

# Threatening social context facilitates pain-related fear learning

Citation for published version (APA):

Karos, K., Meulders, A., & Vlaeyen, J. W. S. (2015). Threatening social context facilitates pain-related fear learning. *The Journal of Pain*, 16(3), 214-225. <https://doi.org/10.1016/j.jpain.2014.11.014>

## Document status and date:

Published: 01/01/2015

## DOI:

[10.1016/j.jpain.2014.11.014](https://doi.org/10.1016/j.jpain.2014.11.014)

## Document Version:

Publisher's PDF, also known as Version of record

## Document license:

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## Threatening Social Context Facilitates Pain-Related Fear Learning

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**Abstract:** This study investigated the effects of a threatening and a safe social context on learning pain-related fear, a key factor in the development and maintenance of chronic pain. We measured self-reported pain intensity, pain expectancy, pain-related fear (verbal ratings and eyeblink startle responses), and behavioral measures of avoidance (movement-onset latency and duration) using an established differential voluntary movement fear conditioning paradigm. Participants (N = 42) performed different movements with a joystick: during fear acquisition, movement in one direction (CS+) was followed by a painful stimulus (pain-US) whereas movement in another direction (CS-) was not. For participants in the *threat* group, an angry face was continuously presented in the background during the task, whereas in the *safe* group, a happy face was presented. During the extinction phase the pain-US was omitted. As compared to the safe social context, a threatening social context led to increased contextual fear and facilitated differentiation between CS+ and CS- movements regarding self-reported pain expectancy, fear of pain, eyeblink startle responses, and movement-onset latency. In contrast, self-reported pain intensity was not affected by social context. These data support the modulation of pain-related fear by social context.

**Perspective:** A threatening social context leads to stronger acquisition of (pain-related) fear and simultaneous contextual fear but does not affect pain intensity ratings. This knowledge may aid in the prevention of chronic pain and anxiety disorders and shows that social context might modulate pain-related fear without immediately affecting pain intensity itself.

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**Key words:** Social context, fear conditioning, pain-related fear, contextual fear, social threat, preparedness.

The importance of pain-related fear in the development and maintenance of chronic pain, originally suggested by fear-avoidance models,<sup>55</sup> has been supported by an increasing number of studies and also

has made pain-related fear a primary target in current treatments.<sup>11,12,24,58</sup> For instance, there is experimental evidence that fear of pain is related to increased pain intensity,<sup>14,15</sup> pain-related disability,<sup>49</sup> defensive reactivity,<sup>8</sup> and behavioral avoidance.<sup>50,54</sup> However, little is known about factors facilitating the development of sustained maladaptive fear of pain, making the prevention of chronic pain challenging.<sup>28</sup>

One relatively novel approach that may shed light on this process is the study of pain in relation to contextual factors.<sup>11,56</sup> For example, there is accumulating evidence in clinical and nonclinical pain research that social context modulates the appraisal, interpretation, and experience of pain and would therefore be a feasible target for intervention.<sup>23</sup> Yet, to our knowledge, the effects of social context modulation on pain-related fear have not been investigated.

Previous research suggests that a threatening social environment is associated with higher levels of acute and chronic pain,<sup>17,37,47</sup> possibly because a threatening context increases anxiety, which in turn has been

Received September 10, 2014; Revised November 17, 2014; Accepted November 22, 2014.

This study has been presented in poster format at the annual Convention for Psychological Science (APS) in San Francisco in 2014.

Development of the MacBrain Face Stimulus Set (Fig 1) was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at [tott0006@tc.umn.edu](mailto:tott0006@tc.umn.edu) for more information concerning the stimulus set.

This study was supported by the Odysseus Grant 'The Psychology of Pain and Disability Research Program' funded by the Research Foundation Flanders (FWO Vlaanderen), Belgium, granted to J.W.S.V. (grant ID = G090208N), and an EFIC-Grünenthal Research Grant (E-G-G ID: 169518451) to A.M. In addition, A.M. is a postdoctoral researcher in FWO Vlaanderen, Flanders, Belgium (grant ID = 12E3714 N).

The authors report no conflicts of interest.

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1526-5900/\$36.00

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<http://dx.doi.org/10.1016/j.jpain.2014.11.014>

shown to increase pain intensity.<sup>27,33,40</sup> The recognition of (social) threat is of paramount importance for a species' survival, facilitating a rapid detection and appraisal of the significance of the threatening stimulus.<sup>18</sup> Therefore, it seems reasonable that the context in which fear learning occurs can modulate learning. A context signaling a threat to survival (eg, social threat) could "prepare" the individual and facilitate fear learning in the interest of promoting effective escape and avoidance of danger.<sup>43</sup> A similar phenomenon in learning theory has been termed "selective associations": Humans show superior fear conditioning with "fear-relevant" stimuli (eg, picture of a snake) and aversive outcomes (eg, a shock) than with fear-irrelevant stimuli (eg, picture of a flower).<sup>36</sup> Similarly, a fear-relevant context could promote faster or stronger acquisition of the conditioned response and/or enhanced resistance to extinction.<sup>35</sup> Consequently, social threat might facilitate the acquisition and impede the extinction of pain-related fear.

Lastly, a threatening context has been shown to lead to contextual fear, which is characterized by a chronic anticipation of threat.<sup>26,31</sup> This was shown in the case of unpredictable pain stimuli, which render the context unsafe and lead to elevated startle responses during the interstimulus interval (ITI).<sup>21</sup> Along the same lines, a threatening social context could also render the context unsafe and lead to contextual fear, which would parallel findings in individuals with social anxiety.<sup>10</sup>

The present study investigated the effects of social context on the acquisition and extinction of pain-related fear as measured by self-report, behavioral avoidance tendencies (reaction times), and psychophysiological reactivity (fear-potentiated startle responses). We hypothesized that a threatening social context facilitates fear learning. Specifically, we predicted for the threatening social context 1) enhanced (ie, faster or stronger) cued pain-related fear acquisition, 2) slowed down extinction of pain-related fear, 3) increased pain intensity ratings, and 4) increased contextual fear (ie, elevated startle responses during the ITI) compared with the safe social context.

## Methods

### Participants

Forty-two healthy individuals (12 males; mean age  $\pm$  standard deviation [SD] = 21  $\pm$  .3 years, range = 17–29) volunteered to participate in the present study. The exclusion criteria were pregnancy; current or history of cardiovascular disease; chronic or acute respiratory disease (eg, asthma, bronchitis); neurologic diseases (eg, epilepsy); any current or past psychiatric disorders; acute and chronic pain; hearing problems; cardiac pacemaker or the presence of any other electronic medical devices; impaired vision that is not corrected for; or use of anxiolytics or antidepressants. Participants were recruited and compensated in 2 ways. First-year psychology students participated in return for course credits ( $n = 5$ , 11.9%), and volunteers recruited from the general student pop-

ulation of the KU Leuven by means of flyers were paid €12 for their participation ( $n = 37$ , 88.1%). Of the 42 participants, 38 (90.5%) were students.

### Ethical Approval

The experimental protocol was approved by the Ethical Committee of the Faculty of Psychology and Educational Sciences of the University of Leuven (Belgium) (registration number = S-55530). All participants provided informed consent prior to participation. It was emphasized that participation was completely voluntary and that participants were allowed to stop the experiment at any time without any negative consequences.

### Apparatus and Experimental Stimuli

#### Software

The entire experiment was run on a Windows XP computer (Dell Optiplex 755) with 2 GB RAM and an Intel Core 2 Duo processor at 2.33 GHz and an ATI Radeon 2400 graphics card with 256 MB of video RAM. Programming of the experiment was done in Affect (version 4.0).<sup>46</sup>

#### Stimulus Material

A joystick (Attack 3; Logitech, Newark, CA) was used to perform the different movements (to the left/right) that served as conditioned stimuli (CSs) in the present experiment. An electrocutaneous stimulus of 2-millisecond duration served as the unconditioned stimulus (pain-US) in the present experiment. The electrical stimulation was delivered by a commercial stimulator (DS7A; Digi-timer, Welwyn Garden City, England) through surface electrodes (1 cm diameter; SensorMedics Corp, Homestead, FL) filled with K-Y gel (Johnson & Johnson, New Brunswick, NJ) that were attached to the wrist of the dominant hand of the participants, with which they also controlled the joystick. To select the intensity level of the pain-US, participants were repeatedly exposed to electrocutaneous stimulation of increasing intensity. They were asked to rate each stimulus on a scale ranging from 0 (feeling nothing) to 10 (worst pain imaginable). The participant was instructed to select a stimulus intensity with a rating of about 8, which was "moderately painful and demanding some effort to tolerate" (mean self-reported stimulus intensity was 8.00, SD = .53, range = 7–9). After selecting the pain stimulus, the participant was informed that he or she would receive a stimulus of maximally this amplitude during the remainder of the experiment. They were also given the possibility to increase or decrease the selected stimulus intensity at this point (mean physical stimulus intensity was 33.79 mA, SD = 18.35, range = 7–99 mA). Social context was manipulated using facial stimuli. Four angry, open-mouthed faces (2 male/2 female) were used to create a threatening social context, whereas 4 happy, open-mouthed faces (2 male/2 female) were used to create a safe social context. Social anxiety research has shown that angry faces increase social threat in both clinical and healthy populations.<sup>5,38</sup> Facial stimuli were taken from the NimStim face stimulus set.<sup>48</sup> The NimStim set

is a collection of 672 naturally posed photographs depicting 8 different expressions: happy, sad, angry, fearful, surprised, disgusted, neutral, and calm. However, because the NimStim facial set is not yet validated in terms of threat value, we conducted a short pilot study including 35 volunteers to test the threat value of the angry facial expressions by asking for each of the 42 pictures "How threatening is this face?" (visual analog scale; 0 = not at all to 100 = very much). We selected the 2 male and 2 female facial stimuli with the highest ratings (male 1:  $M = 70.13$ ,  $SD = 5.18$ ,  $n = 30$ ; male 2:  $M = 70.87$ ,  $SD = 4.68$ ,  $n = 31$ ; female 1:  $M = 61.13$ ,  $SD = 5.28$ ,  $n = 32$ ; female 2:  $M = 61.93$ ,  $SD = 6.08$ ,  $n = 29$ ) from the total of 42 pictures.

## Experimental Setting

All participants were seated in an armchair at about .6 m distance to the computer screen. The experiment was conducted in a sound-attenuated and dimmed experimental room, adjacent to the experimenter's room. Communication was enabled through an intercom system. The experimenter was able to observe the participant via a webcam and monitor physiological responses online by means of a closed-circuit TV installation and computer monitors.

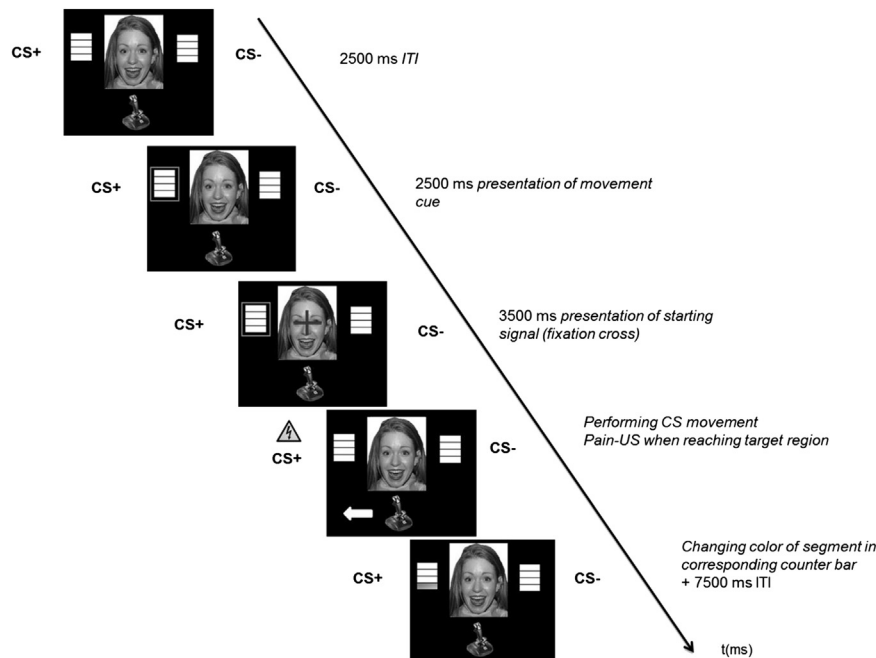
## Procedure

### Voluntary Joystick Movement (VJM) Paradigm

Recently, it has been shown that fear of movement-related pain can be acquired in healthy individuals

via associative learning pathways using a proprioceptive fear conditioning paradigm, using joystick movements as CSs and a painful electrocutaneous stimulus as pain-US.<sup>26</sup> This VJM paradigm has been shown to induce successful acquisition and extinction of cued and contextual pain-related fear in healthy individuals. Moreover, the VJM paradigm allows to measure (passive) fear-motivated behavioral pain avoidance in the form of enhanced response latency and response duration, concurrent with the self-reported fear indices.<sup>25,26,30,31</sup>

The VJM paradigm was adapted to fit the purpose of the present study. Participants were instructed to perform blocks of joystick movements (see Fig 1). A single block consisted of 8 movements that would be executed in the horizontal movement plane (4 left/4 right). All movements were executed as quickly and accurately as possible when prompted by a starting signal "+" (a fixation cross that would appear in the middle of the screen). If the participant started the movement prematurely, an error message would appear, and the cursor would be automatically returned to the center of the screen. Counter bars, which were divided into 4 equal segments, appeared on the left and right sides of the screen. Participants were instructed to move the joystick into the direction indicated by the cue (a green rectangle that appeared around the corresponding counter bar [left/right] prior to the presentation of the fixation cross). On execution of a successful movement, 1 segment of the corresponding counter bar would color blue, so that the participants could keep track of their progress within each block.



**Figure 1.** Overview of an illustrative trial timing in the safe social context. Note that the trials in the threatening social context are identical, with an angry face as stimulus instead of the happy face. The rectangular highlight around the block is used as the movement cue, indicating the direction to which the participant was requested to move. The lightning bolt represents the presentation of the painful electrocutaneous stimulus (pain-US), the central "+" represents the fixation cross serving as the starting signal, and the white arrow represents the CS movement that the participant performs on a trial. CS+ and CS-, respectively, refer to the reinforced movement, that is, left, and the unreinforced movement, that is, right. Successful completion of a movement is indicated by filling a bar on the respective location, that is, left.

## Experimental Design

The experimental session lasted for a total of 75 minutes and consisted of a calibration phase, a practice phase, a startle habituation phase, an acquisition phase, and an extinction phase (see Table 1). A mixed design was employed, implying that all participants ran through all the different phases of the experiment. Half of the participants received the safe context during acquisition and extinction, whereas the other half received the threatening context in both phases. All participants moved the joystick along a horizontal (left/right) movement plane. One movement direction (CS+) was followed by the pain-US (75% reinforcement), whereas the other direction (CS-) was never followed by the pain-US. The direction of the joystick movements that served as the CS+ and CS- was counterbalanced across participants.

### Preparation Phase

After participants arrived at the lab, they were informed about the study orally and in writing. The participants were led to believe that the study concerned the effects of different kinds of distractors (auditory, visual, and somatosensory) on movements (ie, performing the joystick task). They were informed that painful electrocutaneous stimuli (pain-USs) and loud noises (startle noise probes) would be administered during the experiment. After the participants provided informed consent, the electrodes for eyeblink startle responses and the pain-US were attached.

### Practice Phase

Before the start of the practice phase, all participants received verbal information about the joystick task. They were instructed to perform blocks of joystick movements and that 1 block consisted of 8 movements. In total, 1 block of 8 trials (4 left/4 right) was run. During the practice phase, no pain-USs or white noise probes were presented and no facial stimuli were shown in the background.

### Startle Habituation Phase

A startle habituation phase was introduced in order to get participants acquainted with the startle probes during the experiment. Moreover, this procedure prevents possible bias in the startle data because the initial probes usually lead to relatively large startle reactions. Startle

habituation was done within the safe and threatening contexts in order to evaluate baseline startle response to the 2 contexts prior to acquisition. After the lights were dimmed, a total of 4 probes per context were administered with 1 probe per trial. Each trial lasted 15 seconds (with an ITI of 5 seconds). During each trial, 1 startle probe was presented (100 dBA burst of white noise), either randomly between 2 and 7 seconds (2 trials per block) or randomly between 8 and 13 seconds (2 trials per block). During this phase, the participant was wearing headphones, no pain-USs were presented, and no joystick movements were performed.

### Acquisition Phase

The acquisition phase was identical to the practice phase with a few exceptions. First, the pain-US and the startle probes were introduced. Second, a total of 3 blocks with 8 trials were run. Following random group allocation, the acquisition phase was performed in either the safe or the threatening social context. Note that the 2 facial stimuli used for the safe and threatening social contexts were chosen randomly per participant and were kept constant throughout the remainder of the experiment. The total duration of a trial differed per participant based on their movement speed. However, the ITI consisted of a pre-CS interval of 2,500 milliseconds and a post-CS interval of 7,500 milliseconds (see Fig 1 for a trial overview). The pain-US was presented in 75% of CS+ trials, immediately after the movement, whereas it was never presented on CS- trials. A startle probe was presented in every trial. In each block of 8 trials, 4 of the startle probes occurred during the CSs (2 CS+, 2 CS-) and 4 during the ITI (2 before the CSs and 2 after). Participants were never explicitly informed about the contingencies between joystick movements, startle probes, and the pain-US. Rather, they were informed that these stimuli were auditory (startle probes), visual (facial stimuli), and somatosensory (pain-US) distractors during a motor task.

### Extinction Phase

Again, the extinction phase was identical to the acquisition phase. Three blocks of 8 trials were run; however, all trials were run and all trials were run in the acquisition context. Note that no pain-US was presented together with the CS+ movement during the extinction phase, and the timing of the startle probes again was identical to the acquisition phase.

**Table 1. Experimental Design**

GROUPS (N = 42)	PRACTICE (8 TRIALS)	HABITUATION (8 TRIALS)	ACQ1-3 (24 TRIALS)	EXT1-3 (24 TRIALS)
Threat (n = 21)	4 × CS+	[4 Probes] <sup>Threat</sup>	3 × $\begin{bmatrix} 4 \times CS+ \\ 4 \times CS- \end{bmatrix}^{\text{Threat}}$	3 × $\begin{bmatrix} 4 \times CS+ \\ 4 \times CS- \end{bmatrix}^{\text{Threat}}$
Safe (n = 21)	4 × CS-	[4 Probes] <sup>Safe</sup>	3 × $\begin{bmatrix} 4 \times CS+ \\ 4 \times CS- \end{bmatrix}^{\text{Safe}}$	3 × $\begin{bmatrix} 4 \times CS+ \\ 4 \times CS- \end{bmatrix}^{\text{Safe}}$

NOTE. CS+ and CS-, respectively, refer to the movement that is followed by the pain-US during the acquisition phase (75% reinforcement), and the movement that is never followed by the pain-US. No pain-US is presented in the extinction phase. Threat and Safe, respectively, refer to the threatening social context (angry facial stimuli), and the safe social context (happy facial stimuli).

## Outcome Measures

### Eyeblink Startle Modulation

The human startle reflex was measured as a psychophysiological indicator of fear, as it is modulated by emotional experiences and particularly potentiated by fear-evoking stimuli. Similarly, there is evidence for modulation of the human startle reflex by brain areas responsible for affective processing such as the amygdala and the affective anterior cingulate cortex.<sup>39</sup> Orbicularis oculi electromyographic (EMG) activity was recorded with 3 Ag/AgCl SensorMedics electrodes (.25 cm diameter; SensorMedics Corp) filled with electrolyte gel. Using an exfoliating cream, we scrubbed the participants' skin to reduce interelectrode resistance. Subsequently electrodes were placed on the left side of the face according to the site specifications proposed by Blumenthal et al.<sup>2</sup> The raw signal was amplified by an isolated bioamplifier with bandpass filter (LabLinc v75-04; Coulbourn Instruments LLC, Whitehall, PA). The recording bandwidth of the EMG signal was between 90 Hz and 1 kHz ( $\pm 3$  dB). The signal was rectified on-line and smoothed by a Coulbourn multifunction integrator (LabLinc v76-23 A) with a time constant of 20 milliseconds. The EMG signal was digitized at 1,000 Hz from 200 milliseconds before the onset of the auditory startle probe until 1,000 milliseconds after probe onset. The startle probe itself was a 100 dBA burst of white noise with instantaneous rise time presented binaurally for 50 milliseconds through stereo headphones (Sennheiser, Old Lyme, CT).

### Reaction Time Measures

#### Movement-Onset Latency

Movement-onset latency was defined as the time from the moment the starting signal ("+" = red fixation cross) appeared on the screen until the participants left the start region. The start region was operationalized as an invisible and small circle around the fixation cross in the center of the screen. Coordinates (in centimeters) for this start region were calculated for a 17-inch computer screen:  $x = 15.8$ ,  $y = 12.5$ , and the radius of this circle,  $r = .4$ .

#### Response Duration

Similarly, the duration of the response was measured as the time from leaving the start region until the participant successfully completed the movement (eg, reaching the target region) to the left or right. The target regions were operationalized by a larger (invisible) circle around the middle of the screen, keeping the distance to each of the 2 target regions constant. Completing a movement (ie, reaching the target region) was operationalized by moving the invisible cursor beyond this larger circle. Coordinates (in centimeters) for this large circle were calculated for a 17-inch computer screen:  $x = 15.8$ ,  $y = 12.5$ , and the radius of this circle,  $r = 13.6$ . In line with earlier research, movement-onset latency was conceptualized as an indicator of avoidance ten-

dencies, whereas the response duration served as a proximal measure of avoidance.<sup>26,32</sup>

### Verbal Ratings

#### Anticipatory Fear of Movement-Related Pain and US Expectancy

In order to assess whether differential learning occurred and as a proxy for pain-related fear,<sup>3</sup> US-expectancy ratings were obtained. Twice per block (once per movement direction), participants indicated how much they expected the painful stimulus to occur on an 11-point Likert-type scale (range = 0–10) with anchors "not at all" to "very much." Similarly, participants were asked twice per block prior to the movement (once per movement direction) "How afraid are you to perform this movement?" rating it on an 11-point Likert-type scale ranging from 0 to 10 with the anchors "not at all" and "very afraid." Note that both expectancy and fear questions are presented at the moment that the movement direction is highlighted, so participants know which movement has to be performed next.

#### Retrospective Pain Intensity and Perceived Threat of Pain

After the end of each block in the acquisition phase, participants were asked the following questions: 1) "How painful did you find the painful stimuli in the last block?" and 2) "How threatening did you find the painful stimuli in the last block?," which they had to rate on an 11-point Likert-type scale ranging from 0 to 10. The anchors were 1) "not painful at all" and "very painful" and 2) "not threatening at all" and "very threatening."

#### Retrospective Affective Valence and Arousal of the Facial Stimuli

Participants had to rate valence and arousal of the facial stimuli using the Self-Assessment Manikin scale<sup>7</sup> consisting of 5 pictographs. Participants had to rate retrospectively how they felt when being presented with the 2 facial stimuli (after the habituation and the acquisition phase). All responses were scored from 1 ("very happy/not at all aroused") to 5 ("very unhappy/very aroused"). These measures were included as a manipulation check for the social context manipulation.

### Statistical Analyses and Data Reduction

We used PsychoPhysiological Analysis, a modular script-based computer program, to analyze fear-potentiated startle responses. The program calculated the peak amplitudes, defined as the maximum of the response curve within 21 to 175 milliseconds after the startle probe onset. All startle waveforms were also visually inspected off-line, and technical abnormalities and artifacts were eliminated with the software. Each peak amplitude was scored by subtracting its baseline score (averaged EMG level between 1 and 20 milliseconds after probe onset). Afterwards, raw scores were transformed into z-scores to account for interindividual differences in physiological reactivity. In the graphs we used t-scores,

a linear transformation of the z-scores, for easier visualization of the data. Averages were calculated per block, per group during the CS movements (CS+ and CS-) and the ITI.

For the statistical analyses of the movement-onset latency and response duration, data from the practice phase were omitted. Trials with reaction times greater than 3,000 milliseconds (for latency) and less than 300 milliseconds (for latency and duration), as well as trials with reaction times deviating more than 2.5 SDs from the participants' mean reaction time, were defined as outlier responses and excluded. The remaining data were used to calculate mean reaction times for each participant, per CS movement, and per experimental block (averaged across 4 movements). This resulted in some trials without response but never enough to discard all data from a single participant. As a result, all 42 participants were included in the statistical data analysis.

Separate mixed repeated measures analyses of variance (RM ANOVAs) were carried out to examine the acquisition and extinction effects on the different dependent measures. To test for acquisition effects, a 2 [Stimulus Type (CS+/CS-)] × 2 [Group (threat/safe)] × 3 [Block (ACQ1, ACQ2, ACQ3)] mixed RM ANOVA was run on all outcome variables except for eyeblink startle. A 2 [Group (threat/safe)] × 3 [Stimulus Type (CS+/CS-/ITI)] × 3 [Block (ACQ1, ACQ2, ACQ3)] mixed RM ANOVA was run for eyeblink startle responses. Similarly, to test for fear extinction effects, a 2 [Stimulus Type (CS+/CS-)] × 2 [Group (threat/safe)] × 4 [Block (ACQ3, EXT1, EXT2, EXT3)] mixed RM ANOVA was run, and a 2 [Group (threat/safe)] × 4 [Block (ACQ3, EXT1, EXT2, EXT3)] × 3 [Stimulus Type (CS+/CS-/ITI)] mixed RM ANOVA was run for eyeblink startle responses. Greenhouse-Geisser corrections are reported when appropriate. Uncorrected degrees of freedom and corrected *P* values are reported together with  $\epsilon$  and the effect size indication  $\eta_p^2$  for main and interaction effects and Cohen's *d* for planned comparisons.<sup>9,19,34</sup> Planned comparisons were carried out to test our a priori hypotheses. Holm-Bonferroni was used to correct for multiple testing and keep the experiment-wise  $\alpha$  at .05. All statistical analyses were run using Statistica 12 (StatSoft, Inc, Tulsa, OK).

## Results

### US Characteristics

First, there was no significant difference in chosen painful stimulus intensity ( $t[40] = -.31, P = .76$ ) ( $M_{\text{threat}} = 34.67 \text{ mA}, SD = 21.35, n = 21$ ;  $M_{\text{safe}} = 32.9 \text{ mA}, SD = 15.27, n = 21$ ) or self-reported painful stimulus intensity ratings ( $t[40] = 1.16, P = .25$ ) ( $M_{\text{threat}} = 8, SD = .45, n = 21$ ;  $M_{\text{safe}} = 8.19, SD = .6, n = 21$ ) between the safe group and the threat group.

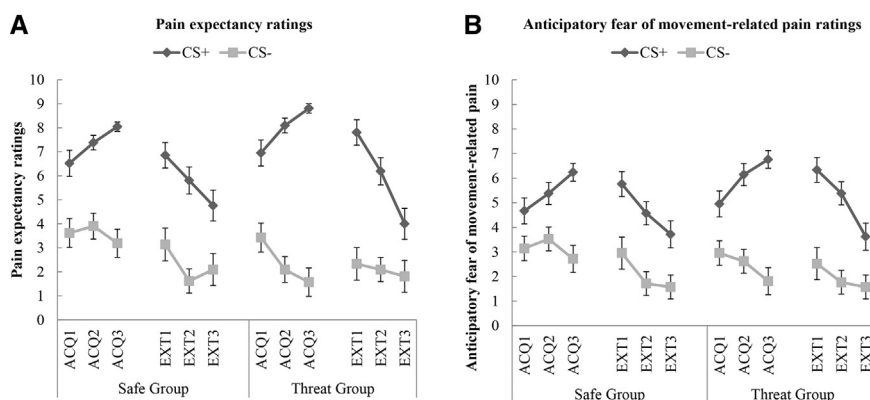
### Social Context Manipulation

As anticipated, angry faces were rated as more unpleasant ( $F[1, 40] = 30.58, P < .001, \eta_p^2 = .43$ ) and more arousing on the Self-Assessment Manikin scale ( $F[1, 40] = 20.72, P < .001, \eta_p^2 = .5$ ) than happy faces, independent of time point or group. Also, threatening faces elicited greater startle responses at baseline, prior to acquisition, as compared to the happy faces ( $t[41] = 10.26, P < .001, d = 3.20$ , confidence interval [CI] = 2.27, 4.14), indicating overall that the manipulation of social context was successful.

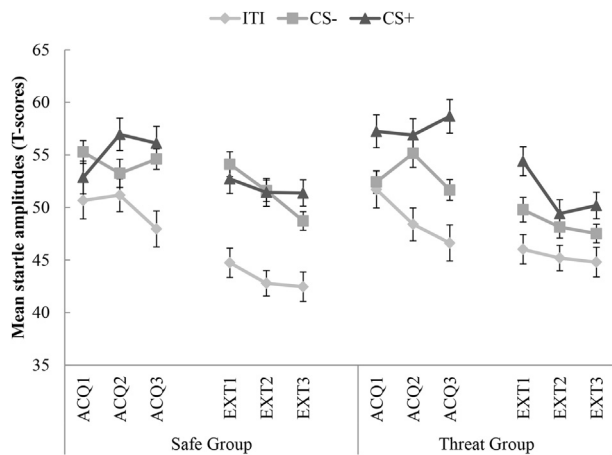
### Hypothesis 1: Enhanced Acquisition of Cued Pain-Related Fear in the Threatening Social Context

#### Anticipatory US Expectancy

The difference between the CS+ and CS- grew larger across acquisition in both groups (Stimulus Type × Block interaction;  $F[2, 80] = 13.01, P < .001, \epsilon = .87, \eta_p^2 = .25$ ), but contrary to our expectation, there were no differences between the groups (3-way interaction;  $F[2, 80] = 1.8, P = .17, \eta_p^2 = .02$ ) (see Fig 2). This analysis confirms that all participants learned that the CS+ predicted the pain-US and that the CS- did not. Testing our a priori hypotheses, planned between-groups comparisons at the end of acquisition (ACQ3) revealed that the difference between CS+ and CS- was more pronounced in the threat group than in the safety group ( $F[1, 40] = 6.87, P = .01, d = .83, CI = .18, 1.47$ ). This pattern suggests that differential expectancy learning



**Figure 2.** Mean self-reported pain expectancy ratings (A) and anticipatory fear of movement-related pain ratings (B) (+SEs) for the CS movements during acquisition (ACQ1-3) and extinction (EXT1-3) separately for the safe group and the threat group. Abbreviation: SE, standard error term based on mixed analysis estimates.



**Figure 3.** Mean eyeblink startle amplitudes (+SEs), transformed into t-scores, for the CS movements (CS+/CS-) and during ITI, during acquisition (ACQ1-3) and extinction (EXT1-3) separately for the safe group and the threat group. Abbreviation: SE, standard error term based on mixed analysis estimates.

during acquisition was stronger in the threatening social context than in the safe group.

### Anticipatory Fear of Movement-Related Pain

Anticipatory fear ratings were in line with the US expectancy ratings. Both groups acquired a differential fear response across the acquisition blocks (Stimulus Type  $\times$  Block;  $F[2, 80] = 19.95, P < .01, \epsilon = .85, \eta_p^2 = .33$ ), with increasingly higher fear ratings for the CS+ movements than the CS- movements. Again, there was no difference between the groups in the course of acquisition (3-way interaction;  $F < 1$ ) (see Fig 2), indicating that both groups successfully learned the CS-US contingencies. Testing our a priori hypotheses, we continued the analysis with planned between-group comparisons. Similar to the expectancy ratings, the difference in fear between CS+ and CS- at the end of acquisition tended to be larger in the threat group than in the safe group ( $F[1, 40] = 3.24, P = .08, d = .57, CI = -.06, 1.2$ ), although this difference did not reach statistical significance. This

finding again provides limited support for the idea that the threatening social context leads to stronger acquisition, characterized by increased differentiation between a painful (CS+) and a nonpainful (CS-) movement.

### Eyeblink Startle Modulation

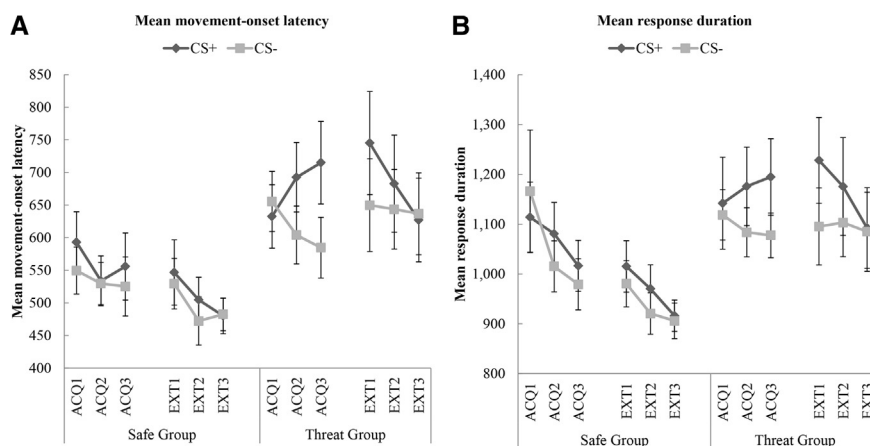
In line with our hypotheses, the course of acquisition differed between the 2 groups (3-way interaction;  $F[4, 160] = 2.53, P = .05, \epsilon = .88, \eta_p^2 = .06$ ) (see Fig 3). To test our a priori hypotheses, we conducted planned between-group comparisons at the end of acquisition. Again, differentiation between the CS+ and the CS- tended to be greater in the threat group than in the safe group, but did just fail to reach statistical significance ( $F[1, 40] = 3.8, P = .05, d = .62, CI = -.02, 1.25$ ). We further explored this finding with planned within-group comparisons, showing that by the end of acquisition (ACQ3), participants in the threat group had higher startle amplitudes to the CS+ than to the CS- ( $F[1, 40] = 12.35, P < .001, d = 1.11, CI = .45, 1.78$ ). Interestingly, this differential response was absent in the safe group ( $F = .57$ ).

### Movement-Onset Latency

Confirming our hypotheses, also movement-onset latency for the painful and nonpainful movements differed between the 2 groups across acquisition (3-way interaction;  $F[2, 80] = 5.33, P < .01, \epsilon = .88, \eta_p^2 = .12$ ) (see Fig 4). Planned within-group comparisons indicate that by the end of the acquisition, participants in the threat group were slower to initiate painful movements than the safe movements ( $F[1, 40] = 8.36, P < .01, d = .91, CI = .26, 1.57$ ), illustrating (passive) behavioral avoidance. In contrast, there was no difference between the painful and nonpainful movements, in the safe group ( $F < 1$ ). This nicely fits with the eyeblink startle findings, showing differential fear learning in the threat group but not in the safe group.

### Response Duration

Contrary to our expectations, response duration for the 2 movements did not differ between the 2 groups



**Figure 4.** Mean movement-onset latency (A) and response duration (B) (+SEs) for the CS movements (CS+/CS-), during acquisition (ACQ1-3) and extinction (EXT1-3) separately for the safe group and the threat group. Abbreviation: SE, standard error term based on mixed analysis estimates.



across acquisition blocks (3-way interaction;  $F < 1$ ) (see Fig 4). There was also no differential response between painful and nonpainful movements across acquisition (Stimulus Type  $\times$  Block;  $F[2, 80] = 1.5, P = .23, \varepsilon = .72, \eta_p^2 = .04$ ).

In summary, we found support for our hypothesis that a threatening social context leads to stronger acquisition of differential fear of movement-related pain. Specifically, anticipatory self-reports (fear and expectancy ratings), eyeblink startle amplitudes, and movement-onset latency clearly show that differentiation between the painful and the nonpainful movements is facilitated in the threatening social context compared to the safe social context.

## ***Hypothesis 2: Slowed Extinction of Pain-Related Fear in the Threatening Social Context***

### **Anticipatory US Expectancy**

In accordance with our hypotheses, we found a significant 3-way interaction ( $F[1, 40] = 3.2, P = .02, \eta_p^2 = .07$ ; see Fig 2). This interaction was driven by the aforementioned group difference in differential pain-related fear at the end of acquisition ( $F[1, 40] = 6.87, P = .01, d = .83, CI = .18, 1.47$ ). At the end of extinction, there was no difference between the groups anymore, demonstrating similar extinction curves ( $F < 1$ ). Planned within-group comparisons showed that at the end of extinction, CS+ movements still elicited higher expectancy ratings than CS- movements in the threat group ( $F[1, 40] = 8.29, P < .01, d = .91, CI = .26, 1.56$ ) and the safe group ( $F[1, 40] = 12.29, P < .01, d = 1.11, CI = .44, 1.77$ ). This shows that fear responses to the painful movements were not fully extinguished by the end of the extinction phase. There was no evidence for resistance to extinction in the threatening social context.

### **Anticipatory Fear of Movement-Related Pain**

Again, contrary to our expectation, the rate of extinction did not differ between the 2 groups (3-way interaction;  $F < 1$ ) (see Fig 2). Both groups showed equal extinction of fear responding (Stimulus Type  $\times$  Block;  $F[1, 40] = 12.75, P < .001, \eta_p^2 = .24$ ), evidenced by a significant decline in fear response toward the CS+ compared to the CS- from the end of acquisition to the end of extinction. Planned within-group comparisons showed that at the end of extinction, CS+ movements still elicited higher fear ratings than CS- movements in the threat group ( $F[1, 40] = 11.02, P < .01, d = 1.1, CI = .39, 1.71$ ) and the safe group ( $F[1, 40] = 12.07, P < .01, d = 1.1, CI = .43, 1.76$ ), again indicating that extinction was not complete at the end of extinction.

### **Eyeblink Startle Modulation**

Paralleling the other outcome measures and contrary to our expectations, the 2 groups tended to differ in their extinction pattern (3-way interaction;  $F[6, 240] = 2.06, P = .06, \eta_p^2 = .05$ ); however, this interaction was not statistically significant (see Fig 3). Overall, eyeblink startle

responses were lower at the end of extinction than at the end of acquisition, indicating startle probe habituation (main effect Block;  $F[3, 120] = 21.02, P < .0001, \eta_p^2 = .34$ ). As discussed earlier, there was no difference between CS+ and CS- at the end of acquisition ( $F = .57$ ), and consequently, CS+ and CS- fear responses declined equally during extinction ( $F < 1$ ). However, in the threat group, where differential acquisition took place ( $F[1, 40] = 12.35, P < .001, d = 1.11, CI = .45, 1.78$ ), we see a significant decline in fear for the CS+ ( $F[1, 40] = 17.51, P < .001, d = 1.32, CI = .64, 2.01$ ) but not for the CS- ( $F[1, 40] = 4.65, P = .04, d = .68, CI = .05, 1.32$ ). Note that  $P = .04$  was no longer statistically significant after Holm-Bonferroni correction ( $P > .025$ ). This demonstrates successful extinction of fear in the threat group.

### **Movement-Onset Latency**

In line with the other outcome measures, extinction learning did not differ between the groups (3-way interaction;  $F = 1.3$ ) (see Fig 4). As mentioned before, there was no difference between CS+ and CS- at the end of acquisition in the safe group ( $F < 1$ ) but only in the threat group ( $F[1, 40] = 8.36, P < .01, d = .91, CI = .26, 1.57$ ). Consequently, although we see no decline in differential responding in the safe group ( $F < 1$ ), there is a decline in differential responding in the threat group ( $F[1, 40] = 10.65, P < .01, d = 1.03, CI = .37, 1.69$ ). This finding indicates successful extinction in the threat group. By the end of extinction, there was no difference between CS+ and CS- movements anymore in the threat group ( $F < 1$ ) or the safe group ( $F < 1$ ).

### **Response Duration**

During extinction, there was also no significant 3-way interaction ( $F < 1$ ) (see Fig 4). Overall, participants became quicker in their movements (main effect Block;  $F[3, 120] = 4.1, P > .01, \eta_p^2 = .09$ ). Because there was no differential acquisition in either group, it was impossible to test for extinction.

## ***Hypothesis 3: Increased Pain Intensity in the Threatening Social Context***

### **Self-Reported Pain Intensity and Threat Ratings**

Neither social context nor block influenced pain intensity ratings (2-way interaction;  $F < 1$ ). Similarly, threat of pain ratings also did not differ between blocks or between groups (2-way interaction;  $F[4, 160] = 1, P = 1, \varepsilon = .62$ ). These findings indicate that despite a simultaneous modulation of pain-related fear, social context did not affect threat of pain or perceived pain intensity, which contradicts our hypothesis that a threatening social context leads to increased pain intensity ratings.

## ***Hypothesis 4: Increased Contextual Fear in the Threatening Social Context***

Because we did not include a self-report measure for contextual fear, the following analysis will focus on

eyeblick startle modulation and the behavioral indices (movement-onset latency and response duration).

### Eyeblink Startle Modulation

Prior to acquisition, threatening faces elicited greater startle responses at baseline (ie, habituation phase), as compared to the happy faces ( $t[41] = 10.26$ ,  $P < .001$ ,  $d = 3.20$ ,  $CI = 2.27, 4.14$ ), indicating that a threatening social context leads to elevated levels of stimulus-aspecific contextual fear compared to the safe social context. Planned between-group comparisons at the end of acquisition (ACQ3) show that there was no difference in contextual fear (startle amplitude to the ITI probes) between the 2 groups ( $F < 1$ ). Subsequently, to test our a priori hypothesis, we performed planned between-group comparisons at the end of extinction (EXT3). The probes presented during the context (ITI probes) tended to elicit higher startles amplitudes in the threat group than in the safe group ( $F[1, 40] = 3.55$ ,  $P = .07$ ,  $d = .59$ ,  $CI = -.04, 1.23$ ); however, this effect failed to reach statistical significance.

### Movement-Onset Latency

During acquisition, participants in the threat group tended to be generally slower to initiate their movements than participants in the safe group (main effect Group;  $F[1, 40] = 3.09$ ,  $P = .08$ ,  $\eta_p^2 = .07$ ), although this effect did not reach statistical significance. However, during extinction, participants in the threat group still persisted to initiate all their movements slower than participants in the safe group, which reached statistical significance ( $F[1, 40] = 5.23$ ,  $P = .03$ ,  $\eta_p^2 = .11$ ). This indicates a main effect of the social context at baseline and after extinction but not during acquisition, with participants in the threatening social context being slower than participants in the safe social context.

### Response Duration

Changes in response duration tended to differ between the 2 groups across the acquisition blocks (Block  $\times$  Group;  $F[2, 80] = 3.22$ ,  $P = .05$ ,  $\epsilon = .71$ ,  $\eta_p^2 = .07$ ) (see Fig 4), but this effect did just not reach statistical significance. To test our a priori hypothesis, we conducted planned within-group comparisons. Participants in the safe group became quicker in their movements during acquisition ( $F[1, 40] = 7.47$ ,  $P < .01$ ,  $d = .86$ ,  $CI = .21, 1.51$ ), whereas movement duration remained constantly higher ( $F < 1$ ) in the threat group. This indicates a motor training effect in the safe group but not in the threat group. One explanation might be that possible training effects are overruled or impaired by another effect of the threatening context itself. During extinction, there was also no significant 3-way interaction ( $F < 1$ ). Testing our a priori hypothesis, we performed planned between-group comparisons. During extinction, movements in the threat group were slower than in the safe group ( $F[1, 40] = 4.53$ ,  $P = .04$ ,  $\eta_p^2 = .10$ ), independent of stimulus type ( $F < 1$ ), which is in line with the movement-onset latency findings.

In sum, we found support for our hypothesis that a threatening social context leads to contextual fear at baseline. There is some evidence that the threat context also led to contextual fear during extinction and that this fear is still present even after cued pain-related fear is extinguished; however, the effect failed to reach statistical significance. Moreover, a threatening social context led to overall slower movement-onset latency and response duration, which could be a reflection of elevated contextual fear.

## Discussion

We investigated the effects of social context (threatening vs safe) manipulations on the acquisition and extinction of fear of movement-related pain, pain intensity, and behavioral avoidance tendencies. As hypothesized, the threatening social context enhanced cued pain-related fear acquisition by facilitating differential fear learning compared to the safe social context (Hypothesis 1). This was evident in all self-report measures and was especially pronounced in the eyeblink startle responses and movement-onset latency, for which in the safe group no differential learning occurred at all. Unexpectedly, we did not find evidence for resistance to extinction of pain-related fear in the threat group (Hypothesis 2). Both groups showed equal, albeit incomplete, differential extinction to the painful movement on all outcome measures. Also unexpectedly, pain intensity ratings did not increase in the threatening social context (Hypothesis 3). Self-reported pain intensity and threat of pain ratings did not differ between groups or across blocks, demonstrating that a modulation of cued fear of pain and contextual fear does not necessarily change reported pain intensity. In line with Hypothesis 4, the findings demonstrate evidence for contextual fear in the threatening social context. Eyeblink startle responses to the context (ITI) and arousal were elevated in the threat group at baseline and tended to remain elevated after extinction. Additionally, movement-onset latency and response duration were longer in the threat group than in the safe group. Strikingly, these effects persisted even after differential fear responding was extinguished, demonstrating a main effect of the threat context that is independent from the CS-US association.

The present findings fit within the framework of evolutionary preparedness,<sup>35</sup> showing that a threatening social context, but not a safe social context, “prepares” us to efficiently distinguish between safe and threatening cues, which facilitates the avoidance of danger. These findings extend earlier research that has been limited to the association between 2 fear-relevant stimuli in the context of selective associations.<sup>36</sup> A threatening social context led to stronger fear acquisition, facilitating the differentiation between a nonpainful and painful movement. This effect was particularly pronounced in the psychophysiological fear indices (ie, eyeblink startle responses) and the behavioral correlates. Although there was evidence for differential learning in both groups regarding self-reported fear ratings, this differentiation was completely absent in the safe

group concerning eyeblink startle responses. Similarly, results from the response latencies show evidence for (passive) behavioral avoidance in response to the CS+ in the threat group but not in the safe group. This finding supports earlier research on response system divergence (ie, psychophysiological, behavioral, and self-reported measures of fear).<sup>45</sup> Independent of this dissociation, we demonstrated robust facilitation of differential fear learning in the threatening social context.

Additionally, a threatening social context led to more generalized, contextual fear, which was present at baseline and persisted after extinction. Movements in the threatening social context were initiated more slowly and took longer than in the safe social context independent of movement direction. This behavioral pattern might indicate behavioral “freezing”—a common defensive response in animals in response to threat that is characterized by reduced body motion<sup>22</sup>—and has recently also been demonstrated in humans in response to social threat.<sup>41</sup> It should be noted that freezing itself might also be conditioned.<sup>44</sup> Moreover, the threatening social context elicited elevated ITI eyeblink startle responses, even before the acquisition procedure. A similar effect has been shown in response to unpredictable painful stimuli, another form of threatening context.<sup>31</sup> Importantly, these markers of contextual fear persisted after the differential fear response was extinguished, even though in the case of ITI startle responses the effect was only marginally significant. That is, the participants did not fully habituate to the threatening social context and still showed evidence for contextual fear, possibly because of the evolutionary salience of a threatening social context.<sup>29</sup> This finding is interesting for current contextual fear–conditioning theories. According to Grillon, a threatening context promotes contextual fear and the undifferentiated anticipation of danger, which in turn decreases when an organism shows adaptive cued fear learning, allowing it to effectively differentiate between safety and danger.<sup>20</sup> Support for this view comes from research into unpredictable aversive stimuli. In a predictable context, no association between the context and the US is formed because there is a better predictor for the US, the CS, limiting contextual fear and promoting adaptive cued fear learning.<sup>13</sup> In an unpredictable context, where specific threat and safety cues are absent, contextual fear develops, demonstrating the chronic anticipation of danger.<sup>26,51</sup>

In contrast, we showed that contextual fear was present in spite of and persisted beyond cued fear learning. A single study showed that unpredictability caused by exposure to unpredictable shocks (US-only) without the presentation of discrete cues (CSs) also led to persisting contextual fear. In this case, contextual fear was also still evident in a subsequent phase of the experiment, when a predictable CS–US relationship was presented.<sup>28</sup> Social threat may be another context in which contextual fear is elicited, even if predictable cued fear learning is possible. This supports the evolutionary significance of a threatening social context as an efficient cue for impending threat, activating an array of behavioral (eg, freezing, eyeblink startle modulation,

arousal), emotional, and cognitive (facilitation of differential fear learning) processes to prepare for danger, which even remains salient after the actual threat (eg, painful electrical stimulation) subsides.<sup>35</sup> This finding is clinically relevant because anxiety patients are also characterized by elevated baseline contextual fear responses and greater sensitivity to threatening contexts, making it an important marker for the development and maintenance of anxiety disorders.<sup>20</sup> By analogy, chronic exposure to a threatening social context, such as in bullying,<sup>57</sup> could facilitate the development and maintenance of anxiety disorders and pain disorders (ie, fibromyalgia), which can be highly comorbid.<sup>1</sup>

It is noteworthy that despite a direct modulation of cued and contextual fear, social context did not directly modulate pain intensity *per se*. This provides further evidence for the observation that although there seems to be a robust relationship between pain-related fear and the development and maintenance of disability,<sup>58</sup> the relationship between pain-related fear and actual pain is less clear. For example, clinical observations have shown that reductions in pain-related fear in exposure treatment are directly related to changes in pain-related disability, whereas there is only a delayed effect on pain intensity itself.<sup>52</sup> The findings of the current study pose a challenge for models positing that pain becomes chronic because of pain-related fear alone.<sup>16</sup> However, the present study cannot speak to possible delayed effects on pain intensity.

The present study was limited in the following ways. First, static rather than dynamic facial stimuli were used to manipulate the social context. Although the validity of these stimuli has been confirmed,<sup>6,41</sup> the ecological validity is limited. Nevertheless, we were able to demonstrate robust and strong effects of these stimuli on fear learning with respect to self-report, behavioral, and psychophysiological measures. Future research should replicate the current findings with active social manipulations (eg, a confederate) to increase ecological validity. Second, although earlier studies found that social threat can affect subjective pain intensity ratings,<sup>37</sup> we did not find any effect of social context on pain. One possible explanation is that a threatening social context did not affect the perceived threat of the painful stimulus. According to a cognitive appraisal model of pain, the idiosyncratic interpretation of a stimulus determines how strongly it is perceived.<sup>53</sup> In this study, the social context did not modulate the perceived threat value of pain and hence did not affect self-reported pain intensity ratings. Still, it would be insightful to measure pain sensitivity with more sensitive measures or measures that are less prone to social desirability such as the nociceptive flexion reflex.<sup>42</sup> Third, it may be noted that the joystick task was not exclusively Pavlovian. Even though the order of movements or movement direction were not under direct control of the participants (in line with Pavlovian learning principles), the movements themselves could also be framed in instrumental learning terms. However, instrumental learning is thought to involve Pavlovian learning processes as well.<sup>4</sup> These in turn could elicit Pavlovian conditioned

responses such as in the present study (ie, fear). Consequently, whether the paradigm is described in Pavlovian or instrumental terms will likely not affect the conclusions of the present study.

Despite these limitations, there are 2 important strengths of this study. First, we successfully adapted the validated voluntary joystick movement paradigm for the study of social context effects on the acquisition and extinction of pain-related fear.<sup>26,29</sup> We have demonstrated that the paradigm offers the unique possibility to independently study the effects of social context on several important constructs related to pain-related fear (self-report, psychophysiology, and behavioral avoidance). Second, to our knowledge, this is the

first study to demonstrate a modulation of differential pain-related fear conditioning by social context, justifying scientific attention to contextual factors in fear and pain research.<sup>11,56</sup> A threatening social context led to stronger acquisition of pain-related fear and elicited contextual fear, but did not affect pain intensity. Future research should extend these findings to chronic pain populations and implement ecologically valid social manipulations.

## Acknowledgments

The authors thank Jeroen Clarysse for his technical support.

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