

# Role of induced negative and positive emotions in sensitivity to itch and pain in women

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## Summary

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**Background** Itch and pain are common symptoms in skin disease. It has been suggested that negative emotions may play a role in itch and pain. To date, however, the role of emotions has only been studied for pain in experimental studies, not yet for itch.

**Objectives** To investigate the effects of negative and positive emotions on the sensitivity to itch and pain.

**Methods** Film fragments were used to induce a negative or positive emotional state in healthy women. Itch and pain were induced using the following somatosensory stimuli: electrical stimulation, histamine iontophoresis and the cold pressor test.

**Results** Results showed that the scores for itch and pain evoked by histamine and the cold pressor test, respectively, were significantly higher in the negative than in the positive emotion condition, whereas tolerance thresholds to electrical stimulation and the cold pressor test, and stimulus unpleasantness scores did not differ between the two conditions.

**Conclusions** These findings for the first time indicate in an experimental design that emotions play a role in sensitivity to somatosensory sensations of both itch and pain.

Itch is a common symptom in patients with skin disease. Approximately 50% of patients with a skin disease suffer from itch on a chronic basis.<sup>1</sup> The sensation of itch is part of the body's defence system and acts as a warning signal for potential threat to the skin. It is well known that itch has many similarities to pain.<sup>2,3</sup> Both sensations are part of the somatosensory system, informing one about objects in the external environment. Moreover, itch and pain are also nociceptive sensations, which implies that they are part of the body's defence system, warning of potential threat or ongoing harm, such as harmful movements or invaders of the skin. Next to the sensory-discriminative aspects of itch and pain, it is known that both also encompass affective-motivational components.<sup>4,5</sup> However, in contrast to pain, the role of emotions in itch has not been investigated systematically. It is assumed that there is a reciprocal relationship between pain and mood.<sup>6</sup> For example, depressive symptoms are more common in patients with chronic pain than in healthy subjects,<sup>6,7</sup> and pain-free subjects with depressive symptomatology are, on average, two times more likely to develop chronic musculo-

skeletal pain than pain-free subjects without depressive symptoms.<sup>8,9</sup> Moreover, negative and positive emotions induced by mood induction procedures have been shown to influence the experience of pain differently. Negative emotions are associated with increased pain perception, whereas positive emotions are associated with reduced pain perception in healthy subjects and patients with chronic pain.<sup>10-15</sup> Next to pain intensity, unpleasantness, also called affective pain, seems to be influenced by the valence of the emotional state. Thus, unpleasant emotions are associated with a higher unpleasantness to somatosensory stimuli than are pleasant emotions.<sup>12,16-18</sup> Furthermore, tolerance to stimuli may be influenced by emotions, as some studies have shown that negative emotions are associated with a lower tolerance than are positive emotions,<sup>19,20</sup> although others have not consistently found such an effect.<sup>10,21</sup> Regarding itch, there is some evidence that negative emotions are correlated with higher levels of itch symptoms in patients with chronic skin disease.<sup>22-24</sup> In addition, there are indications that experimentally induced stress can heighten the levels of itch felt by healthy subjects.<sup>25,26</sup>

Although it seems likely that emotions play a role in the perception of itch, experimental studies investigating the role of negative and positive emotions in itch are lacking. The aim of the present study was to investigate for the first time whether negative and positive emotions influence both itch and pain sensations. The subjects' emotions were manipulated by using film fragments, one of the most effective and standardized methods for inducing both negative and positive emotions.<sup>27</sup> Different quantitative sensory testing stimuli, mechanical, electrical and histamine, were applied to induce itch and pain sensations. Individual psychological characteristics, such as anxiety sensitivity, alexithymia and neuroticism, were assessed because these variables may influence the emotion induction procedure or the experience of physical sensations such as pain.<sup>28,29</sup> We expected that the levels of itch and pain evoked by the stimuli and the perceived unpleasantness would be higher when negative emotions were induced than when positive emotions were induced. The difference in tolerance thresholds between the negative and positive emotion conditions was explored.

## Materials and methods

### Participants

Seventy-seven participants were recruited via the human subject pool management system of the university (Sona Systems, Tallinn, Estonia) and via advertisements distributed on the campus of the Radboud University Nijmegen, the Netherlands. Fifty-nine healthy female subjects aged 18 years and older (mean age 21.4, SD 2.4) participated in the study. The subjects were Dutch (85%) or German (15%) and all could speak and write Dutch fluently; 56% of the subjects had a partner (14% were married or living with their partner) and 71% used oral contraceptives. On arrival at the test facility, the subjects were asked to indicate their current levels of itch and pain on a visual analogue scale (VAS) ranging from 0 (no itch/pain at all) to 10 (worst itch/pain imaginable). Mean levels of itch and pain on the day of testing were 0.2 (SD 0.6) and 0.3 (SD 1.0), respectively. There were no significant differences between the two experimental conditions (see Emotion induction) with regard to age, body mass index, educational level, use of oral contraceptives, and current itch and pain on the day of testing.

Prior to testing, subjects were screened by means of questionnaires (see Self-report questionnaires) and a standardized interview regarding traumatic life events, which was based on

the items of the Negative Life Events and Trauma Questionnaire.<sup>30</sup> Exclusion criteria were severe morbidity (e.g. multiple sclerosis, diabetes mellitus, heart or lung diseases, skin disease), psychiatric disorders (e.g. depression, anxiety), use of a pacemaker, and chronic itch or pain complaints either currently or in the past. Four subjects were excluded from participation because they used medication [antidepressants ( $n = 2$ ), antiviral drugs ( $n = 1$ ) or medication for treatment of attention deficit disorder ( $n = 1$ )], four subjects were excluded because of chronic itch or pain complaints, and 10 subjects were excluded because of direct or indirect experience with emotional, sexual or physical violence.

### General procedure

The study protocol was approved by the regional medical ethics committee of Arnhem/Nijmegen. Self-report questionnaires were sent to the participants in the week preceding the experiment. On arrival at the test facility, participants were informed about the study and all gave their informed consent prior to investigation. Participants had earlier been asked not to drink black tea or coffee 1 h before testing. Subjects who satisfied the inclusion criteria were randomly assigned to one of the two experimental conditions: the positive emotion condition ( $n = 30$ ) or the negative emotion condition ( $n = 29$ ).

A flow diagram of the experiment is given in Figure 1. Positive and negative emotions were induced by showing the subjects either positive or negative film fragments. After each film fragment, subjects reported their experience of positive and negative emotions. For the somatosensory stimuli (electrical stimulation, histamine iontophoresis and the cold pressor test), subjects were asked to rate the perceived levels of itch, pain and unpleasantness on a VAS ranging from 0 (no itch/pain) to 10 (the worst itch/pain imaginable). Stimuli were administered by two female investigators. Lastly, subjects were debriefed about the goal of the experiment and encouraged to contact the experimenter after the experiment if they felt any distress after the experiment. None of the subjects contacted the experimenter afterwards.

After the subjects were shown a neutral film fragment (see Emotion induction), they were familiarized with the stimuli in a pretest trial with the electrical stimulation. After a 5-min interval, emotions were induced using the first condition-specific (either positive or negative) film fragment (see Emotion induction), after which the electrical tolerance threshold was measured twice. After an interval of 10 min, the second condition-specific film fragment (in the same direction as the

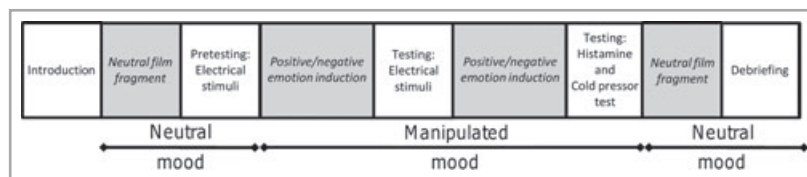


Fig 1. Flow diagram of the experiment. Order of application of the somatosensory stimuli and the film fragments.

first film fragment) was shown. Immediately thereafter, histamine was applied by iontophoresis; 5 min later the cold pressor test was administered. At the end of the experiment, the subjects looked at another neutral film fragment (see Emotion induction).

## Emotion induction

### Emotion manipulation

For the positive and negative emotion conditions, two fragments were used from commercially available feature films. Film fragments for the positive emotion condition were extracted from a humorous film (*Happy Feet*, dir. G. Miller, Warner Bros, 2006) and lasted 4:01 and 6:31 min. Film fragments for the induction of negative emotions, as also used in earlier studies,<sup>31,32</sup> contained scenes with strongly aversive content (extreme violence) and lasted 3:39 and 6:15 min (*Irreversible*, dir. G. No , 120 Films, 2002). Each film fragment was introduced by a slide, shown for 30 s, that briefly introduced the context of the film fragment and asked participants to identify as strongly as possible with the feelings and emotions of the main character in the film fragment. In this way, we attempted to involve the subjects in the film in order to evoke a maximal effect for emotion manipulation. The text was set against a background picture and with music from the respective film. All film fragments were extracted from and shown in the original language version with Dutch subtitles, using a DVD player and a 70-cm diameter TV screen.

### Neutral emotion

All subjects were shown two neutral film fragments lasting 4:04 min containing emotionally neutral nature scenes (*Romanisches Europa*, Discovery Channel HD). One fragment ('Buttes Chaumont Park in Paris') was shown at the beginning and one at the end ('Entlang der Maas') of the experiment.

### Self-reported emotions

After each film fragment, the subjects were asked to rate to what extent they experienced positive feelings (cheerful, elated, happy) and negative feelings (tense, stressed, nervous) at that moment, using a four-point Likert scale ranging from 1 (not at all) to 4 (very strong). The means of the three negative and the three positive emotions were calculated separately to obtain total scores for negative and positive emotions. In the negative emotion condition, Cronbach's alphas for the negative emotions were 0.86 and 0.91 for the first and second film fragment, respectively, and the Cronbach's alphas for the positive emotions in the positive emotion condition were 0.96 and 0.98, respectively. In addition, subjects were asked whether they had seen the film fragments before and they reported how much they had felt involved in the film fragments on a VAS ranging from 0 (not at all) to 10 (very strong). Subjects were also asked to rate both the pleasantness

and unpleasantness of the film fragments on a VAS ranging from 0 (not at all) to 10 (very strong).

## Somatosensory stimuli

After negative or positive emotions had been induced, quantitative sensory testing (QST) stimuli were applied in the following order: electrical stimulation, histamine iontophoresis and the cold pressor test. Subjects were asked to report the levels of itch and/or pain the stimuli evoked on a VAS ranging from 0 (no itch/pain at all) to 10 (the worst itch/pain imaginable) several times during the application of histamine and the cold pressor test, and once during measurements of the electrical tolerance threshold. Mean VAS itch and VAS pain scores were calculated for each stimulus separately. Level of unpleasantness was indicated by the subjects once for each stimulus on a VAS ranging from 0 to 10.

## Electrical stimulation

Cutaneous electrodes were applied to the nondominant forearm, 2 cm distal to the epicondyle of the humerus (C5 dermatome). After the neutral film fragment, and after the first condition-specific film fragment, electrical stimulation was administered using a constant current nerve stimulator (Pajunk, Geisingen, Germany). Electrical stimuli consisted of 0.3-ms pulses at a 100-Hz frequency with a continuously increasing intensity of  $\sim 0.2 \text{ mA s}^{-1}$ . Subjects were asked to report the electrical tolerance threshold, which was defined by 'the moment that the sensation becomes unbearable and you want to stop directly'. Thresholds were measured twice with a 30-s interval between measurements, and mean intensities were calculated. Levels of itch and pain were assessed before electrical stimulation (none of the subjects rated itch and pain levels higher than a score of 2.0). After the threshold measurements, subjects were asked to report, on a VAS, the severity of itch and pain elicited by the electrical stimuli and the unpleasantness of the stimuli.

## Histamine iontophoresis

Histamine was applied by iontophoresis (Chattanooga Group, Hixson, TN, U.S.A.). Histamine dihydrochloride (0.5%) was dissolved in a gel of 2% methylcellulose in distilled water and 2.5 mL was placed in an electrode (Iomed Iogel Iontophoresis Electrode medium; Chattanooga Group). This electrode was applied to the dominant forearm, 2 cm distal to the lateral epicondyle of the humerus (C5 dermatome). The reference electrode (area  $25.8 \text{ cm}^2$ ) was applied to the skin on the lateral side of the triceps brachial muscle. Current level was set at 0.4 mA and histamine was delivered for 2.5 min. Levels of itch and pain were assessed before histamine iontophoresis (100% and 98% of the subjects rated itch and pain with scores of 2.0 or lower, respectively). During histamine application, the subjects reported VAS itch scores every 30 s and afterwards scored the unpleasantness of the stimulus on a VAS.

### Cold pressor test

Levels of itch and pain were assessed before the cold pressor test (80% and 98% of the subjects rated itch and pain with scores of 2.0 or lower, respectively). Subjects were instructed to place their dominant hand in a tank of cold water (mean temperature 3.9 °C; SD 0.4) 'for as long as possible' until the moment they could no longer tolerate it. Participants were unaware of the upper time limit of 3 min. The immersion time was recorded, and subjects were asked about the pain they experienced on a VAS every 10 s during the first 30 s and subsequently every 30 s. The participants scored the unpleasantness of the stimulus at the moment they withdrew their hand.

### Self-report questionnaires

The self-report questionnaires used have previously been shown to have satisfactory reliability and validity. Questionnaires were sent to the participants 1 week before the experiment. The Hospital Anxiety and Depression Scale (HADS)<sup>33</sup> was used to screen for anxiety and depression. The HADS consists of two subscales: a seven-item depression subscale (Cronbach's alpha in the present study was 0.70) and a seven-item anxiety subscale (Cronbach's alpha = 0.76) (total alpha = 0.84). Items were scored on a four-point scale ranging from 0 to 3. The Anxiety Sensitivity Index (ASI) was used to measure the subjects' fear of potential negative consequences of anxiety-related symptoms and sensations.<sup>34</sup> The ASI consists of 16 items, rated on a five-point Likert scale (1 = very little, 2 = little, 3 = some, 4 = much, 5 = very much). The total score was obtained by summing the scores for the 16 items (range 0–64): Cronbach's alpha was 0.79 in this study. Negative affectivity was measured with the neuroticism subscale of the Eysenck Personality Questionnaire. Cronbach's alpha in this study was 0.87. The Bermond–Vorst Alexithymia Questionnaire was used to measure the degree to which a person is able or inclined to describe or communicate his or her emotional reactions, to define his or her arousal states, and the degree to which someone can be emotionally aroused by emotion-inducing events.<sup>35</sup> The 40 items were rated on a five-point Likert scale ranging from 1 (this definitely applies to me) to 5 (this in no way applies to me) and the total score was obtained by summing all 40 items: Cronbach's alpha was 0.90 in this study.

### Statistics

All analyses were performed using SPSS 16.0 for Windows (SPSS, Chicago, IL, U.S.A.). Variables were checked for normal distribution. Subjects were excluded from analyses if they had a minimum mean score for the intended emotions, i.e. positive emotions for the positive emotion condition and negative emotions for the negative emotion condition, which was 1.0 (minimum level) for one or both of the condition-specific film fragments. As a manipulation check for the emotion induction

procedure, repeated measures analysis of variance (ANOVA) was conducted for the two experimental conditions separately with, as within-subject variables, the mean score for the negative or positive emotions during the neutral film fragment and during the first or second condition-specific film fragment.

Hypotheses were tested by using multivariate analyses of variance (MANOVA) with the condition (negative and positive emotion condition) as the independent variable, and VAS pain (electrical stimulation and cold pressor test), VAS itch (electrical stimulation and histamine) and VAS unpleasantness (electrical stimulation, histamine and cold pressor test) for the different stimuli separately as dependent variables (one-tailed). Only if the MANOVA results were significantly different, or tended to be significantly different between the conditions, were post hoc ANOVAs performed to investigate the effects for each stimulus separately.

Pearson correlation coefficients were calculated between the valence scores attributed to the film fragments and the stimuli outcome measures (VAS itch, VAS pain, VAS unpleasantness, and tolerance thresholds) for the negative and positive emotion conditions separately (pleasantness for the positive emotion condition and unpleasantness for the negative emotion condition). Lastly, Pearson correlation coefficients were calculated between scores of the questionnaires measuring individual psychological characteristics (anxiety sensitivity, neuroticism and alexithymia) and the mean of the intended (negative or positive) emotions as well as the VAS scores (itch, pain and unpleasantness) and tolerance thresholds of the sensation evoked by the different stimuli for both the negative and positive emotion conditions.

## Results

### Emotion manipulation check

Three subjects in the negative emotion condition were excluded from the analyses, because their mean score for the negative emotions was 1.0, the minimum, for one or both of the condition-specific film fragments. Thirty-seven per cent of the subjects in the positive emotion condition had seen the film fragments before, while none of the subjects in the negative emotion condition had seen the fragments before, which was significantly different between groups [ $\chi^2$  (1,  $n = 56$ ) = 22.2,  $P < 0.001$ ]. Ninety per cent and 93% of the subjects in the positive emotion condition felt moderately or highly involved (i.e. VAS involvement of 5.0 or higher) with the first and second film fragments, respectively. In the negative emotion condition, 69% and 92% of the subjects felt moderately or highly involved with the first and second film fragments, respectively. Involvement with the film fragments was rated significantly higher in the positive compared with the negative emotion condition ( $F_{1,54} = 6.12$ ,  $P < 0.05$ ) for the first film fragment, but was not significantly different between the conditions for the second film fragment ( $F_{1,54} = 0.07$ ,  $P = 0.80$ ). Mean unpleasantness ratings for the film fragments in the negative emotion condition were 8.1

(SD 1.3) and 8.8 (SD 1.1), and mean pleasantness ratings for the film fragments in the positive emotion condition were 8.0 (SD 1.0) and 7.9 (SD 1.4), for the first and second film fragments, respectively.

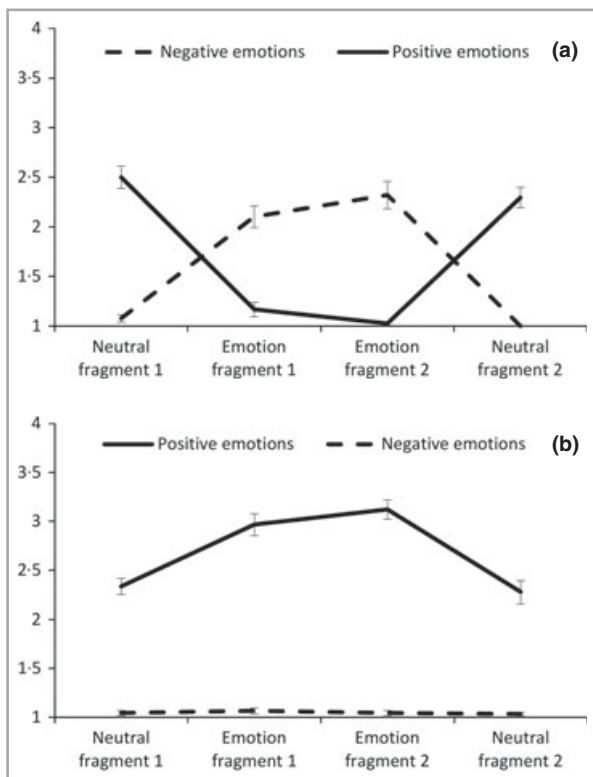
Means and SDs of the negative (tense, uptight, nervous) and positive (elated, cheerful, happy) emotions for the neutral as well as the condition-specific film fragments are shown in Figure 2a (negative emotion condition) and Figure 2b (positive emotion condition). In the negative emotion condition, negative emotions were significantly higher after the first ( $F_{1,25} = 70.05, P < 0.001$ ) and second ( $F_{1,25} = 71.17, P < 0.001$ ) film fragment than after the neutral film fragment, and positive emotions were significantly lower ( $F_{1,25} = 140.50, P < 0.001$  for the first and  $F_{1,25} = 186.10, P < 0.001$  for the second negative film fragments) in comparison with the neutral film fragment. In the positive emotion condition, positive emotions were significantly higher after the first ( $F_{1,29} = 37.08, P < 0.001$ ) and second ( $F_{1,29} = 70.66, P < 0.001$ ) film fragments than after the neutral film fragment, and negative emotions were around the minimum score during all film fragments (see Fig. 2a,b). Mean scores for the intended emo-

tions were significantly higher in the positive (mean 3.0, SD 0.6) than in the negative (mean 2.1, SD 0.6) emotion condition ( $F_{1,54} = 30.0, P < 0.001$ ).

**Sensitivity to somatosensory stimuli: visual analogue scale (VAS) scores for pain, itch and unpleasantness**

Table 1 gives the mean scores for VAS pain, VAS itch, and VAS unpleasantness for the negative and positive emotion conditions. MANOVA (one-sided) results for the level of itch evoked by the stimuli (electrical stimulation, histamine iontophoresis) showed that VAS itch scores were significantly higher in the negative emotion condition than in the positive emotion condition [Wilks' lambda ( $\Lambda$ ) = 0.90,  $F_{2,53} = 2.95, P < 0.05$ ]. Univariate tests showed that VAS itch scores were significantly higher in the negative than in the positive emotion condition for histamine iontophoresis ( $F_{1,54} = 5.95, P < 0.05$ ), while itch evoked by electrical stimulation did not differ between the experimental conditions ( $F_{1,54} = 0.09, P = 0.38$ ). MANOVA (one-sided) results for pain evoked by the stimuli (electrical stimulation and cold pressor test) showed that VAS pain scores were significantly higher in the negative condition than in the positive emotion condition ( $\Lambda = 0.90, F_{2,53} = 3.06, P < 0.05$ ). For each stimulus separately, univariate tests showed that the level of pain evoked by the cold pressor test was significantly higher in the negative emotion condition than in the positive emotion condition ( $F_{1,54} = 4.19, P < 0.05$ ), while there was no significant difference between the conditions in pain elicited by electrical stimulation ( $F_{1,54} = 0.11, P = 0.38$ ). MANOVA (one-sided) results for the VAS unpleasantness of the somatosensory stimuli showed no significant differences between the two experimental conditions ( $\Lambda = 0.92, F_{3,52} = 1.53, P = 0.11$ ).

**Table 1** Levels of itch, pain and unpleasantness evoked by the somatosensory stimuli applied after induction of negative or positive emotions



**Fig 2.** (a) Negative emotion condition. Mean ( $\pm$  SEM) self-reported negative (dashed line) and positive (solid line) emotions in the negative emotion condition after the first neutral film fragment, the two condition-specific negative film fragments and the second neutral film fragment. (b) Positive emotion condition. Mean ( $\pm$  SEM) self-reported negative (dashed line) and positive (solid line) emotions in the positive emotion condition after the first neutral film fragment, the two condition-specific positive film fragments and the second neutral film fragment.

VAS scores	Negative emotion condition (n = 26)	Positive emotion condition (n = 30)
<b>VAS pain</b>		
Electrical stimulation	3.9 (2.6)	4.2 (2.4)
Cold pressor test	5.2 (1.9)	4.1 (2.1)
<b>VAS itch</b>		
Electrical stimulation	2.8 (3.3)	2.5 (2.3)
Histamine iontophoresis	4.3 (1.7)	3.0 (2.0)
<b>VAS unpleasantness</b>		
Electrical stimulation	6.2 (2.4)	6.2 (2.3)
Histamine iontophoresis	5.5 (2.3)	4.9 (2.6)
Cold pressor test	7.5 (1.9)	6.5 (2.3)

Mean (SD) levels of itch, pain and unpleasantness evoked by the different somatosensory stimuli, indicated on a visual analogue scale (VAS) ranging from 0 to 10, in the negative and positive emotion conditions.

The mean electrical tolerance threshold intensity and mean cold pressor immersion time were 5.4 mA (SD 1.8) and 83.4 s (SD 59.3), respectively, in the negative emotion condition, and 5.7 mA (SD 3.3) and 98.5 s (SD 61.9), respectively, in the positive emotion condition. Explorative MANOVA analyses showed that tolerance thresholds did not significantly differ between emotion conditions ( $\Lambda = 0.98$ ,  $F_{2,53} = 0.43$ ,  $P = 0.66$ ).

### Correlations of induced emotions

The measures of sensitivity (VAS itch, VAS pain, VAS unpleasantness, and tolerance thresholds) were not significantly correlated with the pleasantness ratings of the film fragments in the positive emotion condition. In the negative emotion condition, (borderline) significant correlations were found between a higher unpleasantness rating of the film fragments and lower electrical ( $r = -0.38$ ,  $P = 0.05$ ) and cold pressor ( $r = -0.47$ ,  $P < 0.05$ ) tolerance thresholds, and higher VAS unpleasantness scores for electrical stimulation ( $r = 0.38$ ,  $P = 0.05$ ) and higher VAS pain scores during the cold pressor test ( $r = 0.37$ ,  $P = 0.06$ ). The individual psychological characteristics of neuroticism, anxiety sensitivity and alexithymia were not significantly correlated with the self-reported negative and positive emotions or the tolerance thresholds or VAS itch, VAS pain and VAS unpleasantness, except for significant correlations between a higher anxiety sensitivity and higher scores on the negative emotions for film fragments 1 ( $r = 0.46$ ,  $P < 0.05$ ) and 2 ( $r = 0.48$ ,  $P < 0.05$ ), between higher levels of anxiety sensitivity and higher VAS pain scores during the cold pressor test ( $r = 0.43$ ,  $P < 0.05$ ) in the negative emotion condition, and between higher levels of neuroticism and a lower level of electrically evoked pain ( $r = -0.46$ ,  $P < 0.05$ ) in the positive emotion condition.

### Discussion

This study showed for the first time that people experience higher levels of itch elicited by histamine when they are in a negative, rather than a positive, emotional state, and replicated previous findings that pain levels elicited by the cold pressor test are increased when a person is in a negative, rather than a positive, emotional state. In contrast, emotional state did not significantly affect the perceived unpleasantness of the somatosensory stimuli, or the tolerance thresholds for electrical and cold pressor stimulation.

Our findings that the levels of experimentally induced itch were higher when negative compared with positive emotions were induced, are consistent with the findings of preliminary studies investigating emotional stress and itch.<sup>25,26</sup> The findings for higher levels of pain evoked by the somatosensory stimuli when negative emotions, rather than positive emotions, were induced, are in line with previous findings of emotion induction in pain processing.<sup>10,12,14,16,20,21,36</sup> The effects of emotion manipulation on sensitivity to itch and pain were most pronounced for histamine iontophoresis and the cold pressor test when compared with the sensations induced

by electrical stimulation. This difference may be due to several reasons. Histamine iontophoresis and the cold pressor test induce distinct sensations of itch or pain, respectively, whereas electrical stimulation generally evokes more ambiguous sensations. Moreover, electrical stimulation was applied after the first condition-specific film fragment, whereas histamine and the cold pressor test were tested after the second film fragment. The effects of emotion manipulation may be stronger after a longer duration of exposure (i.e. after viewing of both fragments instead of only the first fragment), and the physiological reactions attributed to emotion manipulation may be delayed.<sup>10,37,38</sup>

The individual psychological characteristics anxiety sensitivity, alexithymia and neuroticism were not related to the self-reported negative and positive emotions or the outcome measures of the sensory stimuli and therefore did not influence our main results, indicating that these variables do not, or only minimally, contribute to the effects of emotions on sensitivity to itch and pain. This may be related to the study sample which consisted of healthy subjects with generally low scores for these individual characteristics, or to the fact that these characteristics are not of direct relevance to pain or itch sensitivity. Future studies might address the relevance of other psychological concepts, such as pain- or itch-related fear, as possible essential components in the worsening of chronic pain<sup>39</sup> or itch.

The question remains as to which mechanisms underlie the effect of emotions on itch and pain sensations. Emotions are processed by deactivation or activation of various brain regions, e.g. the anterior cingulate cortex (ACC), posterior cingulate cortex, (dorsolateral) prefrontal cortex and insula, areas which are also activated during (the anticipation of) pain and itch sensations.<sup>2,40–45</sup> That these brain areas are common to both emotions and to pain and itch could support there being a close link between affective states and these somatosensory sensations. In addition, emotional stimuli could either lead to analgesia, e.g. by external, attention-demanding stressors, or to hyperalgesia, e.g. due to anticipatory anxiety about pain.<sup>41</sup> Descending endogenous modulation processes of itch and pain, for example through conditioned modulation,<sup>4,46</sup> may play a role in the modulatory effects of cognitive and affective factors on these sensations. This is supported by earlier studies indicating that cognitive expectations regarding pain and pain catastrophizing can influence pain perception by these modulatory mechanisms.<sup>47,48</sup> Moreover, the effects of expectations on pain in placebo analgesia are also influenced by the affective quality of the pain sensation and by the internal affective state of the individual during the pain.<sup>49</sup> In addition, cholecystokinin, one of the key mediators in nociceptive hyperalgesia, is involved in both anxiety and pain modulation,<sup>50</sup> while brain areas involved in pain expectations, e.g. rostral ACC, thalamus and insula, are in part similar to those involved in emotions.<sup>41,51</sup> Future research should focus on disentangling the processes by which affective and cognitive factors interactively and differentially affect the modulatory processing and perception of itch and pain.

There are some limitations of the study that need to be addressed. Firstly, while the film fragments were effective in producing the intended emotions, as shown by the self-reported negative and positive emotions, the duration of the emotion induction procedure or the time in between this procedure and application of the sensory stimuli may not have been long enough to bring about physiological effects,<sup>10,37</sup> which could explain the lack of emotion-induced differences in itch and pain evoked by the electrical stimulation, the first stimulus applied. In future research, longer film fragments could be used or the time in between emotion manipulation and sensitivity measurements should be longer to evoke larger effects. Secondly, we cannot exclude that interaction effects between stimuli may have influenced the results. For example, some subjects still felt histamine-induced itch when the cold pressor test was applied. However, because pain can inhibit itch, residual itch is not expected to influence the levels of pain induced by the cold pressor test. In addition, although the interaction between stimuli was minimized by applying them in an order in which the least aversive stimulus of the shortest duration (electrical stimulation) was applied first and the stimulus with the longest sensation duration and associated with the largest autonomic responses (the cold pressor test) was applied last, the fixed stimulus order could have had an order effect. Thirdly, although emotions differed significantly across conditions, positive emotions were slightly higher than negative emotions for the respective emotion induction. This may also be a result of the neutral film fragment which may have had an elative effect on the emotional state in both conditions. Future research should also include an experimental condition without a neutral film fragment. Fourthly, we only included women in the present study. As earlier research has indicated that women and men differ in their perception and reaction to emotional stimuli<sup>27</sup> and in their sensitivity to sensory stimuli,<sup>52</sup> future research should also include men.

This study has several implications for clinical practice. Because negative emotions can contribute to the aggravation of patients' symptoms of itch and pain and, consequently, to their quality of life, health professionals may also attend to the presence of psychological distress in these patients. It is important to monitor patients for heightened levels of negative emotions. Patients with both high levels of negative emotions and high levels of physical symptoms of itch and pain may benefit from psychological treatments<sup>53,54</sup> such as cognitive behavioural therapy, and relaxation and stress-management training.

To conclude, the present study indicates for the first time within an experimental design that emotions not only influence the experience of somatosensory sensations of pain, but also of itch. The induction of negative emotions in comparison to positive emotions is associated with higher levels of itch and pain elicited by specific itch and pain stimuli, respectively. Future research should investigate whether emotions might, like the perception of itch and pain in healthy subjects, influence the symptoms of patients with chronic itch and

pain, and especially in patients who are distressed. Negative emotions can aggravate symptoms of itch and pain, and these symptoms may, in turn, also influence the emotional state, which may ultimately lead to a vicious cycle of symptom exacerbation. Psychological treatments could be increasingly aimed at disrupting this cycle of itch and pain amplification by negative emotions, and especially in patients with high levels of psychological distress (e.g. depressive symptoms or anxiety).

### What's already known about this topic?

- Skin diseases are often associated with symptoms of itch and pain.
- It is well known that negative emotions can result in an increase in pain.
- There is preliminary evidence for an association between emotions and itch, but the direct influence of negative emotions on itch has not been experimentally investigated.

### What does this study add?

- This study demonstrates that negative emotions can lead to higher levels of itch and pain.
- As symptoms of itch and pain may be associated with more negative emotions, we speculate that, in patients with chronic itch or pain, negative emotions may be part of a vicious cycle of symptom worsening.

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