Viewing a needle pricking a hand that you perceive as yours enhances unpleasantness of pain

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A B S T R A C T

"Don't look and it won't hurt" is commonly heard advice when receiving an injection, which implies that observing needle pricks enhances pain perception. Throughout our lives, we repeatedly learn that sharp objects cause pain when penetrating our skin, but situational expectations, like information given by the clinician prior to an injection, may also influence how viewing needle pricks affects forthcoming pain. How both previous experiences and acute situational expectations related to viewing needle pricks modulate pain perception is unknown. We presented participants with video clips of a hand perceived as their own being either pricked by a needle or touched by a Q-tip, while concurrently applying painful or nonpainful electrical stimuli. Intensity and unpleasantness ratings, as well as pupil dilation responses, were monitored. Effects of situational expectations about the strength of electrical stimuli were investigated by manipulating the contingency between clips and electrical stimuli across experimental blocks. Participants were explicitly informed about the contingency. Intensity ratings of electrical stimuli were higher when a clip was associated with expectation of painful compared to nonpainful stimuli, suggesting that situational expectations about forthcoming pain bias perceived intensity. Unpleasantness ratings and pupil dilation responses were higher when participants viewed a needle prick, compared to when they viewed a Q-tip touch, suggesting that previous experiences with viewing needle pricks primarily act upon perceived unpleasantness. Thus, remote painful experiences with viewing needle pricks, together with information given prior to an injection, differentially shape the impact of viewing a needle prick on pain perception.

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1. Introduction

Picture yourself looking at the needle of a syringe when receiving an injection. You know by experience that the needle prick will hurt. Additionally, situational aspects, such as the belief that the medical professional will prick you gently, modulate expectations about forthcoming pain. Previous studies using semantically meaningless cues showed that expectations about the strength of pain alters pain perception, rendering moderately painful stimuli more painful when strong pain is anticipated, compared to when weak pain is anticipated [1,6,15,18]. How situational expectations

concerning upcoming pain and previous experiences with viewing needles pricking one's body interact and modulate pain perception is unknown.

Pain perception essentially comprises a *sensory-discriminative* component reflecting intensity and spatiotemporal aspects, and an *affective-motivational* component relating to unpleasantness and disturbing character of pain [2,21,30]. These components are thought to be processed in partially distinct cortical networks [24,30] and can be behaviorally monitored by ratings of intensity and unpleasantness. Studies investigating the influence of viewing needle pricks on pain processing suggest that eye-witnessing injury caused by sharp objects modulates activity in cortical areas involved in the processing of both pain components. One study, in which participants watched clips of a needle pricking a hand in extrapersonal space while receiving painful stimuli at their own hand, showed modulations in regions associated with the processing of the sensory-discriminative component [33]. Another study demonstrated that threatening participants' own hands or incorporated body parts (i.e., artificial limbs perceived as one's own) with a

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needle without applying painful stimuli elicits activity in areas involved in anxiety and processing of the affective-motivational component [9]. While these studies suggest that observing needle pricks modulates activity in a widespread cortical network, they do not allow conclusions about the mutual influence of previous experiences with viewing needle pricks and acute situational expectations concerning forthcoming pain.

Here, we mimicked a naturalistic situation in which a needle pricked, or a Q-tip touched an incorporated hand. We presented clips of needle pricks and Q-tip touches and applied spatiotemporally aligned painful or nonpainful intracutaneous electrical stimuli, for which intensity and unpleasantness ratings were obtained. As an index for autonomic nervous system activity, which has been previously associated with the affective-motivational pain component [23], we recorded pupil dilation responses (PDR). Besides clips of needle pricks and Q-tip touches, a control clip of the incorporated hand alone was included. The contrast between control clip and needle and Q-tip clips reflects the impact of viewing an instrument contacting an incorporated hand on pain perception. To examine interactions between previous experiences and acute situational expectations for viewing needle pricks, we varied the contingency between needle pricks and Q-tip touches and the strength of electrical stimulation (painful, nonpainful) across experimental blocks. Prior to each block, participants were informed about the respective contingency, which elicited situational expectations regarding needles and Q-tips. We expected that viewing needle pricks compared to Q-tip touches enhances pain perception and PDR. Situational expectations were assumed to modulate the impact of viewing needle pricks on pain perception.

2. Materials and methods

2.1. Participants

Twenty-eight individuals participated in the study after voluntarily providing written informed consent. One participant was excluded from the analysis due to technical problems during PDR measurement, and 2 participants were excluded because they were outliers in pain ratings (i.e., exceeded 3 SD of group mean). The remaining 25 participants (mean age 26.8 ± 3.4 years; 13 women) were subjected to further analysis. All participants had normal or corrected-to-normal vision and reported no history of neurological or psychiatric illness and no acute pain. Participants were mainly students (n = 21) who were recruited from the participants' pool of the University Medical Center Hamburg-Eppendorf and received monetary compensation for their participation. The study was approved by the Ethics Commission of the Medical Association of Hamburg, Germany.

2.2. Stimuli

The intracutaneous model [5] was used to induce painful and nonpainful electrical stimuli. This pain model is especially suited to simulate needle pricks because painful intracutaneous electrical stimuli evoke a stabbing and sharp sensation resembling a short needle prick. Electrical stimuli (16 ms duration) were applied to the tip of participants' left index finger (Fig. 1A). Prior to each session, individual sensation and pain thresholds were determined. The sensation threshold was defined as the average intensity at which participants were able to detect a certain stimulus. The pain threshold was defined as the average intensity at which participants reported a given stimulus as painful. The thresholds were determined using 5 ascending and descending series of electrical stimuli with successive intensity increments of 0.02 mA. During the experiment, painful stimuli were presented at 2-fold pain
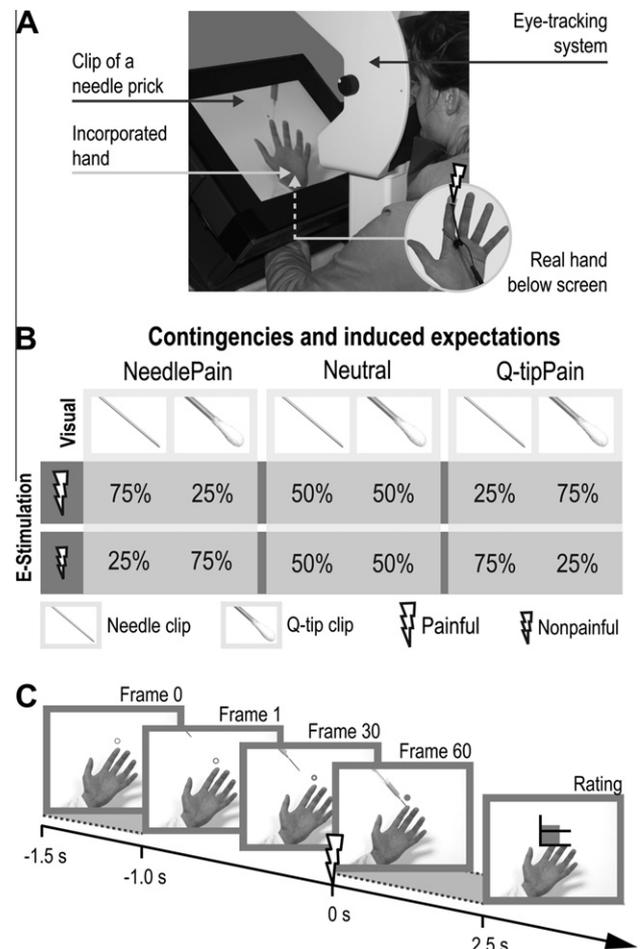
Fig. 1. Experimental setup. (A) Participants placed their left hand palm upwards on a board below the screen to get the impression that they were looking at their own hand. Pupil size was recorded during the trials and intracutaneous electrical stimuli were applied to participants' left index fingers. (B) Illustration of the different experimental conditions. Participants were explicitly informed about the contingency prior to each experimental block. (C) Illustration of a needle clip with electrical stimulation and rating. Simultaneously with the last frame in which the needle pricked the skin, participants received a painful or a nonpainful electrical stimulus (flash symbol). The last frame was maintained on the screen for 2500 ms, after which participants rated the electrical stimulus on a 2-dimensional scale (ordinate: intensity; abscissa: unpleasantness). Participants were asked to cross the horizontal line when an electric stimulus was perceived as being painful. Trial timing was the same for Q-tip and hand alone clips.

threshold (M = 0.36 mA, SD = 0.10 mA) and nonpainful stimuli at 1.5-fold sensation threshold (M = 0.14 mA, *SD* = 0.05 mA).

Visual stimuli comprised 36 naturalistic clips depicting the volar view of a left hand whose index finger was either pricked by a needle or touched by a Q-tip. Similar to previous experiments (e.g., [3,33]), both instruments were attached to a syringe (Fig. 1 and Supplementary Fig. 1). An additional clip of a hand alone served as a control condition. The presentation of each needle and Q-tip clip started with the first frame of the clip, which was presented for 500 ms. The following 60 frames were presented at a rate of 60 Hz and the last frame of the clip sustained on the screen for 2500 ms.

2.3. Procedure

Participants were seated in front of the infrared eye-tracking system (iView X, SensoMotoric Instruments, Teltow, Germany) with their heads secured (Fig. 1A). Visual presentation of needle

pricks and Q-tip touches was spatiotemporally aligned with the application of electrical stimuli. Participants' left hands were placed on a board mounted below a flat screen, so that the position of their hand matched the position of the virtual hand on the screen and they were instructed to imagine that the hand on the screen would be their own. Each experimental trial started with the presentation of a clip (Fig. 1C). Simultaneously with the last frame, which shows the needle that pricked or the Q-tip that touched the finger of the incorporated hand, participants received a painful or a nonpainful electrical stimulus at the respective finger of their own hand. Throughout all clips, participants fixated on a gray-shaded circle located above the left index finger. Starting 1000 ms prior to electrical stimulation, the circle filled from surrounding to center and was complete when the electrical stimulus was presented. This was done to assure that the same temporal information about the occurrence of the electrical stimulus was provided in all clips, including the hand-alone clips. During each trial, pupil size was monitored from the left eye at a sample rate of 500 Hz. Following the presentation of the last frame, participants rated intensity and unpleasantness of the electrical stimulus on a 2-dimensional visual analogue scale using a joystick in their right hand. The visual analogue scale, which was superimposed over the finger of the hand on the screen, ranged between 0 and 100 on the vertical *intensity* axis (0 = no sensation; 40 = beginning of pain experience, marked by a horizontal line; 100 = most intense pain) and 0 to 100 on the horizontal *unpleasantness* axis (0 = not unpleasant at all; 100 = extremely unpleasant). Prior to the experimental session, the experimenter instructed participants to rate the perceived intensity and unpleasantness of electrical stimuli, but not how intense or unpleasant the visual stimulation appeared. Each experimental session consisted of 15 blocks comprising 60 trials each. As key experimental manipulation, blocks differed with respect to contingencies between video clips (needle vs. Q-tip) and strength of electrical stimulation (painful vs. nonpainful). Pain ratings and PDR were obtained in 3 expectation conditions: *Needle-Pain*, *Neutral*, and *QtipPain*. In the *NeedlePain* condition, needle pricks were associated with painful stimulation in 75% (i.e., 15 of 20 trials per block) of all needle clip trials, and Q-tip touches were associated with painful stimulation in 25% (i.e., 5 of 20 trials per block) of all Q-tip clip trials. This association between video clips and painful stimulation was reversed in the *QtipPain* condition (Fig. 1B). Finally, in the *Neutral* condition, both Q-tip and needle clips were associated with painful stimulation in 50% (i.e., 10 of 20 trials per clip and block) of all needle clip and Q-tip clip trials. Importantly, before each block, participants were explicitly informed about the contingency of the stimuli by a pictorial instruction presented on the screen and an additional verbal instruction given by the experimenter. In all expectation conditions, the hand-alone control clips were uniformly paired with painful and nonpainful electrical stimuli and were presented in 33% of trials within each block. Twenty hand-alone trials were presented in each experimental block, whereby 10 trials were paired with painful and 10 trials were paired with nonpainful stimulation. Thus, the contingency for the hand-alone clips was constant in all expectation conditions. Therefore, hand-alone clips were not subjected to the statistical analysis of the effects of situational expectations on pain perception. After 10% of all trials, a control question was presented to make sure that participants attended to the clips ("Which clip was shown in the previous trial?"). The presentation of the control question was randomized over trials. To assure a balanced presentation of the different expectation conditions, experimental blocks (3 *Neutral*, 6 *NeedlePain*, and 6 *QtipPain*) were presented in pseudo-randomized order, that is, within each 5 consecutive blocks, 1 *Neutral*, 2 *NeedlePain*, and 2 *QtipPain* blocks were randomly presented. Trials within each block were presented in random order. Prior to each block, the eye-tracking system was

calibrated, and after the experimental session, participants rated the degree of embodiment of the hand seen on the screen.

2.4. Embodiment questionnaire

To measure the degree of experienced embodiment of the hand viewed on the screen, a questionnaire was used that addressed factors predictive for the proprioceptive displacement observed in classic studies on the rubber hand illusion (adapted from [17]). The questionnaire comprised 10 items, including questions on ownership (e.g., "It seemed like I was looking directly at my own hand, rather than at a videotaped hand"), location (e.g., "It seemed like my hand was in the same location as the hand in the clip"), and agency (e.g., "It seemed like I was in control of the hand on the screen"). All questions were rated on a 6-point Likert scale (1 = "strongly disagree," 6 = "strongly agree"). The original questionnaire [17] was translated into German and wording was slightly modified because a videotaped hand instead of a rubber hand was used in the present study (e.g., the term "rubber hand" was replaced by "hand in the clip").

2.5. Data analysis

Prior to statistical analysis, outlier trials were removed from pain ratings. To this end, the mean of intensity and unpleasantness ratings was calculated over nonpainful and painful trials separately, pooled across contingency conditions and clips. Trials in which the ratings were below or above 3 SD were omitted from further analyses. The PDR data were screened and corrected for outliers in a similar way as has been done in previous studies ([27,31]; see supplemental material). Eye blinks and other artifacts were removed in an interval ranging from 200 ms before to 200 ms after blink or artifact onset. Trials were excluded from further analyses if 50% of the sample points within the baseline interval, ranging from -1000 to -500 ms before electrical stimulus onset, or the analysis interval, ranging from -200 prior to electrical stimulation to 1300 ms after electrical stimulation, were artifactual. For all included trials, periods containing artifacts were linearly interpolated [27]. The PDR to electrical stimulation was normalized by subtracting the baseline and subsequently dividing by the baseline. To establish the presence of significant effects in PDR and to define a time interval for further analyses, point-wise running *t*-tests between the needle prick and the Q-tip touch trials were computed. To account for alpha error accumulation in multiple testing, time intervals were defined as being significantly different if each sample point within a 100-ms interval reached a threshold of $P < 0.001$.

Repeated-measures analyses of variance (ANOVAs) were conducted on intensity and unpleasantness ratings as well as on the PDR. The analysis consisted of 2 levels. The first level contrasted the effect of needle and Q-tip clips on ratings and PDR. Intensity and unpleasantness ratings were subjected to separate ANOVAs with the factors Visual Stimulation (needle vs. Q-tip clip), Expectation (*QtipPain*, *Neutral*, *NeedlePain*), and Electrical Stimulation (painful vs. nonpainful). Furthermore, the relationship between intensity and unpleasantness ratings and PDR was investigated by calculating Pearson's *r* correlation coefficients between difference values (i.e., viewing needle pricks vs. viewing Q-tip touches) of pain ratings and difference values of PDR in the 3 expectation conditions. The second level of analysis was conducted to examine the impact of viewing an instrument contacting a hand on pain and PDR as compared to viewing a hand alone. Because hand-alone clips were uniformly paired with painful and nonpainful electrical stimuli in all expectation conditions and thus, were never subject to contingency manipulations, we averaged the electrical stimulus ratings obtained for needle, Q-tip, and hand-alone clips over expectation conditions prior to statistical testing. Separate ANOVAs were

Table 1
Analysis of variance for viewing needle pricks vs viewing Q-tip touches.

	df	Intensity		Unpleasantness		Pupil dilation response	
		F	P-value	F	P-value	F	P-Value
Visual stimulation (VS)	1 (24)	0.00	0.956	5.68[*]	0.025	37.64[**]	0.000
Expectation (E)	2 (48)	0.63	0.535	0.56	0.577	1.02	0.368
Electrical stimulation (ES)	1 (24)	158.75[**]	0.000	84.09[**]	0.000	56.77[**]	0.000
VS × E	2 (48)	4.14[*]	0.046	5.47[*]	0.018	1.13	0.332
VS × ES	1 (24)	4.67[*]	0.041	0.34	0.563	1.16	0.292
E × ES	2 (48)	0.53	0.590	0.68	0.511	1.50	0.235
VS × E × ES	2 (48)	1.70	0.194	0.50	0.608	0.34	0.713

Note: Values enclosed in parentheses represent error degrees of freedom (*df*).
[*] $P < 0.05$.
[**] $P < 0.01$.

conducted for intensity ratings, unpleasantness ratings, and PDR using the factors Visual Stimulation (needle, Q-tip, and hand-alone clip), and Electrical Stimulation (painful vs nonpainful). Since a large number of electrical stimuli (n = 900, 450 stimuli were painful) was administered in the experiment, it may be that habituation effects influenced the present findings [4,8]. To examine the possible influence of habituation on the effects in intensity and unpleasantness ratings, additional 4-way ANOVAs were conducted, in which the factor Time was entered (first and last 50% of trials within each condition).

3. Results

3.1. Effects of viewing needle pricks vs Q-tip touches

The ANOVA of intensity ratings using the factors Visual Stimulation (needle prick vs. Q-tip touch), Expectation (*NeedlePain*, *Neutral*, *QtipPain*), and Electrical Stimulation (painful vs. nonpainful) revealed a significant main effect of Electrical Stimulation ($F[1,24] = 158.75$, $P < 0.001$; Table 1). Ratings were higher for painful compared to nonpainful stimuli (Fig. 2A). Moreover, a significant interaction of Electrical Stimulation × Visual Stimulation was observed ($F[1,24] = 4.67$, $P = 0.041$), indicating that, across Expectation conditions, the presentation of a needle clip compared to a Q-tip clip led to slightly higher intensity ratings of painful stimuli (needle clip, M = 52.43; Q-tip clip, M = 51.97; $t[24] = 1.39$, $P = 0.178$) and to slightly lower-intensity ratings of nonpainful stimuli (needle clip, M = 21.46; Q-tip clip, M = 21.89; $t[24] = -1.42$, $P = 0.170$). The ANOVA also revealed a significant Expectation × Visual Stimulation interaction ($F[2,48] = 4.16$, $P = 0.046$). Follow-up comparisons that were conducted separately for the 3 expectation conditions indicated a trend towards higher ratings when a needle clip compared to a Q-tip clip was presented in the *NeedlePain* condition (needle clip, M = 37.45; Q-tip clip, M = 35.82; $t[24] = 1.96$, $P = 0.061$) and a trend towards higher ratings when the Q-tip clip compared to the needle clip was seen in the *QtipPain* condition (needle clip, M = 36.39; Q-tip clip, M = 37.72; $t[24] = -1.94$, $P = 0.065$). No significant differences were found in the *Neutral* condition (needle clip, M = 36.99, Q-tip clip, M = 37.26; $t[24] = -0.82$, $P = 0.408$). Thus, the difference in intensity ratings (needle prick minus Q-tip touch clips) was positive in the *NeedlePain* condition, around zero in the *Neutral* condition, and negative in the *QtipPain* condition (Fig. 2B). The difference values obtained in the *NeedlePain* condition significantly differed from those obtained in the *Neutral* ($t[24] = -2.18$, $P = 0.039$)
and the *QtipPain* conditions ($t[24] = -2.10$, $P = 0.047$), demonstrating that situational expectations about forthcoming pain biases perceived stimulus intensity towards the expected direction.

The ANOVA of unpleasantness ratings revealed a significant main effect of Electrical Stimulation ($F[1,24] = 84.09$, $P < 0.001$;
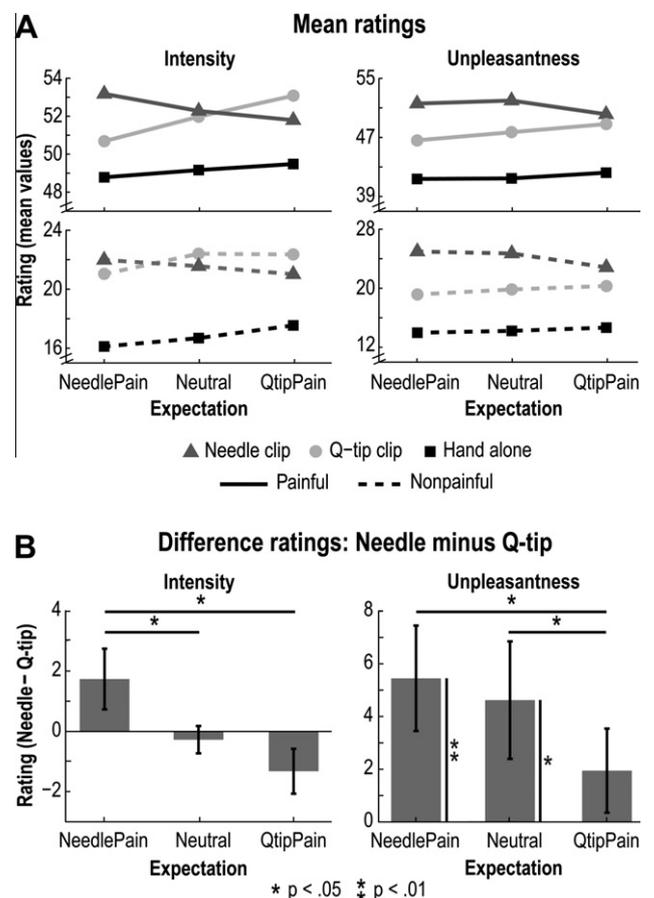
Fig. 2. Influence of visual stimulation and expectation on subjective ratings of electrical stimuli. (A) Left panel: painful (upper panel) and nonpainful (lower panel) stimuli were perceived as more intense when the respective clip was associated with painful stimulation (e.g., the needle clip in the *NeedlePain* condition led to higher ratings than the Q-tip clip). Right panel: electrical stimuli were perceived as more unpleasant when participants viewed needle pricks compared to when they viewed Q-tip touches. (B) Difference ratings for the contrast needle prick minus Q-tip touch clips. Left panel: The difference in intensity ratings was positive in the *NeedlePain* condition and negative in the *QtipPain* condition. Moreover, the difference value in the *NeedlePain* condition significantly differed from those in the *Neutral* and the *QtipPain* condition. Right panel: the difference in unpleasantness ratings differed significantly from zero in the *Neutral* and the *NeedlePain* condition and the difference value was larger in the *NeedlePain* and *Neutral* compared to the *QtipPain* condition.

Table 1). Painful stimuli were perceived as more unpleasant than nonpainful stimuli. In addition, a significant main effect of Visual Stimulation ($F[1,24] = 5.68$, $P = 0.025$) showed that, across expectation conditions, unpleasantness ratings were larger when electrical stimuli were presented with needle clips compared to Q-tip
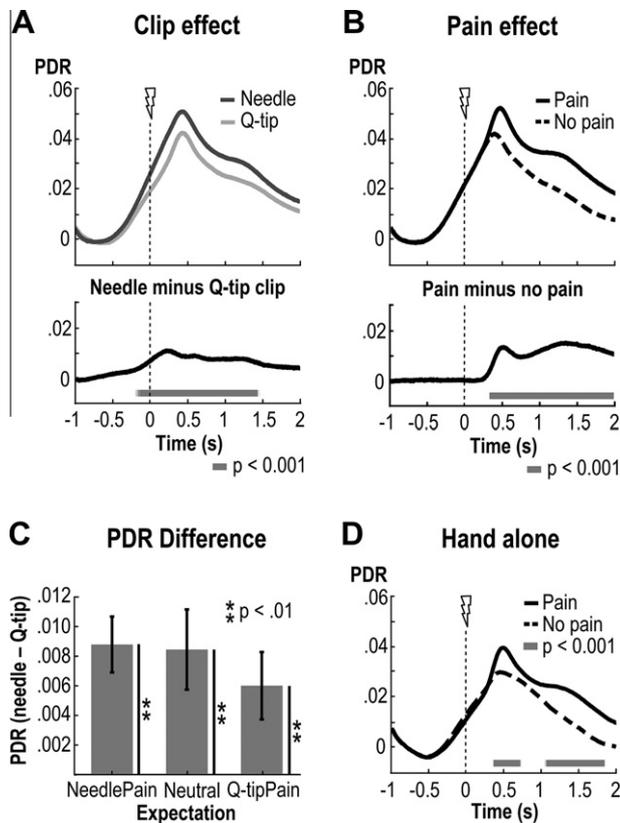
Fig. 3. Traces of the pupil dilation response (PDR). (A) PDR was larger when viewing needle pricks compared to viewing Q-tip touches (pooled across trials with painful and nonpainful stimulation). The traces differed on average about 200 ms before electrical stimulus onset (lower panel). (B) Painful stimuli (merged across needle and Q-tip clips) evoked larger PDR than nonpainful stimuli. Traces diverged about 300 ms after electrical stimulus onset (lower panel). (C) Magnitude of change between viewing needle pricks and Q-tip touches. Viewing needle pricks evoked higher PDR (mean from −200 to 1300 ms) than viewing Q-tip touches in all expectation conditions. (D) PDR traces for painful and nonpainful stimuli in hand-alone control trials. Traces differed from about 300 ms poststimulus. The flash symbol signifies electrical stimulation onset.

clips. The effect of Visual Stimulation on unpleasantness ratings differed between expectation conditions, as indicated by a significant Expectation × Visual Stimulation interaction ($F[2,48] = 5.47$, $P = 0.018$). Follow-up comparisons showed that electrical stimuli were perceived as significantly more unpleasant when presented with a needle prick clip compared to a Q-tip touch clip in the *NeedlePain* (needle clip, M = 38.21; Q-tip clip, M = 32.75; $t[24] = 2.87$, $P = 0.008$) and in the *Neutral* condition (needle clip, M = 38.49; Q-tip clip, M = 33.78; $t[24] = 2.38$, $P = 0.026$), while no significant effects were observed in the *QtipPain* condition (Fig. 2B). To further investigate whether the effects on pain ratings may be influenced by habituation to electrical stimuli, ratings were subjected to 4-way ANOVAs, comprising the factors Visual Stimulation, Expectation, Electrical Stimulation, and Time (first and last 50% of trials). For intensity ratings, a significant Time × Electrical Stimulation interaction was observed ($F[1,24] = 6.37$, $P = 0.019$). Nonpainful stimuli were perceived similarly intense in the first (M = 21.43) and last (M = 21.95) 50% of trials ($t[24] = −0.47$, $P = 0.646$), whereas painful stimuli were perceived as more intense in the first (M = 53.42) compared to the last (M = 50.86) 50% of trials ($t[24] = 2.22$, $P = 0.036$). Thus, there was a habituation effect for painful but not for nonpainful stimuli. Importantly, no other significant effects concerning the factor Time were found, suggesting that habituation effects did not influence the findings described
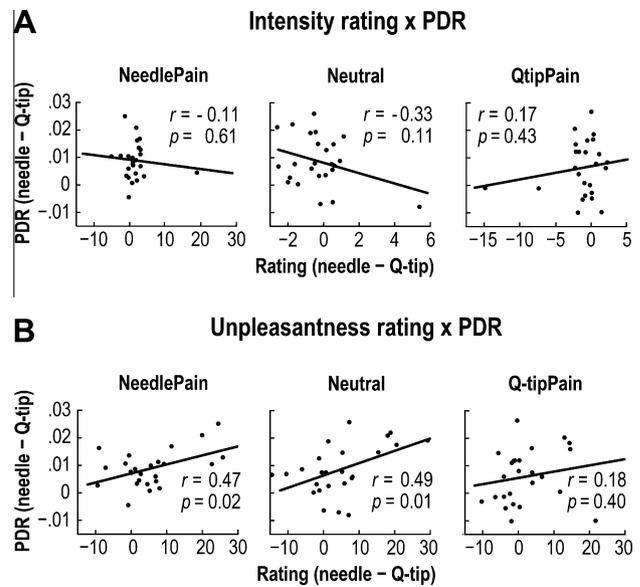
Fig. 4. Pearson's *r* correlations between subjective ratings and the pupil dilation response (PDR). (A) Correlation between intensity rating and PDR (mean from −200 to 1300 ms with relation to onset of electrical stimulation). No significant correlations were found. (B) Correlation between unpleasantness rating and PDR. Significant correlations were observed in the *Neutral* and the *NeedlePain* condition.

above. The ANOVA for unpleasantness ratings did not reveal any significant effects regarding the factor Time.

For the analysis of PDR, data points within a time interval ranging from −200 to 1300 ms (around electrical stimulation) were averaged and used as dependent variables. This interval was selected based on running *t*-tests (corrected for multiple testing), which indicated significant differences between the traces for needle and Q-tip clips at this time range (Fig. 3A; PDR traces were further examined in 2 control experiments; see supplementary material). The ANOVA for PDR revealed a significant main effect of Electrical Stimulation ($F[1,24] = 56.77$, $P < 0.001$; Fig. 3B) due to a larger PDR to painful compared to nonpainful stimuli. Moreover, a significant main effect of Visual Stimulation indicated larger PDR when participants viewed a needle prick compared to when they viewed a Q-tip touch ($F[1,24] = 37.64$, $P < 0.001$; Fig. 3C and Supplementary Fig. 2). Next, the relationship between the effects in intensity and unpleasantness ratings (Fig. 2B) and PDR (Fig. 3B) was investigated. Pearson's *r* correlation coefficients were computed between the difference values (i.e., viewing needle pricks minus viewing Q-tip touches) of pain ratings and the difference values of PDR in the 3 expectation conditions. No significant correlations were found between intensity ratings and PDR in all conditions and between unpleasantness ratings and PDR in the *QtipPain* condition (Fig. 4A). Significant positive correlations, however, were observed between unpleasantness ratings and PDR in the *Neutral* ($r = 0.49$, $P = 0.014$) and the *NeedlePain* conditions ($r = 0.47$, $P = 0.017$, Fig. 4B), suggesting an association between the effects in PDR and stimulus unpleasantness ratings.

3.2. Effects of viewing an instrument contacting an incorporated hand

To investigate the more general impact of viewing an instrument contacting an incorporated hand on pain perception, electrical stimulus ratings and PDR were averaged over expectation conditions and ANOVAs for intensity ratings, unpleasantness ratings, and PDR, using the factors Visual Stimulation (needle, Q-tip, and hand-alone clip) and Electrical Stimulation (painful vs nonpainful), were conducted (Table 2). The ANOVA of intensity ratings

Table 2
Analysis of variance for viewing needle pricks vs viewing Q-tip touches.

	df	Intensity		Unpleasantness		Pupil dilation response	
		F	P-value	F	P-value	F	P-value
Visual stimulation (VS)	2 (48)	31.85**	0.000	11.31**	0.001	36.84**	0.000
Electrical stimulation (ES)	1 (24)	180.28**	0.000	93.32**	0.000	84.61**	0.000
VS × ES	2 (48)	5.83*	0.013	0.09	0.833	2.91	0.064

Note: Values enclosed in parentheses represent error degrees of freedom (*df*).
* $P < 0.05$.
** $P < 0.01$.

revealed a significant main effect of Electrical Stimulation, due to higher ratings to painful compared to nonpainful stimuli ($F[1,24] = 180.28$, $P < 0.001$; Fig. 2A). Additionally, a significant main effect of Visual Stimulation showed that electrical stimuli were perceived as more intense when participants viewed an instrument contacting the incorporated hand compared to when they viewed the hand alone ($F[2,48] = 31.85$, $P < 0.001$; Fig. 2A, needle and Q-tip clip vs. hand-alone clip). A significant interaction of Electrical Stimulation × Visual Stimulation ($F[2,48] = 5.83$, $P = 0.013$) indicated that this effect was stronger for nonpainful (needle clip, M = 21.46; Q-tip clip, M = 21.89; hand-alone clip, M = 16.74) compared to painful stimuli (needle clip, M = 52.43; Q-tip clip, M = 51.97; hand-alone clip, M = 49.15).

The ANOVA of unpleasantness ratings revealed a significant main effect of Electrical Stimulation ($F[1,24] = 93.32$, $P < 0.001$; Fig. 2A). Ratings were higher for painful compared to nonpainful stimuli. Furthermore, a significant main effect of Visual Stimulation ($F[2,48] = 14.17$, $P = 0.001$; Fig. 2A) indicated that electrical stimuli were perceived as more unpleasant when participants viewed an instrument contacting the incorporated hand compared to when they viewed the hand alone, and as most unpleasant when a needle clip was presented (needle, M = 37.76; Q-tip, M = 33.69; hand-alone clip, M = 27.94).

Finally, the ANOVA of pupil data showed enhanced PDR when painful stimuli compared to nonpainful stimuli were applied, as expressed by a main effect of Electrical Stimulation ($F[1,24] = 84.61$, $P < 0.001$; Fig. 3D). Moreover, a significant main effect of Visual Stimulation ($F[2,48] = 36.84$, $P < 0.001$; compare Fig. 3B and D) showed that viewing a needle prick and a Q-tip touch led to stronger PDR than viewing a hand alone.

3.3. Embodiment of the hand in the clip and control for visual attention

The questionnaire inquiring the degree of embodiment of the hand viewed on the screen showed that participants generally had the impression that they were looking at their own hand (mean = 3.65 ± 1.13; 20 of 25 participants scored higher than 3). Highest scores were obtained on items that relate to the feeling that the viewed hand was at the location of their own hand and which express a causal relationship between the viewed and the experienced event (item 6, 4.68 ± 1.25; item 7, 4.28 ± 1.49; item 8, 4.64 ± 1.32). In addition, participants correctly answered the control question on visual attention ("Which clip was shown in the previous trial?"; asked after 10% of all trials) in 89.4% of all occurrences, demonstrating that participants attended to the clips.

4. Discussion

This study examined the impact of viewing a needle pricking an incorporated hand on the perception of concurrently presented painful and nonpainful electrical stimuli. A particular strength of our study is that it allowed for the investigation of interactive effects between previous experiences and acute situational expecta-

tions regarding the probability that the subsequent stimulation would be painful. Based on previous experience, an encounter with a sharp object (such as a needle) is more likely to be followed by pain than an encounter with a blunt object (such as a Q-tip). Hence, the experimentally induced expectations were either in line with, or contrary to, the expectations derived from previous experience. The key findings were that the influence of situational expectations about forthcoming pain, induced by explicitly manipulating the contingency between the presentation of needle clips or Q-tip clips and the occurrence of painful or nonpainful stimulation across experimental blocks, was most robustly reflected in the perceived stimulus intensity. Furthermore, the general effect of viewing a needle prick compared to viewing a Q-tip touch was primarily reflected in perceived stimulus unpleasantness and in responses of the autonomic nervous system (ANS), expressed by PDR.

Situational expectations about forthcoming pain with regard to video clips, raised by contingency information provided prior to the experimental blocks, biased the perceived intensity of electrical stimuli. Irrespective of the viewed event, needle prick or Q-tip touch, stimulus intensity ratings tended to be higher when participants expected the event to be accompanied by painful compared to nonpainful electrical stimuli. In our experiment, the clips of needle pricks and Q-tip touches served as cues for the electrical stimuli. In this respect, our finding is in line with previous studies using semantically meaningless cues to induce expectations about the strength of forthcoming painful and nonpainful stimulation [1,6,15,18,25]. For instance, moderately strong pain stimuli were perceived as more painful when preceded by cues signaling high pain compared to cues signaling low pain [1]. Together, this suggests that expectations about forthcoming pain triggered by semantically meaningful and semantically nonmeaningful cues act upon pain perception in a similar way. Information provided prior to viewing an injection bias the perceived intensity of the painful needle prick towards the expected direction.

Both painful and nonpainful electrical stimuli were perceived as more unpleasant when participants viewed a needle prick, compared to when they viewed a Q-tip touch or a hand alone. This effect was paralleled by an enhancement in PDR. The finding that viewing needle pricks enhances responses of the ANS and increases the perceived unpleasantness of electrical stimuli fits with previous studies showing that affective stimuli from other sensory modalities modulate pain processing and pain perception ([10,13,26,32,35,36]; this is also true for tactile processing [34]). Several of these studies suggested that affective stimuli influence perceived unpleasantness but not perceived intensity of painful stimuli [13,22,36]. Moreover, studies that presented video clips depicting needle pricks inflicted upon another person's body found activations in cortical areas processing the affective-motivational pain component ([7,19], but see [33]). Thus, our study suggests that, similar to what has been found for the processing of visual stimuli depicting other people's pain [7,19], viewing painful stimulation attributed to one's body modulates the affective-motivational component of pain. Of particular interest is also that the

effects on stimulus unpleasantness ratings were modulated by situational expectations about forthcoming pain. This implies that both factors, previous experiences made throughout lifetime that sharp objects cause pain and situational expectations, mutually affect the perceived unpleasantness of painful stimuli.

Another important finding is that the effects on stimulus unpleasantness ratings were correlated with the effects on PDR. A previous study demonstrated that modulations in pain perception triggered by hypnotic suggestions are reflected in ANS activity [23]. This study showed that ANS activity, measured by heart rate, positively correlated with perceived unpleasantness but not with perceived intensity. Thus, ANS activity may primarily reflect the perceived unpleasantness of painful stimulation. Of particular interest in the present study was that the PDR traces evoked by viewing needle pricks and Q-tip touches differed already about 200 ms prior to the onset of electrical stimulation. A recent study showed that the mere threatening of a rubber hand, perceived as being one's own, with a needle increases activity in the anterior cingulated cortex – a brain region involved in anticipation of pain and ANS regulation [9]. Thus, it can be speculated that the enhanced anticipatory PDR in the present study indicates activity changes in cortical regions involved in the processing of the affective-motivational pain component. This would also fit with the observation that viewing needle pricks most robustly led to enhanced stimulus unpleasantness ratings.

The general effect of viewing an instrument (needle or Q-tip) contacting the incorporated hand compared to viewing the incorporated hand alone was expressed by enhanced stimulus intensity and unpleasantness ratings as well as by a stronger PDR. Since a temporal cue, in this case a fixation circle that filled from surrounding to center, signaled the onset of the electrical stimulus in all clips, it is unlikely that temporal cueing, as such, can account for these effects. Observing pain and touch evokes activity in brain areas that are also involved in the processing of painful and tactile stimuli [14,19,20]. Hence, visual stimuli, which have been regularly paired with pain or touch, may lead to the anticipation of these stimuli as soon as the respective visual input is presented. Moreover, the present study demonstrates that compared to viewing a hand alone, viewing painful and nonpainful events, especially those that are attributed to oneself, enhances the perceived strength of concurrently presented painful and nonpainful stimuli.

When interpreting our results, it is important to emphasize that the visual stimuli were spatiotemporally aligned with the electrical stimuli. Research on processing of stimuli across modalities consistently showed that stimuli that are spatially and temporally aligned are more likely to be integrated than stimuli that are not aligned [28,29]. Thus, our setup may have facilitated the cross-modal bias of viewing a needle pricking an incorporated hand on pain perception. Due to the spatial alignment of visual and electrical stimuli, the visual stimuli were presented in peripersonal space. Previous studies demonstrated that salient sensory stimuli (e.g., threatening stimuli) presented in the proximity of the body facilitate the processing of stimuli from other modalities [11,16]. Along the same lines, the visual percept of the needle approaching the incorporated hand (i.e., entering the peripersonal space) may have impacted on the processing of concurrently presented electrical stimuli in the present study. While previous studies showed that affective pictures influence pain perception, even if presented in extrapersonal space [10,13,32,35], another study, in which clips of needle pricks were presented in extrapersonal space, could not observe modulations in pain ratings [33]. Thus, it is likely that the spatiotemporal alignment of stimuli in peripersonal space may further increase cross-modal biasing of semantically relevant visual input on pain perception [12]. Future studies may address this interesting issue.

Taken together, our study reveals several important findings. Firstly, situational expectations about forthcoming pain modulate the perceived intensity of painful and nonpainful stimuli towards the expected direction. This finding has practical implications for clinicians who may be advised to provide information that reduces patients' expectation about the strength of forthcoming pain prior to an injection. Secondly, increase of ANS activity, including anticipatory responses and enhancement of perceived unpleasantness mainly reflects the impact of previous experiences with viewing needle pricks on concurrently presented painful and nonpainful stimuli. This suggests that previously learned associations between visual and painful stimuli primarily modulate the affective-motivational pain component. Finally, viewing an instrument (needle or Q-tip) stimulating an incorporated hand compared to viewing a hand alone while receiving pain, leads to enhanced intensity and unpleasantness ratings as well as enhanced ANS activity. This finding provides empirical evidence in favor of the common advice not to look at the needle prick when receiving an injection.

Conflict of interest statement

Acknowledgments

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.pain.2012.02.010.

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