimuli (saw-tooth shape) started at a baseline temperature of 3 °C below the individual pain threshold and increased with a heating rate of 4 °C/s. The stimuli peaked at a temperature of 3 °C above heat pain threshold and returned at a cooling rate of 4 °C/s. There were three runs. Temporal summation was determined as the averaged differences between sensations evoked by trains of stimuli and single stimuli in a way that high scores meant strong temporal summation. As pointed out above, the physical intensity of stimulation was tailored to the individual heat pain threshold and, thus, the quantity of temporal summation might be directly influenced by the individual level of pain thresholds. In fact, heat pain thresholds and ‘raw’ temporal stimulation scores correlated significantly ($r = 0.445$, $p < 0.001$). To guarantee independency of these two predictors, temporal summation scores were statistically freed from the influence of heat pain threshold levels. For that purpose, a regression analysis was computed (heat pain threshold as predictor and temporal summation as criterion) and only the residual scores of temporal summation were used in further analyses.

2.2.1.4. Assessment of the affective and bodily distress. The affective and bodily distress state was assessed with three different questionnaires (self-rating scales), namely the German version of the Screening for Somatoform Symptoms (SOMS [46]), the German version of the State-Anxiety Inventory (STAI-X1 [30]) and the Center for Epidemiologic Studies Depression Scale (CES-D; German version: ADS [17]).

The SOMS [46] is a self-rating scale of somatization, which assesses 53 organically unexplained physical symptoms (e.g., headache, low back pain, nausea). The state version of the SOMS was applied where subjects are asked to rate the intensity of each symptom during the last 7 days on a five-point Likert scale. For further analyses we used the sum of all items (“somatization severity index”).

The STAI-X1 [30] is a self-rating scale and contains 20 items that were designed to measure transitory anxiety states – that is, subjective feelings of apprehension, tension, and worry that vary in intensity and fluctuate based on the situation. Items are rated on a five-point rating scale.

The CES-D [17] is a self-rating scale that was designed to assess emotional, somatic and cognitive symptoms of depressive mood during the last week. It contains 20 items that are rated on a four-point Likert scale.

2.2.1.5. Cortisol reactivity. Following the protocol of Pruessner et al. [45], patients were asked to sample morning saliva at the time of awakening and 15, 30, 45 and 60 min thereafter immediately prior to hospital admission, whilst still at home, for two consecutive days. Subjects were required to expectorate 0.5–1.0 ml of saliva into a plastic vial via a short plastic straw (DRG Instruments GmbH, Germany). At 11 p.m. of the first day, the patients ingested a tablet of 0.5 mg dexamethasone (DEX) (Merck, Darmstadt, Germany). This was done to assess the extent of cortisol suppression produced by a small dosage of DEX (Mini-Dexamethasone-Suppression-Test [45]). The patients were informed about the necessity of strictly following the time schedule for saliva sampling and to refrain from eating and brushing teeth before saliva collection, to obtain valid data. Patients stored saliva samples at home in their freezer and passed them after admission to the hospital, where they were stored in a –20 °C freezer until further analyses.

Salivary cortisol was assayed by use of an ELISA kit (DRG Instruments, Germany). The intra-assay coefficient of variation was <5.5% and the corresponding inter-assay coefficient was <6.5%. The analytical sensitivity was 1.48 nmol/l. The competitive immunoassay requires 1.5 h incubation time and shows robust and reproducible performance.

To quantify the cortisol reactivity, two indicators were computed for further analyses: (i) morning cortisol increase during the first hour after awakening (area under the cortisol awakening response curve up to 60 min after awaking on day 1) and (ii) cortisol suppression after DEX (difference between area under the awakening response curve of day 1 and day 2).

2.2.2. The assessment of the criterion variables

As criterion variables, we assessed patients' self-ratings of postoperative pain intensity as well as of pain-related disability, each three and six months after surgery.

2.2.2.1. Postoperative pain intensity. Three months and six months after surgery, patients were asked to rate the average intensity of their postoperative pain during the four last weeks on an 11-point numerical rating scale (NRS). The numerical rating scale was labeled with the verbal anchors “no pain” and “strongest pain imaginable”.

2.2.2.2. Postoperative pain-related disability. Three months and six months after surgery, patients were also asked to complete the Pain Disability Index (PDI) questionnaire [38]. The PDI was designed to assess subjective pain-related disability and consists of seven items measuring the degree to which pain interferes with functioning across a range of activities (e.g., social activities, recreational activities, professional life activities). Scores of each item may range from 0 (no interference) to 10 (total interference). Thus, the maximum PDI-score is 70.

2.2.2.3. Classification of outcome groups. Patients were classified according to their scores for postoperative pain intensity and pain disability in two outcome groups, respectively. This classification was computed separately for each of the two intervals after surgery. Accordingly, there was a Pain Intensity-group low (NRS: 0–2) and a Pain Intensity-group high (NRS: 3–10), both three and six months after surgery. The classification was inspired by findings of Farrar et al. [9], suggesting that meaningful changes in pain intensity on such a scale are indicated by differences of at least two scale units. Similarly, there was a Pain Disability-group low (PDI: 0–8) and a Pain Disability-group high (PDI: 9–70), both three and six months after surgery. The PDI cut-off of 8 was derived from a report by Dillmann et al. [8], that – based on several studies – approximately 95% of chronic pain patients show PDI-scores higher than 8. Table 2 gives an overview of all outcome groups.

Table 2

Number of patients in the outcome groups according to the rated postoperative pain intensity (NRS) and pain-related disability (PDI) three and six months after surgery.

	Group low (NRS 0–2)	Group high (NRS 3–10)
<i>Pain intensity</i>		
Three months post surgery (N = 84)	N = 63 (75%) (NRS mean \pm SD = 0.84 \pm 0.81)	N = 21 (25%) (NRS mean \pm SD = 4.00 \pm 1.10)
Six months post surgery (N = 78)	N = 67 (86%) (NRS mean \pm SD = 0.66 \pm 0.77)	N = 11 (14%) (NRS mean \pm SD = 4.27 \pm 1.74)
	Group low (PDI 0–8)	Group high (PDI 9–70)
<i>Pain-related disability</i>		
Three months post surgery (N = 84)	N = 39 (46%) (PDI mean \pm SD = 2.79 \pm 3.03)	N = 45 (54%) (PDI mean \pm SD = 21.11 \pm 10.02)
Six months post surgery (N = 78)	N = 68 (87%) (PDI mean \pm SD = 1.85 \pm 2.25)	N = 10 (13%) (PDI mean \pm SD = 17.50 \pm 6.79)

NRS, numerical rating scale; PDI, Pain Disability Index.

Not surprisingly, there was an overlap between outcome groups classified according to the two criteria, which resulted in significant results in cross tabulation (60% of the patients were grouped into the same category for the two pain outcome parameters at three months; $\phi = 0.262$, $p = 0.016$; 86% of the patients were grouped into the same category for the two pain outcome parameters at six months; $\phi = 0.396$, $p < 0.001$). However, the interrelation was apparently small enough to justify the assumption of pain intensity and pain disability being independent outcome measures (at least at three months post surgery). We cannot completely rule out that this finding is merely the result of the way we selected our cut-off scores used for defining outcome groups. However, it is also possible that the feeling of disability due to pain can be triggered by the fear of pain in addition to the intensity of pain. Accordingly, loose relationship between outcome variables is not surprising.

2.3. Statistical analysis

All analyses were conducted using SPSS 15.0 for Windows. After having classified patients into the different outcome groups, we computed effect sizes (Cohen's d) to quantify the difference between each low and high outcome groups as regards our predictor variables [5]. This computation was mainly performed to describe the strength of the differences between low and high outcome groups as regards each predictor variable (univariate approach). However, in order to analyse, which of these predictors is best suited to predict our outcome variables, multivariate approaches were required. For that purpose, we used Structural Equation Models (SEMs). We did this in two steps. First, we computed SEMs separately for each predictor group (predictor groups as described in Section 2.2.1.1 to Section 2.1.1.5) to select out of each predictor group those predictors that proved to be significant. We assumed that these preset predictor groups are divergent for good theoretical reasons because they were selected as indicators of different psychological and physiological processes. Following this first step of selecting the best predictors within each group, we went onto step 2, in which we compared these best predictors across theoretical groups in new SEM analyses. The two intervals after surgery, namely three and six months, were always analysed together in one SEM analysis to compare predictors for early and late outcome periods. Postoperative pain intensity and pain-related disability were analysed in separate SEM analyses, because we thought that these outcome variables were indicative of different processes (see Section 2.2.2). The fit of the SEM was estimated by computation of CFI, which suggested fits to be at the least acceptable in 83% of SEM analyses. The relevance of predictors in SEMs was described by the Standardized Regression Weights (SRW) and the corresponding

P -values. Findings were considered to be statistically significant at $\alpha \leq 0.05$.

3. Results

3.1. Description of sample and variables

The descriptive statistics for all the predictor variables assessed as well as for the criterion variables are displayed in Table 1. The grouping of the patients according to the criterion variables into low or high outcome groups is given in Table 2. 25% of the patients still suffered from pain three months post surgery (according to their NRS rating), a figure, which was reduced to 14% after six months. Of those suffering from pain six months after surgery 55% also reported pain three months earlier. These patients with recordable pain intensities rated their pain as moderate (around 4 on our NRS from 0 to 10). High pain-related disability (PDI-scores) was found in 54% of the patients three months after surgery but declined to only 13% six months after surgery. Of those complaining about pain-related disability six months after surgery, 90% had already done so three months earlier. According to our data, pain intensity and pain disability diverged three months after surgery and converged six months after surgery (see also Section 2.2.2 for the correlations between these variables), suggesting more additional influences on pain-related disability besides pain intensity in the early period. Rated pain disability in the high outcome group was still in the lower range of chronic pain patients (PDI-scores in the range of 17 and 21) although clearly above the cut-off of 8 cited for chronic pain patients [8].

3.2. Prediction of postoperative pain intensity

Effect sizes (Cohen's d) for the differences between low and high outcome groups as regards postoperative pain intensity are depicted in Table 3. These effect sizes suggest that the attentional preference for positive words assessed in dot-probe task and morning cortisol are potent predictors for pain intensity both three and six months after surgery. Temporal summation of heat pain and cortisol suppression seem to be potent predictors only for the three months interval after surgery.

Multivariate analyses using SEM, which considered the five groups of predictors separately (within predictor group analyses; *first step*), allowed classifying the dot-probe task parameter, attentional preference for positive words, as a significant predictor for pain intensity six months after surgery (the prediction of pain intensity after three months approached significance) (Table 4a). Furthermore, temporal summation of heat pain and heat pain thresholds significantly predicted postoperative pain intensity

Table 3

Effect sizes (Cohen's *d*) for differences in predictor variables between high and low outcome groups as regards pain intensity and pain-related disability three and six months after surgery.

Predictor variables	Pain intensity		Pain disability	
	Three months	Six months	Three months	Six months
<i>Dot-probe task</i>				
Pain-related words	0.0682	0.2042	0.1990	0.4790
Social threat words	0.0265	0.0495	0.1710	0.1649
Positive words	0.5074	0.6475	0.1658	0.2082
<i>Pain-related questionnaires</i>				
PCS	0.0592	0.3266	0.3016	0.1169
PASS	0.0231	0.0759	0.4501	0.2080
PVAQ	0.2456	0.2492	0.7131	0.5237
<i>Experimental pain sensitivity</i>				
Pressure pain threshold	0.2314	0.1635	0.2125	0.3414
Cold pain threshold	0.3217	0.0239	0.0755	0.7514
Heat pain threshold	0.2859	0.0996	0.1137	0.1770
Temporal summation	0.5240	0.1800	0.1000	0.1800
<i>Affective and bodily distress</i>				
SOMS	0.0246	0.3330	0.2606	0.1784
STAI-X1	0.2801	0.1008	0.2333	0.1899
CES-D	0.1422	0.0657	0.1353	0.5742
<i>Cortisol reactivity</i>				
Morning cortisol	0.6615	0.5074	0.2537	0.1824
Cortisol suppression	0.7532	0.3079	0.1709	0.1193

PCS, Pain Catastrophizing Scale; PASS, Pain Anxiety Symptom Scale; PVAQ, Pain Vigilance and Awareness Questionnaire; SOMS, Screening for Somatoform Disorders; STAI-X1, State-Anxiety Inventory; CES-D, Center for Epidemiology Studies Depression; for medium and strong effects areas are shaded in grey and numbers written in bold ($0.5 \leq d \leq 0.8$ for medium effects, $d > 0.8$ for large effects; Cohen (1988)).

three months after surgery. However, in contrast to the dot-probe task parameter, the prediction by these variables for the longer interval of six months was far from being significant. No other significant predictors were found.

Finally, these 3 predictors, which were prominent by significance in their respective groups of predictors, were compared amongst each other by SEM (between predictor group analyses, *second step*) (Table 5a). Significant (six months) and close to significant predictions (three months) of postoperative pain intensity could only be achieved by the dot-probe task parameter "attentional preference for positive words". The parameters of experimental pain sensitivity failed to reach significance.

The SEM analyses, considering inter-correlations between predictors, were likely to be more conservative statistical approaches. This approach has singled out one predictor, namely the attentional preference for positive words assessed by the dot-probe task. This predictor had already shown its strength in our univariate approach (Cohen's *d* computation) compared to the other predictors.

3.3. Prediction of postoperative pain-related disability

Cohen's *d* for the differences between the low and high outcome groups as regards pain-related disability (PDI-scores) acclaimed relevance for the PVAQ as a potent predictor for pain-related disability both three and six months after surgery (Table 3). Cold pain threshold and CES-D scores also appeared to explain this difference well but only for the longer interval of six months.

The multivariate analyses by SEM, computed separately for the five groups of predictors (within predictor group analyses, *first step*), corroborated the significance of the PVAQ scores but only for the prediction of pain-related disability after three months (Table 4b). Within the group of questionnaires, assessing pain-related emotions and cognitions (PVAQ, PASS and PCS), only the PVAQ proved to be a significant predictor. This might seem surprising, since Cohen's *d* computation suggested some predictive relevance also for the PCS and the PASS. However, they did not prove significant as soon as they were entered together with the

PVAQ into SEM analysis. This does not necessarily point to the irrelevance of the other two concepts but suggests a rather strong overlap (co-variance) with the PVAQ. In addition to the predictive significance of the cold pain threshold and the CES-D scores for the pain-related disability after six months, pressure pain threshold turned out to be a significant predictor for the longer interval post surgery.

Again, the 4 significant predictors, which outstood significantly in their respective groups of predictors, were compared amongst each other in a new SEM (between predictor group analyses, *second step*) (Table 5b). Only the CES-D lost its role as a significant predictor. The PVAQ appeared to be a significant predictor of pain-related disability both three and six months after surgery, whereas pressure and cold pain thresholds did so only for the longer period. Puzzlingly, the two pain thresholds predicted the pain-related disability in reverse directions. High levels of pain disability appeared to be associated with low pressure pain thresholds but high cold pain thresholds.

3.4. Summary of results

Ideally, a potent predictor of postoperative pain should prove to be relevant in all univariate approaches (Cohen's *d*) and multivariate tests (within predictor group SEMs, between predictor group SEMs) both for the intervals of three and six months after surgery. However, none of our predictors could reach this ideal. Nevertheless, two predictors came very close. The dot-probe task parameter, attentional preference for positive words, proved to be very good for the prediction of postoperative pain intensity because even in the cases of non-significant prediction, significance was approached. The second one was the PVAQ for prognosis of pain-related disability, which failed significance only in one of the six tests. Measures of experimental pain sensitivity appeared to be useful for some predictions but not in a comparably consistent fashion as the other two predictors. The rest of our predictors could not convince, although it is agreed that our statistical approach was rather conservative and thus allowed for type-II errors.

Table 4

Results of separate structural equation model (SEM) analyses with predictors grouped into five categories (within predictor group analyses): dot-probe task, pain-related questionnaires (PVAQ, PCS, PASS), experimental pain sensitivity, affective and bodily distress and cortisol reactivity (step 1); criterion variables: outcome groups high and low as regards pain intensity (4a) and pain-related disability (4b).

Predictor variables	Pain intensity				
	Three months		Six months		
	SRW	P	SRW	P	
<i>a</i>					
<i>Dot-probe task</i>					
Pain-related words	-0.008	0.943	-0.043	0.702	
Social threat words	-0.080	0.479	0.003	0.982	
Positive words	0.208	0.063	0.239	0.031	
<i>Pain-related questionnaires</i>					
PCS	0.062	0.696	-0.176	0.271	
PASS	-0.146	0.402	0.024	0.890	
PVAQ	0.192	0.153	0.137	0.308	
<i>Experimental pain sensitivity</i>					
Pressure pain threshold	0.121	0.352	-0.066	0.635	
Cold pain threshold	0.233	0.064	0.025	0.851	
Heat pain threshold	-0.262	0.028	-0.023	0.858	
Temporal summation	-0.239	0.025	0.069	0.546	
<i>Affective and bodily distress</i>					
SOMS	0.061	0.619	0.145	0.239	
STAI-X1	-0.145	0.275	-0.046	0.731	
CES-D	-0.003	0.985	-0.007	0.961	
<i>Cortisol reactivity</i>					
Morning cortisol	0.133	0.459	0.276	0.135	
Cortisol suppression	0.187	0.298	-0.103	0.459	
<i>Pain disability</i>					
		Three months		Six months	
		SRW	P	SRW	P
<i>Dot-probe task</i>					
Pain-related words	-0.134	0.240	-0.164	0.147	
Social threat words	0.048	0.672	-0.060	0.594	
Positive words	0.070	0.240	0.065	0.561	
<i>Pain-related questionnaires</i>					
PCS	-0.043	0.778	-0.025	0.874	
PASS	0.039	0.812	-0.020	0.910	
PVAQ	0.346	0.007	0.184	0.169	
<i>Experimental pain sensitivity</i>					
Pressure pain threshold	0.156	0.259	-0.295	0.021	
Cold pain threshold	-0.062	0.642	0.464	<0.001	
Heat pain threshold	-0.058	0.650	-0.098	0.407	
Temporal summation	0.100	0.379	-0.092	0.381	
<i>Affective and bodily distress</i>					
SOMS	-0.056	0.650	0.161	0.178	
STAI-X1	0.140	0.294	0.207	0.110	
CES-D	-0.106	0.460	-0.323	0.020	
<i>Cortisol reactivity</i>					
Morning cortisol	0.069	0.715	0.294	0.113	
Cortisol suppression	-0.043	0.821	-0.277	0.136	

SRW, Standardized Regression Weights; PCS, Pain Catastrophizing Scale; PASS, Pain Anxiety Symptom Scale; PVAQ, Pain Vigilance and Awareness Questionnaire; SOMS, Screening for Somatoform Disorders; STAI-X1, State-Anxiety Inventory; CES-D, Center for Epidemiology Studies Depression; significant results are marked both by bold letters and shaded areas check edit.

4. Discussion

The aim of the present study was to investigate whether preoperatively assessed psychological and physiological variables help to identify patients with increased intensity of postoperative pain and enhanced pain disability three or six months after surgery. The predictors were grouped into (i) self-report of pain-related cognitions and emotions, (ii) attentional bias to emotional words, (iii) experimental pain sensitivity, (iv) affective and bodily distress, and (v)

cortisol reactivity. The surgical model used (cosmetic thorax surgery) allowed for exclusion of any preoperatively existing pain so that the process of chronification of “truly” postoperative pain could be monitored.

In such patients, an attentional bias for positive words (dot-probe task) and self-reported pain hypervigilance as well as some parameters of experimental pain sensitivity proved to be significant predictors for postoperative pain. Interestingly, state anxiety and depression, for which relevance was claimed by other authors

Table 5

Results of structural equation model (SEM) analyses across the categories (between predictor group analyses): dot-probe task, pain-related questionnaires (PVAQ, PCS, PASS), experimental pain sensitivity, affective and bodily distress and cortisol reactivity with only significant predictors from step 1 included (see Table 4); criterion variables: outcome groups high and low as regards pain intensity (5a) and pain-related disability (5b).

Predictor variables	Pain intensity				
	Three months		Six months		
	SRW	P	SRW	P	
<i>a</i>					
Dot-probe: positive words	0.192	0.075	0.248	0.024	
Heat pain threshold	−0.131	0.227	−0.050	0.651	
Temporal summation	−0.199	0.067	0.084	0.444	
Pain disability					
		Three months		Six months	
		SRW	P	SRW	P
<i>b</i>					
PVAQ	0.410	<0.001	0.300	0.002	
Pressure pain threshold	0.153	0.192	− 0.301	0.007	
Cold pain threshold	0.048	0.684	0.493	<0.001	
CES-D	−0.144	0.161	−0.147	0.126	

SRW, Standardized regression weights; PVAQ, Pain Vigilance and Awareness Questionnaire; CES-D, Center for Epidemiologic Studies Depression; significant results are marked both by bold letters and shaded areas.

[e.g., 18], were not useful predictors. Thus, mainly attention-related parameters allowed for prediction of chronic postoperative pain.

4.1. Predicting postoperative pain intensity

The dot-probe task showed that patients being attentionally biased towards adjectives describing positive experiences were those with higher postoperative pain intensity (three as well as six months after surgery). Interestingly, in our earlier report on acute postoperative pain in the same sample of patients, the tendency of avoiding pain-related words in the dot-probe task proved to be a significant predictor [28]. Similar findings were also obtained by Munafò and Stevenson [37], who were the first to use an attentional task (modified Stroop) to predict postoperative pain (gynaecological surgical procedures). At first glance, it seems a paradox that avoidance of pain-related information or preference of pain-incompatible information predisposes an individual to postoperative pain. However, the following considerations might help to unravel this puzzle: Pre-attentive vigilance for positive events and avoidance of pain-related information might prevent patients from elaborating the current situation (impending surgery, possibility of pain after the intervention). They might thus lack the necessary psychological preparation needed for coping with postoperative pain in its acute phase. Such a failure might have long-term consequences because it predicts pain still after three and six months post surgery. This interpretation revives earlier hypotheses about the effects of repressing and sensitizing. In consequence of the introduction of these concepts, there were some observations that sensitizers compared to repressors seek actively information about threatening medical procedures, show less stress responses and have better medical outcomes [10,51,52,57].

There is more evidence that controlled confrontation with pain or its anticipation is necessary to cope with pain successfully. In the case of acute pain, focusing on its sensory component (but not on its affective component) has appeared to be helpful [3]. Passive coping or denial, on the other hand, is associated with heightened postoperative pain both in its acute [7,21,25] and its chronic form [8]; whereas information on pain plus coping instructions,

helped to reduce postoperative pain in adolescents with high preoperative anxiety [29].

Given that the dot-probe task was applied a day before surgery in a potential phase of preparatory pain coping, an attentional bias towards pain-related stimuli would have been adaptive, leading to timely and adequate coping, instead of a bias for positive stimuli. Only when this attentional bias towards pain-related stimuli is sustained and outlasts the phase of preparation for acute pain, it might become dysfunctional and increases the risk of developing chronic pain problems [6,42,59].

Interestingly, we recently found that preoperative attentional avoidance of social threat words (dot-probe task) was a significant predictor for acute postoperative pain, suggesting attentional avoidance of negative experiences in general to be a negative predictor [27]. In contrast to the present sample, the patients were aged, admitted for tumor surgery and suffering from high levels of psychological distress and this difference between samples might explain the exact type of attentional avoidance or preference. However, it is striking that attentional avoidance of negative information or the preference for positive information has now shown to be predictive in several studies. For sure, these are two independent processes. However, we assume as a common denominator that the processing of pain-related information is not prioritized.

4.2. Predicting postoperative pain disability

Interestingly, ratings of postoperative pain intensity and of pain disability run perfectly different routes as regards their best preoperative predictors. Whereas the best predictor for pain intensity was found on a behavioral level (dot-probe task), the sizeable percentage of those (54%) feeling still disabled due to pain three months after surgery became prominent beforehand by an increased self-report of pain hypervigilance. Those patients, who preoperatively considered themselves to be attentionally absorbed by pain and vigilant to all its forms, felt still unable to restore bodily functions after three and – to a minor degree – after six months. Such a relation appears plausible and suggests a style of behavioral wariness after surgery in individuals biased to monitor pain. Differing influences on the postoperative course of pain intensity and pain disability were also recently described by Katz et al. [22], who found pain disability to be more affected by emotional factors compared to pain intensity. Not surprisingly, the correlation between pain intensity and pain disability was only weak, especially three months after surgery.

Besides pain hypervigilance (PVAQ), preoperatively assessed cold and pressure pain thresholds also predicted pain disability six months after. A negative relationship between preoperative pain thresholds and postoperative pain has been observed in some studies mainly for acute pain [16,19,39,64]. Accordingly, our finding of a negative relationship between preoperative pressure pain thresholds and pain-related disability six months after surgery is new but not surprising. In contrast, the positive relationship between cold pain threshold and pain-related disability is more thought provoking. No earlier studies exist that have shown a similar relationship. Cold pain sensitivity has been associated with psychological genetic polymorphisms in dopamine transmitter pathways, which apparently also increase the risk of postoperative pain [58]. This explanation is helpful for understanding the relationship but not its direction. However, given our relatively small sample size, we cannot exclude that this finding might only be a statistical artifact.

4.3. General discussion and limitations

It is surprising that traditionally used predictors for postoperative pain, most notably depression and anxiety were not very use-

ful in distinguishing between high and low pain outcome groups. In a recent systematic review, depression was classified to be likely correlated with chronic postoperative pain [18]. This cautious conclusion, which we even toned down in our recent review [20], was not corroborated by our present data. The reason for that might have been that our patients were young, had no major pain experiences before and showed only low levels of mood disturbances, which can hardly be called depression. We investigated such a sample on purpose in order to be able to assess early phases of pain chronification, but might thus have missed those relationships developing only in more advanced pain careers. Another puzzling finding was that the relevance of predictors changed between the assessment of postoperative pain three and six months after surgery. Considering the fact that during the course of recovery, cases turned continuously into non-cases, thus changing the sample compositions, this puzzling finding might be better understood. The predictors for refractory cases later in the course of recovery may differ from those of still manageable cases earlier. Similarly, predictors for acute postoperative pain in this sample reported earlier [28] were not all preserved for the prediction of chronic pain reported here. To give one critical example, pain catastrophizing was a useful predictor for the acute but not for the chronic period of postoperative pain. Lastly, the hypothesis promoted by the findings of Geiss et al. [12] that a reduced cortisol secretion in the morning hours and enhanced feedback sensitivity of the HPA axis predict poor outcome after surgery could only be partially corroborated. The seemingly strong univariate effects (effect sizes) in this respect did not survive our multivariate analyses.

There are some limitations to our study. First, we only examined young men with surgical correction of chest malformations (funnel chest). Although this is almost an ideal surgical model for predictor research – as explained before – it is necessary to replicate our findings in other samples of patients, to determine the extent to which our findings can be extrapolated. A second limitation was the rather low rates and low intensities of postoperative pain. This is likely the merit of the current Erlangen pectus repair method, which is less invasive than other methods and allows for less extensive anterolateral mobilization [62,63]. Thirdly, the selection of relevant predictors for postoperative pain was based at first on findings about psychological predictors in the literature but was driven in the course of our analyses by their statistical significance, which requires necessarily replication in independent samples.

In sum, attentional bias toward positive words helped to predict postoperative pain intensity after three and six months, whereas self-reported hypervigilance allowed for predicting pain-related disability at these intervals post surgery. After six months, only a small group of patients were still reporting about pain. In those, pain-related disability was also predicted by the preoperatively assessed pressure and cold pain thresholds in addition to self-reported pain hypervigilance.

5. Conflict of interest statement

There is no conflict of interest.

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