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Affective modulation of brain potentials to painful and nonpainful stimuli

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Abstract

In accordance with the emotional priming hypothesis, emotions seem to modulate pain perception and pain tolerance thresholds. To further evaluate this association, event-related brain potentials (ERPs) elicited by painful and nonpainful electrical stimuli during processing of positive, neutral, and negative valenced pictures were recorded from 30 healthy volunteers. Valence of pictures affected pain ratings and the N150 elicited by painful stimuli, with lowest amplitudes for positive pictures and highest amplitudes for negative pictures. The P260 elicited by painful and nonpainful stimuli was modulated by arousal with reduced amplitudes with arousing (positive or negative) compared to neutral pictures. N150 amplitudes varying with picture valence seem to reflect an affective modulation of pain perception whereas P260 amplitudes varying with picture arousal rather reflect non-pain-specific attentional processes.

Descriptors: Pain, Affect, Emotion, Electrical pain model, Event-related potentials, IAPS pictures

According to the motivational priming hypothesis (Lang, 1995), an organism's emotional state will modify responses to valenced stimuli. Responses triggered by aversive stimuli are facilitated in the context of a negative emotional state and inhibited in the context of a positive emotional state. This prediction was verified repeatedly on the basis of the acoustic startle reflex in animals (e.g., Lang, Davis, & Oehman, 2000) and humans (e.g., Vrana, Spence, & Lang, 1988). Human participants were mainly studied with the affective picture paradigm. The International Affective Picture System (IAPS; Center for the Study of Emotion and Attention [CSEA-NIMH], 1995), a standardized set of affective picture stimuli varying on the emotional dimensions of valence and arousal, can be used for affect induction. The startle reflex is elicited by a startle probe presented during picture viewing and registered on the basis of the electromyogram of the m. orbicularis occuli. Its intensity varies with picture valence; it is enhanced in the context of emotional negative stimuli and dampened in the context of emotional positive stimuli (Lang, Bradley, & Cuthbert, 1990).

Using this affective picture paradigm, Schupp, Cuthbert, Bradley, Birbaumer, and Lang (1997) investigated two measures of the evoked startle response, the startle blink reflex and the event-related potential. They found that these two physiological responses to the startle probe were differentially modified by the emotional context: whereas the blink response was modulated by the valence of the pictures, the amplitude of the P300 of the event-related potential varied with picture arousal, with reduced P300 amplitudes in the context of arousing (negative or positive) picture stimuli compared to nonarousing neutral stimuli.

Based on the motivational priming theory, an organism's emotional state should modulate not only responses to startling stimuli but also to other aversive stimuli. This should be especially true for pain stimuli. The amygdala and the periaqueductal gray (PAG) are known to be crucial for the modulation of the startle response (Davis, 1997; Walker, Cassella, Lee, De Lima, & Davis, 1997) as well as pain responses (Oliveira & Prado, 2001; Pavlovic, 1998). In this study, we measured somatosensory evoked brain potentials to painful and nonpainful stimuli delivered during picture viewing to investigate the motivational priming idea.

In their review article, Keefe et al. (2001) reported several correlational studies suggesting that negative emotional states serve as risk factors that increase the likelihood of pain onset or exacerbation. In addition, there is some experimental evidence that positive mood reduces pain perception whereas negative mood increases pain perception. For example, Zelman, Howlands, Nichols, and Cleeland (1991) found that reading elative, neutral, or depressive mood statements led to increased, unchanged, or decreased pain tolerance, assessed with a cold pressor test. Villemure, Slotnick, and Bushnell (2003) manipulated mood states with pleasant and unpleasant odors and found that odor valence affected pain unpleasantness indirectly through its effect on mood; positive odors elicited positive mood and reduced pain unpleasantness ratings compared to negative odors. Two recent studies (de Wied & Verbaten, 2001; Meagher, Arnau, & Rhudy, 2001) used a modified version of the affective picture paradigm to modulate the participants' emotional state and assessed pain perception with the cold pressor test. De Wied and

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Verbaten presented the pictures simultaneously with the cold pressor test and found that negative pictures were associated with decreased pain tolerance and positive pictures with increased pain tolerance, both compared to neutral pictures. Meagher et al. presented the pictures before the cold pressor test and found that viewing disgust and fear pictures decreased pain thresholds and viewing erotic pictures increased pain thresholds, whereas pain tolerance was not consistently affected by picture content.

The widely used cold pressor test is a tonic pain model (Chen, Dworkin, & Haug, 1989) associated with strong cardiovascular changes, which themselves may influence pain perception (e.g., Rau et al., 1994). Therefore, a generalization to other pain models remains problematic. In addition, previous studies did not adhere to the affective picture paradigm, because the typical within-subjects design of the affective picture paradigm was changed to a between-subjects design: Each group saw only one category of emotional pictures (positive, neutral, or negative) and apart from the study of De Wied and Verbaten, pain stimuli were delivered after the presentation of several pictures of one valence category, whereas startle probe stimuli are typically presented during picture presentation.

However, the main disadvantage of the cold pressor pain model is that it does not allow simultaneous registration of somatosensory evoked potentials (SEPs) as electrophysiological measures related to pain perception. In contrast, an electric pain model allows a close experimental analogy to the typical affective picture paradigm and the registration of somatosensory evoked brain potentials (Bromm & Lorenz, 1998).

To extract those components from the somatosensory evoked potentials that are relevant for the processing of pain, Bromm and Scharein (1982) defined by means of a principal component analysis two components that are part of the N150–P260 complex and correlate significantly with reported pain intensity (Chapman & Jacobson, 1984; Chen & Chapman, 1980; Miltner, Johnson, Braun, & Larbig, 1989).

However, somatosensory evoked late brain potentials are not pain specific and are not specific to the modality of the eliciting stimulus; they vary with the psychological meaning and the demands and task relevance of the stimulus (Picton & Hillyard, 1988). Thus, it is generally acknowledged that the N150–P260 component of the somatosensory evoked potential reflects the activity of neurons involved in a number of different, pain-related and non-pain-related processes (Dowman, 1994). To separate the pain-related and non-pain-related components of potentials elicited by electrical stimulation of the sural nerve, Dowman subtracted somatosensory evoked potentials elicited by pain-threshold stimuli from those generated by supra-pain-threshold stimuli and described a negative difference potential (NDP) 75–240 ms after stimulus onset. Scalp topography, dipole source localization analyses, and intracranial recording studies provide evidence that the NDP is generated by the anterior cingulate cortex and the supplementary somatosensory area (Dowman, 2004). These findings are in line with previous brain electrical source analyses of laser-evoked potentials (Bromm & Lorenz, 1998) revealing a dipole in the prefrontal cortex, probably indicating premotor activity or blink reflex contamination in response to the stimulus, two dipoles localized bilaterally in the secondary somatosensory cortices, and a fourth dipole in the cingulate gyrus, which bound most activity of both the N150 and the P260.

In the present study, we used the well-established affective picture paradigm to further evaluate the effects of emotion on subjective and electrophysiological responses to pain stimuli. Based on the design of Schupp et al. (1997) we presented painful or nonpainful probe stimuli during the viewing of negative, neutral, and positive pictures. Pain reports as well as somatosensory-evoked brain potentials were registered. Based on the motivational priming hypothesis, valence effects were expected for pain ratings and the amplitudes of the N150–P260 complex, however, only for painful but not for nonpainful electrical stimuli.

Methods

Participants

Participants were 30 healthy right-handed paid volunteers (15 female; mean age = 22.8 years; $SD = 3.6$; range 18–30 years) who were free of neurological, psychiatric, or chronic pain disease. Prior to the experiment, they were informed about the experimental procedure and that they would receive 252 electrical stimuli with half of them being painful. The experimental protocol was approved by the ethics committee of the ''Deutsche Gesellschaft für Psychologie'' (DGPs) and informed consent was obtained for all participants.

Stimulus Materials and Design

One hundred and eight color slides were chosen from the International Affective Picture System (Center for the Study of Emotion and Attention, 1995), depicting 36 unpleasant, 36 pleasant, and 36 neutral objects or scenes, resulting in three different picture content categories.[1] Pictures were presented on a 19-in. computer screen.

Three orders of slide presentation were arranged such that, across participants, a particular picture occurred in the first, second, or third block. Picture presentation was arranged in three blocks, each containing 12 pleasant, 12 neutral, and 12 unpleasant slides. In addition, slide order was changed within each block to control local order effects.

The electrical stimuli consisted of single unipolar electrical pulses of 20 ms duration, delivered via a surface bar electrode, which was applied to the left forearm. The bar electrode consisted of two durable gold-plated stainless steel disk electrodes with 9 mm diameter and 30 mm spacing (Nicolet part #019-431400). The stimuli were generated by a battery-driven constant-current stimulator (developed by the University of Konstanz), supplying a maximum of 140 V and a maximum current of 10 mA. In an unpublished pilot study we demonstrated that our electric pain model elicited ERPs comparable to those of other electric pain models (Becker, Haley, Urena, & Yingling, 2000; Bromm &

[1]Criteria for the choice of the pictures were normative ratings (Lang, Bradley, & Cuthbert, 1995) on the dimensions of affective valence and arousal (on a scale ranging from 1 to 9, with low scores indicating low arousal and low pleasure and high scores indicating high arousal and high pleasure). Negative and positive pictures had comparable arousal ratings (6.13 vs. 6.09, respectively). Neutral pictures had low arousal (2.57) and intermediate valence ratings (5.09). The slide numbers were as follows: positive: 2160, 4220, 4250, 4310, 4520, 4599, 1710, 4607, 4608, 4610, 4611, 4640, 4641, 4652, 4658, 4659, 4660, 4670, 4680, 4690, 2050, 5260, 5450, 5470, 5621, 5626, 8170, 8180, 8190, 8200, 8300, 8370, 8420, 8496, 8501, 8080; neutral: 2190, 2320, 2480, 2570, 2580, 2840, 2880, 5390, 5510, 5520, 5530, 5731, 5740, 7000, 7004, 7006, 7010, 7025, 7031, 7035, 7050, 7060, 7080, 7100, 7140, 7150, 7175, 7185, 7187, 7205, 7217, 7233, 7235, 7490, 7491, 7950; and negative: 1070, 1090, 1110, 1120, 1220, 1280, 1300, 2120, 2730, 2800, 3230, 6020, 6190, 6200, 6230, 6260, 6313, 6350, 6370, 6510, 6540, 6550, 6940, 7380, 9040, 9050, 9140, 9181, 9300, 9490, 9600, 9611, 9620, 9630, 9810, 9911.

Lorenz, 1998), with higher N150–P260 amplitudes for painful than for nonpainful stimuli, although both nociceptive and nonnociceptive fibers are activated in this model whereas the original intracutaneous stimulation protocol is thought to activate only nociceptive fibers.

A within-subject design was used. All subjects completed two experimental sessions at the same time on two successive days, one with painful stimulation and one with nonpainful stimulation (order balanced across participants).

Each experimental session consisted of 108 trials (three blocks of 36 trials) with the following sequence: Pictures were presented for 6 s followed by a postpicture processing period of 6 s that was terminated by a soft tone. The following interval consisted of two phases: in the pause phase varying randomly between 4 and 10 s, a blank monitor was presented and the participants had no task. In the subsequent rating phase, participants were asked to rate the intensity of the preceding electrical stimulus (regardless of in which phase the stimulus was applied) on a scale ranging from 0 (*no sensation*) to 4 (*just noticeable pain*) to 10 (*unbearable pain*). During each experimental block, 15 electrical stimuli each were delivered in the picture (between 2500 and 5000 ms after picture onset) and the postpicture period (between 2500 and 5000 ms after picture offset), in both cases equally distributed across the three picture categories. In addition, 12 electrical stimuli were delivered during the pause interval at randomly selected trials.

Procedure

After arrival at the laboratory, participants read and signed informed consent and electrodes were attached.

The pain threshold was assessed. Twelve series of electrical stimuli with ascending and descending intensity in steps of 0.5 mA were applied (maximum stimulus intensity that could be administered was 10 mA), and participants had to rate each electrical stimulus on a scale ranging from 0 (*no sensation at all*) to 4 (*just noticeable pain*) to 10 (*unbearable pain*). The mean value of that intensity that participants rated as "just noticeable pain" was defined as pain threshold. Based on this measurement, painful stimuli were defined as 1 mA above and nonpainful stimuli 1 mA below the individual pain threshold. Mean stimulus intensity was 3.0 mA ($SD = 1.4$) for nonpainful and 5.0 mA ($SD = 1.8$) for painful stimuli.

The participants were then told that a series of slides would be presented and that each picture should be viewed during the entire presentation time. They were also instructed to imagine that they were still watching the slide, continuing to keep the eyes open and fixated on the center of the screen after picture offset until a soft tone terminated this period.

Participants were also told that electrical stimuli would be presented during picture, postpicture, or intertrial intervals. They were instructed to ignore these electrical stimuli and to concentrate on the pictures. Three practice trials with a negative, a neutral, and a positive picture were run to familiarize participants with the trial sequence. These practice trials allowed us to adjust the stimulus intensities when necessary to ensure that the stimuli were actually painful on one day and nonpainful on the other day. After the second experimental session, participants were asked to rate all test pictures on valence and arousal scales ranging from 1 (*very unpleasant* resp. no arousal) to 9 (very pleasant resp. very strong arousal). Both rating scales were presented consecutively and simultaneously with the test picture on the monitor.

Participants made their ratings by pressing one of the designated keys on the computer keyboard.

ERP Recording and Data Analysis

The electroencephalogram (EEG) was measured with Ag-AgCl electrodes (digitized with a sampling rate of 200 Hz) from 11 sites according to the international 10–20 system (A1, A2, F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4), using a Brain-Amp-MR amplifier (Brain Products GmbH) and the software Brain Vision Recorder Version 1.01b (Brain Products GmbH). Data were bandpass-filtered (0.5–50 Hz) on-line. All channels were recorded with an A1 reference and converted to linked-ears reference off-line. The ground electrode was located on the chest. Vertical and horizontal eye movements were recorded using miniature Ag-AgCl electrodes.

Off-line EEG analysis was performed with the computer software Brain Vision Analyzer Version 1.04 (Brain Products GmbH): Electroencephalograms were bandpass-filtered (0.5–30 Hz) and corrected for horizontal and vertical ocular artifacts (Gratton, Coles, & Donchin, 1983). Epochs registered -200 ms before to 500 ms after onset of the electrical stimuli were baseline corrected with reference to the mean baseline interval (-200 to 0 ms) and then averaged for each participant and each experimental condition. ERP components were quantified on the basis of mean amplitudes calculated over time windows defined on the basis of visual inspection (time windows were centered on the maxima of the effects) and the literature (Bromm & Lorenz, 1998; Miltner et al., 1989). For N150 and P260, the time windows were 100–150 ms and 220–350 ms after stimulus onset, respectively. If not otherwise indicated, means $\pm$ *SD*s are reported.

ERP components were analyzed with repeated-measures ANOVAs. If necessary, Greenhouse–Geisser corrections were applied. Significant effects were followed up by comparisons of means using the Bonferroni procedure. A significance level of .05 (two-tailed) was used for all analyses.

Results

Picture Ratings

Table 1 depicts the mean valence and arousal ratings for the three picture categories. For valence ratings and arousal ratings, separate one-way repeated-measures ANOVAs with the factor Picture Content (positive vs. neutral vs. negative) were performed. Both analyses revealed significant effects of Picture Content (valence, $F[2,58] = 268.8$, $p < .001$; arousal, $F[2,58] = 66.6$, $p < .001$).

Follow-up comparisons of means, using the Bonferroni procedure, showed that for valence ratings all pairs of means were significantly different from each other (all $ps < .001$). For arousal ratings the difference between the positive and the negative slide condition ($p < .14$) was not significant, whereas all other differences were significant (all $ps < .001$).

Polynomial analysis of variance revealed a significant linear, $F(1,29) = 331.8$, $p < .001$, and a significant quadratic effect for

Table 1. *Mean Valence and Arousal Ratings with Standard Deviation for All Slide Types*

Picture content	Valence ratings	Arousal ratings
Positive	6.8 ± 0.8	5.4 ± 1.4
Neutral	5.5 ± 0.5	3.4 ± 1.3
Negative	2.8 ± 0.7	5.9 ± 1.2

The scores ranged from 1 (low pleasure, low arousal) to 9 (high pleasure, high arousal).

valence ratings, $F(1,29) = 48.8$, $p < .001$, and a significant linear, $F(1,29) = 4.3$, $p < .048$, and a significant quadratic effect, $F(1,29) = 123.4$, $p < .001$, for arousal ratings.

Pain Ratings

Figure 1 depicts the mean pain ratings as a function of experimental condition. A repeated-measures ANOVA with the factors Painfulness (painful vs. nonpainful), Period (picture vs. postpicture period), and Picture Content (positive vs. neutral vs. negative) revealed significant effects of Painfulness, $F(1,28) = 216.7$, $p < .001$, Period, $F(1,28) = 55.3$, $p < .001$, and Picture Content, $F(2,56) = 25.1$, $p < .001$, as well as a significant Period $\times$ Picture Content interaction, $F(2,56) = 4.1$, $p < .023$. As can be seen in Figure 1, higher pain ratings were obtained for painful (4.4 ± 0.9) than for nonpainful stimuli (2.2 ± 0.5), and also for stimuli applied during the postpicture period (3.4 ± 0.6) compared to stimuli applied during the picture period (3.2 ± 0.5).

The Picture Content $\times$ Period interaction was followed up by separate ANOVAs for both processing periods that revealed a significant effect of Picture Content for both the picture, $F(2,56) = 17.7$, $p < .0001$, and the postpicture period, $F(2,56) = 20.8$, $p < .0001$. For the picture period, pain ratings were significantly lower during the processing of positive compared to neutral ($p < .0001$) and negative pictures ($p < .0001$). For the postpicture period, pain ratings were lower for positive compared to negative pictures ($p < .0001$), and lower for neutral compared to negative pictures ($p < .0001$). A polynomial analysis of variance revealed significant linear effects (picture period: $F[1,28] = 30.9$, $p < .0001$, postpicture period: $F[1,28] = 36.3$, $p < .0001$) for the factor Picture Content, but no quadratic effect (picture period: $F[1,28] = 2.4$, n.s., postpicture period: $F(1,28) = 2.7$, n.s.).

Event-Related Brain Potentials (ERPs)

Both painful and nonpainful stimuli elicited ERPs with an early negative peak in the time range between 100 and 150 ms (N150) and a late positive amplitude between 220 and 350 ms (P260). Mean N150 and P260 amplitudes for all conditions and electrodes are shown in Tables 2 and 3. The N150 had maximal amplitudes at frontal-right electrodes, whereas the P260 had a bilateral distribution and an activity focus at the vertex, with the highest amplitudes at central leads, lower amplitudes at posterior leads, and smallest amplitudes at frontal leads. Amplitudes were larger for painful stimuli than for nonpainful stimuli and larger during the postpicture period than during the picture period. Furthermore, the amplitude of the components varied depending on the affect manipulation.

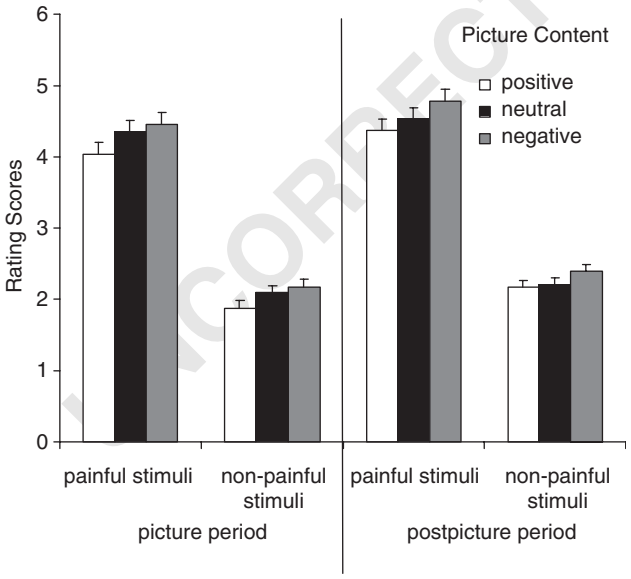

Figure 1. Mean pain ratings with standard errors separate for all picture contents, picture and postpicture processing period, and painful and nonpainful stimuli. The scores ranged from 0 (*no pain*) via 4 (*just noticeable pain*) to 10 (*unbearable pain*).

Repeated-measures ANOVAs with the within-subject factors Painfulness (painful vs. nonpainful), Period (picture vs. postpicture processing period), Picture Content (positive vs. neutral vs. negative) and Electrodes were computed separately for the N150 and the P260 components.

N150. The overall ANOVA showed a significant main effect for Painfulness, $F(1,29) = 10.49$, $p < .003$, with larger amplitudes for painful (-1.418 ± 5.3 μV) than for nonpainful stimuli (0.556 ± 3.4 μV), a significant main effect for Period, $F(1,29) = 13.64$, $p < .001$, with larger amplitudes for stimuli applied during the postpicture period (-0.968 ± 4.6 μV) than for stimuli applied during the picture period (0.105 ± 4.0 μV), and a significant main effect for Electrodes, $F(8,232) = 21.19$, $p < .001$, with larger amplitudes at Fz, F4, Cz, and C4 than at other electrode sites. The three-way interaction Painfulness $\times$ Picture Content $\times$ Electrodes was not significant, $F(16,464) = 1.230$.

A significant Painfulness $\times$ Picture Content interaction, $F(2,58) = 3.60$, $p < .04$, was followed up by separate ANOVAs for painful and nonpainful stimuli. Only for painful stimuli was a significant main effect of Picture Content found, $F(2,58) = 3.58$, $p < .042$, with a significant difference between the positive and the negative picture conditions ($p < .041$, see Figure 2); all other differences were not significant. A polynomial analysis of variance revealed a significant linear trend for the factor Picture Content, $F(1,29) = 6.91$, $p < .014$, but no quadratic trend, $F(1,29) = 1.4$. Follow-up tests for nonpainful stimuli revealed no significant main effect of Picture Content.

A significant Picture Content $\times$ Electrodes interaction, $F(16,464) = 2.16$, $p < .048$, was followed up by separate ANOVAs for each electrode site. For no electrode site was a significant main effect of Picture Content found. However, a polynomial analysis of variance for the recordings at Cz revealed a significant linear trend, $F(1,29) = 4.50$, $p < .043$, but no quadratic trend, $F(1,29) = 0.34$, for the factor Picture Content.

A significant Painfulness $\times$ Electrodes interaction, $F(8,232) = 20.54$, $p < .001$, was followed up by separate ANOVAs for each electrode site. Significant effects of Painfulness were found for Fz, F4, C3, Cz, and C4, but not for F3 and the parietal electrode sites.

Finally, a significant Period $\times$ Electrodes interaction, $F(8,232) = 9.23$, $p < .001$, was followed up by separate ANOVAs for each electrode site, revealing significant effects of Period for Fz, F4 C3, Cz, C4, and Pz, but not for F3, P3, and P4.

P260. The overall ANOVA returned a significant main effect of Painfulness, $F(1,29) = 24.04$, $p < .001$, with larger amplitudes for painful (12.453 ± 4.4 μV) than for nonpainful stimuli (9.770 ± 3.9 μV), a significant main effect of Period, $F(1,29) = 40.0$, $p < .0001$, with larger amplitudes for stimuli applied during the postpicture period (12.172 ± 3.9 μV) compared

Table 2. *Mean N150 Amplitudes with Standard Deviation for All Picture Contents, Picture and Postpicture Processing Period, Painful and Nonpainful Stimuli, and All Electrodes*

		Painful		Nonpainful	
Electrodes	Picture content	Picture	Postpicture	Picture	Postpicture
F3	positive	0.36 ± 4.82	− 1.31 ± 6.12	1.38 ± 3.09	0.37 ± 4.54
	neutral	0.04 ± 5.83	0.06 ± 5.90	1.06 ± 4.14	0.15 ± 4.20
	negative	− 0.10 ± 5.18	− 0.92 ± 5.85	1.04 ± 3.95	1.51 ± 5.24
Fz	positive	− 2.87 ± 6.35	− 4.79 ± 7.56	− 0.03 ± 3.89	− 1.54 ± 5.33
	neutral	− 3.81 ± 7.12	− 3.91 ± 7.89	− 0.72 ± 5.13	− 1.51 ± 4.77
	negative	− 3.82 ± 6.38	− 5.09 ± 7.33	− 0.61 ± 4.86	− 0.27 ± 5.50
F4	positive	− 1.67 ± 6.02	− 2.81 ± 6.72	0.53 ± 4.03	− 0.24 ± 4.90
	neutral	− 2.24 ± 5.98	− 2.10 ± 6.99	0.23 ± 4.83	− 0.43 ± 4.66
	negative	− 2.62 ± 5.89	− 3.17 ± 6.83	0.62 ± 4.61	0.92 ± 5.80
C3	positive	− 0.62 ± 4.87	− 3.79 ± 7.47	0.77 ± 3.34	− 1.37 ± 4.25
	neutral	− 1.69 ± 6.17	− 2.69 ± 7.63	0.64 ± 4.48	− 1.48 ± 4.59
	negative	− 2.18 ± 5.75	− 4.22 ± 6.56	0.49 ± 4.49	0.27 ± 4.49
Cz	positive	− 3.12 ± 7.50	− 7.48 ± 10.64	0.53 ± 5.93	− 2.44 ± 6.69
	neutral	− 4.88 ± 9.24	− 6.46 ± 10.97	0.04 ± 7.09	− 2.29 ± 7.36
	negative	− 5.86 ± 9.01	− 8.92 ± 10.41	− 0.27 ± 6.92	− 0.78 ± 6.97
C4	positive	− 1.47 ± 6.33	− 4.13 ± 8.29	0.37 ± 4.60	− 1.73 ± 5.79
	neutral	− 2.95 ± 7.17	− 3.37 ± 7.90	− 0.36 ± 5.90	− 1.77 ± 5.77
	negative	− 3.57 ± 7.36	− 5.06 ± 7.67	− 0.33 ± 5.74	− 0.44 ± 5.58
P3	positive	1.13 ± 4.06	1.49 ± 6.48	1.81 ± 2.72	0.72 ± 3.83
	neutral	0.54 ± 5.13	− 0.13 ± 7.24	1.17 ± 3.47	1.94 ± 3.80
	negative	4.31 ± 4.93	1.91 ± 5.97	3.66 ± 3.67	1.75 ± 3.72
Pz	positive	3.21 ± 4.86	3.56 ± 7.12	3.45 ± 3.24	2.03 ± 4.34
	neutral	2.38 ± 6.25	1.52 ± 7.29	2.90 ± 4.16	3.49 ± 4.77
	negative	3.56 ± 6.28	1.89 ± 6.97	2.78 ± 4.38	1.34 ± 4.12
P4	positive	2.59 ± 4.93	3.19 ± 6.32	2.34 ± 3.15	1.55 ± 4.31
	neutral	2.23 ± 5.52	0.22 ± 6.67	1.95 ± 3.64	0.24 ± 4.30
	negative	1.61 ± 5.32	1.39 ± 6.06	1.77 ± 4.05	2.82 ± 3.65

to the picture period (10.051 ± 4.0 μV), and a significant main effect of Electrodes, $F(8,232) = 59.32$, $p < .001$, with largest amplitudes at central leads, smaller amplitudes at parietal leads, and even smaller amplitudes at frontal leads. There was no significant main effect of Picture Content, $F(2,58) = 2.21$, and no significant interaction of Picture Content × Electrodes, $F(16,464) = 0.95$.

Table 3. *Mean P260 Amplitudes with Standard Deviations for All Picture Contents, Picture and Postpicture Processing Period, Painful and Nonpainful Stimuli, and All Electrodes*

		Painful		Nonpainful	
Electrodes	Picture content	Picture	Postpicture	Picture	Postpicture
F3	positive	6.89 ± 4.15	10.20 ± 3.71	5.74 ± 3.30	8.04 ± 3.86
	neutral	8.30 ± 4.36	9.74 ± 4.51	7.13 ± 3.03	7.97 ± 4.48
	negative	7.77 ± 3.93	9.84 ± 4.28	6.07 ± 3.99	8.09 ± 4.04
Fz	positive	8.62 ± 5.07	11.82 ± 4.73	7.16 ± 4.32	9.46 ± 4.48
	neutral	10.28 ± 5.44	11.59 ± 5.40	8.66 ± 4.44	9.46 ± 4.63
	negative	9.48 ± 4.26	11.74 ± 5.05	7.62 ± 4.84	9.63 ± 4.42
F4	positive	7.41 ± 4.49	10.30 ± 4.20	5.76 ± 3.78	8.28 ± 4.48
	neutral	8.81 ± 5.05	10.47 ± 4.56	7.38 ± 4.21	7.98 ± 4.25
	negative	8.42 ± 3.91	10.41 ± 4.61	6.85 ± 3.97	8.68 ± 3.90
C3	positive	11.03 ± 5.49	14.63 ± 4.83	7.81 ± 3.70	11.15 ± 4.37
	neutral	12.83 ± 5.49	14.46 ± 5.77	9.62 ± 3.89	10.46 ± 4.99
	negative	12.17 ± 4.72	14.37 ± 5.72	8.36 ± 4.65	11.44 ± 4.55
Cz	positive	16.35 ± 8.09	19.85 ± 7.68	12.62 ± 6.12	16.06 ± 6.89
	neutral	18.83 ± 8.29	19.63 ± 8.43	14.90 ± 6.55	15.80 ± 6.78
	negative	17.33 ± 7.14	19.76 ± 8.58	13.41 ± 7.23	16.63 ± 6.49
C4	positive	12.11 ± 5.87	15.16 ± 5.41	9.34 ± 4.50	12.44 ± 5.29
	neutral	13.87 ± 6.05	15.22 ± 5.79	11.08 ± 5.37	11.83 ± 5.54
	negative	13.24 ± 4.75	15.30 ± 6.26	10.36 ± 5.52	12.91 ± 5.14
P3	positive	9.46 ± 4.38	11.95 ± 5.74	6.48 ± 3.99	9.26 ± 4.52
	neutral	10.68 ± 5.15	12.01 ± 5.19	8.04 ± 4.34	8.76 ± 4.97
	negative	10.01 ± 4.17	12.09 ± 6.02	6.67 ± 4.38	9.93 ± 4.09
Pz	positive	12.65 ± 5.71	15.61 ± 7.05	9.42 ± 5.01	12.66 ± 5.20
	neutral	14.52 ± 6.52	15.68 ± 6.42	11.26 ± 5.29	12.02 ± 5.44
	negative	13.31 ± 4.90	15.84 ± 7.25	9.87 ± 5.45	13.09 ± 4.66
P4	positive	10.25 ± 4.93	12.32 ± 6.00	7.51 ± 4.19	10.00 ± 4.59
	neutral	11.56 ± 5.93	12.52 ± 5.30	8.70 ± 4.55	9.27 ± 4.79
	negative	10.84 ± 4.38	12.92 ± 6.11	7.91 ± 4.93	10.52 ± 4.35

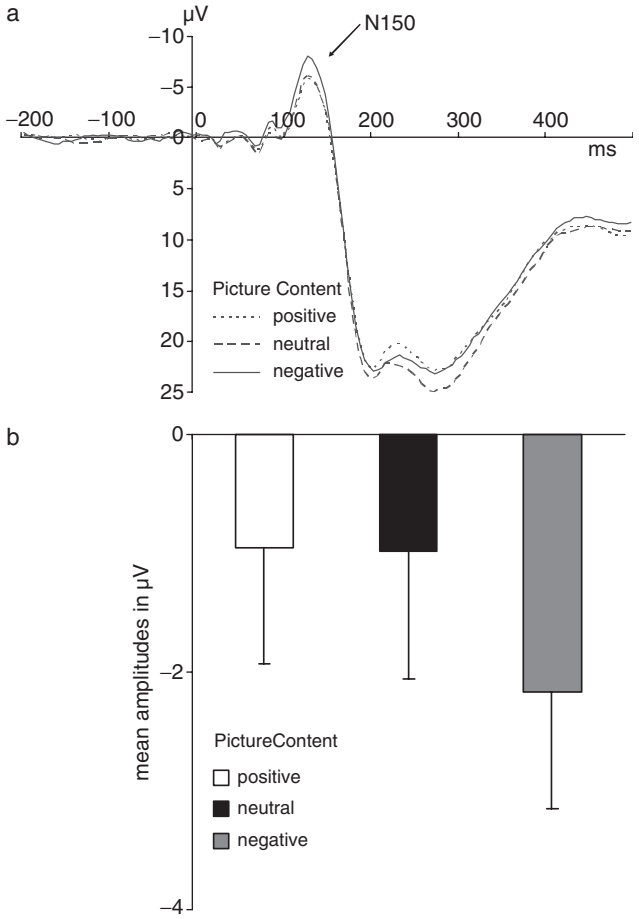

Figure 2. A: Grand average ERP waveform at Cz elicited by painful electrical stimuli differentiated for picture contents. B: Bar graphs depict mean N150 amplitudes with standard errors differentiated for picture contents averaged across electrodes.

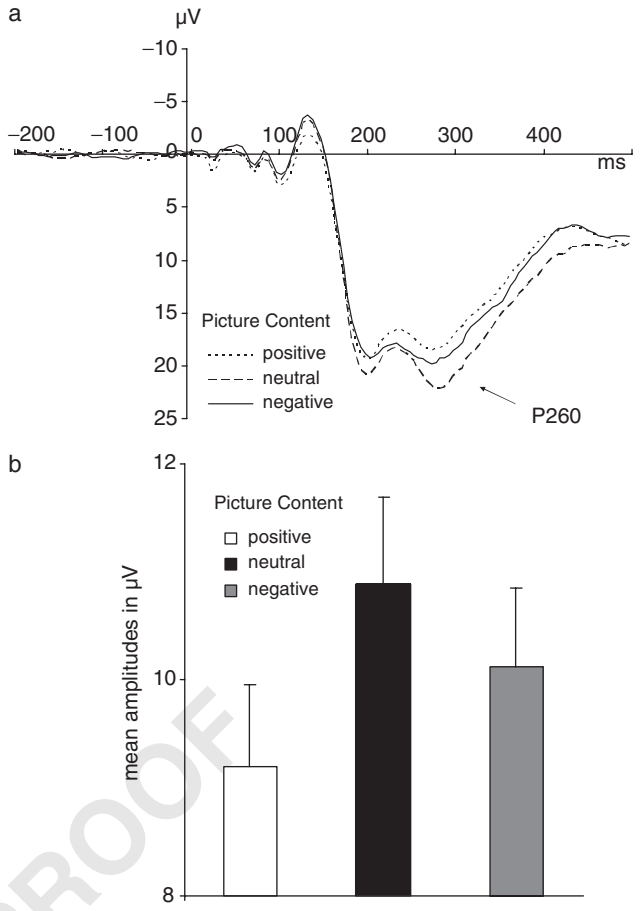

Figure 3. A: Grand average ERP waveform at Cz elicited by electrical stimuli (painful and nonpainful) differentiated for picture contents. B: Bar graphs depict mean P260 amplitudes with standard errors differentiated for picture contents averaged across electrodes.

A significant Period × Picture Content interaction, $F(2,58) = 5.68$, $p < .006$, was followed up by separate ANOVAs for the picture and the postpicture processing periods. As can be seen in Figure 3, during picture processing, a significant effect of Picture Content, $F(2,58) = 7.96$, $p < .001$, was due to smaller amplitudes for positive and negative compared to neutral pictures. However, follow-up comparisons confirmed a significant difference only between positive and neutral pictures, $p < .003$. A polynomial analysis of variance for the picture processing period revealed a marginally significant quadratic effect, $F(1,29) = 3.25$, $p < .082$, but no linear effect, $F(1,29) = 1.55$, $p < .223$, for the factor Picture Content.

For the postpicture processing period, no significant effect for Picture Content was found.

Furthermore, a significant interaction of Painfulness × Electrodes, $F(8,232) = 5.88$, $p < .001$, was followed up by separate ANOVAs for each electrode site. The analyses revealed a significant effect for Painfulness for all electrode sites ($ps < .007$).

Pain Ratings and ERPs during the Pause Interval

Mean pain ratings for stimuli during the pause interval were 4.471 ± 0.9 for painful stimuli and 2.244 ± 0.5 for nonpainful stimuli. A repeated-measures ANOVA with the factors Period (picture vs. postpicture vs. pause interval) and Painfulness (painful vs. nonpainful) revealed significant main effects for Painfulness, $F(1,28) = 218.63$, $p < .001$, and Period, $F(2,56) = 15.42$, $p < .001$, but no significant interaction between the two factors. Follow-up comparisons revealed lower pain ratings for the picture period compared to the postpicture period ($p < .001$) and the pause interval ($p < .007$).

Furthermore, we compared the ERPs obtained in both picture processing periods and those obtained in the intertrial interval separately for the N150 and the P260 component and computed repeated-measures ANOVAs with the factors Period (picture period vs. postpicture period vs. pause interval), Painfulness (painful vs. nonpainful), and Electrodes. Only effects involving the factor Period will be reported.

For N150, the overall ANOVA showed a significant effect of Period, $F(2,58) = 4.04$, $p < .030$, with smaller amplitudes for stimuli during picture processing ($0.105 \pm 4.0\ \mu V$) than for stimuli during postpicture processing ($-9.968 \pm 4.6\ \mu V$) and during the pause interval ($-0.411 \pm 5.3\ \mu V$).

For P260, the overall ANOVA revealed a significant main effect of Period, $F(2,58) = 140.57$, $p < .001$, with higher amplitudes for stimuli evoked during the pause interval ($17.248 \pm 5.1\ \mu V$) than for stimuli during the postpicture period ($12.172 \pm 3.9\ \mu V$) and even less for stimuli during the picture period ($10.051 \pm 4.0\ \mu V$).

Discussion

The present experiment used the affective picture paradigm to examine the effects of affect on the perception and processing of electrical pain stimuli. Picture stimuli varying on the dimensions of arousal and valence were presented and electrical stimuli above and below the individually determined pain threshold were delivered during the picture and the postpicture processing period. Arousal and valance ratings for pictures assessed after the experiment confirmed a linear effect of valence with lowest ratings for negative pictures and highest ratings for positive pictures, and a quadratic effect of arousal with low arousal ratings for neutral pictures and high arousal ratings for positive and negative pictures. In addition, pain ratings assessed during the experiment validated the pain threshold assessment procedure. A pain rating of 4 represented just noticeable pain, and ratings for nonpainful stimuli were below 4, while ratings for painful stimuli were significantly higher and above 4.

ERPs triggered by painful and nonpainful electrical stimuli showed characteristics in line with previous studies (e.g., Bromm & Scharein, 1982; Miltner et al., 1989; Schupp et al., 1997): N150 and P260 amplitudes were enlarged for painful stimuli in comparison to nonpainful stimuli, and furthermore, stimuli delivered within the postpicture processing period elicited larger SEP amplitudes and pain rating scores than stimuli applied within the picture processing period. This latter effect may be due to an allocation of attention to the electrical stimuli during the postpicture processing period despite the instruction not to focus on the electrical stimuli during both processing periods. This is consistent with the finding of Miltner et al. (1989) that attention, focused to or away from electrical pain stimuli, influences both pain perception and the pain-evoked brain potential, with smaller pain ratings and amplitudes of the pain-evoked brain potential when attention is distracted from the electrical pain. However, our finding is not in line with Dowman (2001, 2002, 2004), who found reduced pain ratings but enlarged NDP amplitudes when subjects' attention was distracted from pain stimuli by visual stimuli (Dowman, 2001), heterotopic cold pain stimuli (Dowman, 2002), and invalid cuing stimuli (Dowman, 2004). This discrepancy may be explained by the use of different paradigms to distract participants' attention. Whereas Dowman misdirected the participants' attention to another modality or stimulus localization using distinct but invalid cuing stimuli, Miltner et al. as well as the present study distracted participants with attention-demanding tasks (word puzzles, picture viewing) during which unpredictable pain stimuli were delivered.

Most important, manipulations of affect did influence the pain perception as reflected in pain ratings and ERPs. Pain ratings for painful and nonpainful electrical stimuli were modulated by the valence of the affective foreground pictures, with highest ratings during the processing of negative pictures and lowest ratings during the processing of positive pictures. This finding confirms previous reports based on the cold-pressor test (de Wied & Verbaten, 2001; Meagher et al., 2001) by realizing a phasic pain model and a typical affective picture paradigm in one study. Our findings strongly support the motivational priming hypothesis assuming that responses triggered by aversive stimuli are facilitated in the context of a negative emotional state and inhibited in the context of a positive emotional state (Lang, 1995). This valence modulation was also present for nonpainful electrical stimuli. We assume that the nonpainful stimuli were also aversive although below the painful range (see Bromm & Meier, 1984).

Because the pain ratings were obtained at the end of each trial, it cannot be excluded that the affective modulation of the pain ratings was due to a mood congruency effect of memory (Bower, 1981), that is, that unpleasant stimuli might have a relative memory advantage under negative mood in comparison to positive mood. Thus, at the end of the trial, when subjects were asked how painful the electrical stimulus was, they may have had more difficulty recalling the stimulus when given during the positive picture condition and consequently may have given it a lower rating than when it was given during the negative picture condition. If so, the affective modulation of the pain ratings would not reflect an altered pain perception but an altered storage of the painful stimulus in memory dependent on the emotional state. However, this would not argue against the motivational priming hypothesis, but just show the other side of the same coin: Lang, Bradley, and Cuthbert (1990) proposed that emotional valence is a general information processing category with sensory, central, and response-processing implications.

The present experimental manipulation allowed registration of somatosensory ERPs as physiological measures of pain processing. The N150, a typical component of the pain evoked brain potential (Bromm & Scharein, 1982), varied with the valence of the affective foreground stimuli with largest and lowest amplitudes during processing of negative and positive pictures, respectively. Again, this finding may be interpreted as support of the motivational priming hypothesis (Lang, 1995). Interestingly, we found this effect only for painful stimuli but not for stimuli in the nonpainful range, indicating that the modulation of the N150 amplitude is pain specific. This pain specificity of the N150 may also explain why Schupp et al. (1997) did not find a modulation of early ERP components (e.g., N100) triggered by startle stimuli. In contrast to the pain specificity of the N150, the registered pain ratings may mirror a somatosensory dimension from not noticeable via unpleasant to painful, and this may explain why we found an affect modulation for painful and nonpainful stimuli.

Considering the experiment as a distraction task with varying levels of difficulty, a possible alternative interpretation of our findings may be that the participants paid more attention to the positive and less to the negative (due to avoidance) and neutral (because of their being boring) pictures. However, Lang, Greenwald, Bradley, and Hamm (1993), measuring affective, visceral, and behavioral reactions while participants were viewing pictures, found a linear relationship between interest and ranked arousal ratings as well as between viewing durations and ranked arousal ratings, even more so when arousal ranks were adjusted for valence ratings. Because there was no significant difference between the arousal ratings for the positive and negative pictures used in our study, it seems implausible that attention could explain the effects of emotional valence on the pain ratings and the SEP components.

The present study also revealed affect modulation effects for the P260. The P260 amplitudes were modulated by the arousal dimension of the pictures with smaller amplitudes when arousing (positive or negative) compared to neutral pictures were processed. This effect, on the one hand, was observable for painful and nonpainful stimuli, but, on the other hand, was only present during the picture processing period and not during the postpicture processing period. Schupp et al. (1997) observed enhanced P300 amplitudes triggered by startle stimuli during the processing of neutral compared to arousing stimuli. Considering the processing of the pictures and probe stimuli as a dual task con-

dition, Schupp et al. argued that the direction of attention to a primary task in the visual modality in general causes attenuation of P300 amplitudes triggered by probe stimuli (Donchin, Kramer, & Wickins, 1986).

The only significant difference in P260 amplitudes was between the positive and the neutral picture condition. Thus, an alternative interpretation of the results would be that the amplitudes of the P260 are smaller for stimuli during positive pictures compared to neutral pictures and that there is no difference between P260 amplitudes for stimuli elicited during neutral and negative picture processing. This interpretation would be in line with previous studies that found that the affective modulation of pain perception was mainly due to differences between positive and neutral pictures, whereas differences between negative and neutral pictures were less pronounced (de Wied & Verbaten, 2001; Weisenberg, Raz, & Hener, 1998; Zelman et al. 1991). However, the polynomial ANOVA revealed no significant linear trend but a marginally significant quadratic picture category effect ($p < .082$) and, in addition, the visual inspection of the characteristics of the SEPs suggests that SEPs elicited during negative picture processing resemble those evoked during positive picture processing and not those evoked during neutral picture processing. Therefore, the amplitudes of the P260 may be modulated by the arousal of the affective pictures.

The P260 component measured in this experiment strongly resembles the P300 measured by Schupp et al. (1997). Both components were relatively late positive ERP components elicited by aversive stimuli and showed a comparable modulation by the affective foreground. But, in contrast to the typical cognitive P300 with a maximum at Pz and a peak latency between 300 and 600 ms (Verleger, 1997), our P260 was more prominent at Cz than at Pz and had a peak latency around 265 ms, which is typical for a late positive component of somatosensory evoked potentials (Bromm & Lorenz, 1998).

The arousal modulation of the P260 seems to reflect allocation of attention to arousing stimuli. This line of argument is supported by the fact that we found a P260 modulation for both painful and nonpainful stimuli in the present study, and attention allocation to pictures should be independent of the quality of the probe stimuli. In addition, the overall reduced P260 amplitudes during the picture processing period compared to the postpicture processing period and the pause interval suggest an overall stronger allocation of attention to pictures in the picture processing period. Therefore, the attentional modulation effects should be more likely to be detected during the picture processing period, and this was actually the case.

For both the N150 and the P260 components, no Electrode Location $\times$ Picture Content interaction was found. This means that the data of this study may not help to determine which brain areas are involved in the affective modulation of the SEP components. As mentioned above, dipole analyses of the pain-evoked potential revealed generators in the prefrontal cortex and in the anterior cingulate cortex (Bromm & Lorenz, 1998; Dowman, 2004). Interestingly, Rainville, Duncan, Price, Carrier, and Bushnell (1997) found a pain-related activity in the anterior cingulate cortex that was specifically modulated by changes in pain unpleasantness in their positron emission tomography study, suggesting that the anterior cingulate cortex might be an important site for the affective modulation of pain. Royet et al. (2002) found that the prefrontal cortex is activated by stimuli with either positive or negative hedonic value, and Coghill, Sang, Maisog, and Iadarola (1999) found that this same area is also activated by painful thermal stimuli.

In conclusion, the valence of affective foreground stimuli did affect pain ratings. In addition, the N150 and the P260 components of the ERPs elicited by painful and nonpainful stimuli were differently modulated by an affective foreground. Whereas the arousal modulation of the P260 seems to reflect a non-pain-specific enhanced allocation of attention to arousing stimuli, the N150 amplitude was the only component that was linearly modulated by the valence dimension, and this effect appeared to be pain specific. These findings are in accordance with the emotional priming hypothesis that, on the basis of the present findings, was confirmed for the processing of pain stimuli.

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