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Fear of pain changes movement

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ORIGINAL ARTICLE

Fear of pain changes movement: Motor behaviour following the acquisition of pain-related fear

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Abstract

Background: According to current fear-avoidance models, changes in motor behaviour (e.g. avoidance) are a key component in the development and maintenance of chronic pain complaints. Yet, experimental research assessing actual behavioural changes following painful events is relatively sparse. This study investigated the effects of pain anticipation on changes in motor behaviour using a fear conditioning paradigm and robot-generated standardized movement trajectories of the upper extremities.
Methods: Pain-free participants ($N = 20$) performed clockwise and counterclockwise fixed, circular movements with a robotic arm without receiving visual feedback. During fear acquisition, moving in one direction (CS+) was paired with a painful stimulus (pain-US) whereas moving in the other direction (CS−) was not. During the subsequent extinction phase, the pain-US was omitted. We assessed self-reported pain-related fear and urge to avoid the movement, as well as several behavioural measures: Velocity, acceleration, exerted force and force direction.
Results: Movements that were paired with pain were associated with increased self-reported pain-related fear and urge to avoid. Moreover, movements that were associated with pain were performed faster, more forcefully and more accurately than movements that were not associated with pain. All these differences diminished during the extinction phase.
Conclusions: The present study demonstrates the utility of robot-generated force feedback in the study of pain-related fear and associated changes in motor behaviour.
Significance: Fear of pain changes movement: Movements associated with pain are performed faster, with more force and higher accuracy than movements that are not associated with pain. These changes can inform us how fear of pain translates into avoidance and escape behaviour, two important constructs in the maintenance of chronic pain.

1. Introduction

The fear-avoidance model (Vlaeyen and Linton, 2000; Crombez et al., 2012) proposes a mechanism for the development and maintenance of chronic pain complaints. The model predicts that pain-related fear and catastrophic beliefs about pain result in behavioural avoidance of feared movements/activities which can be adaptive in the short term but leads to functional disability in the long term (Trost et al., 2012; Vlaeyen and Linton, 2012).

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Experimental, cross-sectional and prospective studies in clinical populations as well as clinical analogue studies found support for the fear-avoidance model, mainly focusing on the development of pain-related fear and anxiety in chronic pain (Crombez et al., 1999, 2012; Leeuw et al., 2007; Zale et al., 2013). Despite its prominent role in the model, the study of actual behavioural changes following acquisition of pain-related fear has received far less attention.

It has been proposed that individuals with pain-related fear alter the way in which they move, possibly with the goal to avoid pain (Thomas and France, 2007). Such adaptations of motor behaviour might increase the risk for subsequent injury, explaining the relationship between pain-related fear and disability. Indeed, there is evidence that patients with low back pain avoid motion of the lumbar spine and demonstrate reduced velocity and acceleration when performing reaching movements (Thomas and France, 2007; Thomas et al., 2008a). However, the aforementioned studies are correlational and to our knowledge, no study thus far has investigated changes in motor behaviour following experimentally induced acquisition of pain-related fear in pain-free participants.

The current study presents a novel, ecologically valid and flexible paradigm using the HapticMaster, which is a 3-degrees of freedom (right/left, down/up and back/forward), force-controlled robotic arm. Our goal was to explore changes in motor behaviour following acquisition of pain-related fear in pain-free participants. We examined speed (i.e. velocity and acceleration) and the direction of the movement (i.e. force direction). In addition, we also measured the force with which participants direct their movements (Van der Linde and Lammertse, 2002).

We developed a novel, pain-relevant fear conditioning paradigm, in which the HapticMaster was used to perform circular movements in the horizontal plane which served as conditioned stimuli (CSs), and a painful electrocutaneous stimulus served as the unconditioned stimulus (pain-US). One movement direction (e.g. clockwise) (CS+) was paired with the pain-US, whereas the other (e.g. counterclockwise) was not (CS−). It has been shown previously that pain-related fear can be acquired through associative learning, using joystick movements (Meulders et al., 2011).

We hypothesized that the CS+ elicits increased (1) pain-related fear (e.g. higher self-reported fear) and (2) avoidance tendencies (i.e. more self-reported urge to avoid) compared with the CS−. More importantly, we expected (3) changes in motor behaviour following fear acquisition. Specifically, we expected differences between movements associated with pain and movements not associated with pain with regard to velocity, acceleration, exerted force and force direction. Considering the lack of prior research in this area, we do not make specific predictions about the direction of these changes. Lastly, we expect that the aforementioned differences (4) diminish during the extinction phase when the pain-US it omitted.

2. Methods

2.1 Participants

Twenty pain-free individuals (12 females; mean age ± SD (range) = 22.15 ± 1.93 (19–28) years) participated in the present study. Three participants were left-handed. Individuals with heart disease, chronic or acute pain (anywhere in the body), current or past diagnosis of depression or anxiety disorders, chronic or acute respiratory problems, neurological disorders (e.g. epilepsy), pregnancy, severe joint or muscle problems or the presence of any other severe medical condition were excluded from participation in this study. Participants received either 2.5 course credits or a financial remuneration of €7.50 for their participation. The experimental protocol was approved by the Ethical Review Committee of the Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, The Netherlands (registration number: ECP-111 12_02_2012).

2.2 Apparatus and experimental stimuli

2.2.1 HapticMaster

The HapticMaster (HM) (see Fig. 1) is a force controlled robot arm (Moog Inc. FCS Robotics, East Aurora, NY, USA) (Van der Linde and Lammertse, 2002). It has 3-degrees of freedom and it allows for a wide range of movement. Additionally, the HM has a force controlled haptic interface that allows simulating weight and force and can thus mimic real-life, pain-relevant movements thereby increasing ecological validity. In addition, the HM allows for the precise measurement of behavioural indices, such as velocity, acceleration and force. Specifically, it is possible to study the changes in these behavioural indices following pain-related fear acquisition.

In the current study, participants were asked to perform fixed, circular (r = 12.5 cm) movements in

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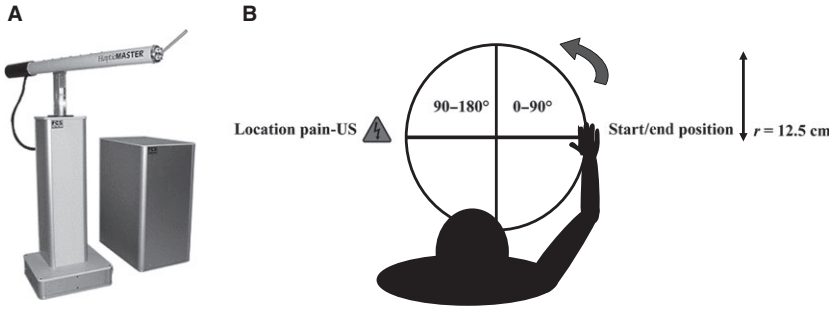

Figure 1 Overview of the HapticMaster (A) and one of the circular movements (B; a counterclockwise movement). During CS+ acquisition trials, the pain-US was administered when the hand crossed at 180° of the movement.

a horizontal plane with the HM (see Fig. 1). Note that the HM allows for movements in all directions but for the purpose of this experiment, movements were restricted to the horizontal plane and a fixed circular movement trajectory in a clockwise or counterclockwise fashion. The starting location of the circular movement was indicated by haptic feedback. Movement direction served as conditioned stimulus (CS), with one movement direction (CS+; e.g. counterclockwise) being consistently paired (100% reinforcement) with a painful electrocutaneous stimulus (pain-US), whereas the other movement direction (CS−; e.g. clockwise) was never paired with the pain-US. Which movement direction served as the CS+ was counterbalanced across participants. The beginning of a new trial was indicated by an auditory starting signal. The inter-trial interval (ITI) was 10 s.

2.2.2 Painful unconditioned stimulus (pain-US)

An electrocutaneous stimulus of 2 ms duration served as the pain-US. The stimuli were generated by a constant current stimulator (DS7A, Digitimer, Welwyn Garden City, UK) and delivered to the wrist of the dominant hand through two 1-cm surface Ag/AgCl EMG electrodes filled with K-Y gel (Johnson & Johnson, New Brunswick, NJ, USA). Note that a calibration procedure was carried out to determine the individual pain tolerance level for each participant (see Section 2.6).

2.2.3 Software

The experiment was run on a computer (HP Compaq 8200 Elite SFF) with Windows 7 Professional with an Intel® Core™ i5-2500 Processor. Synchronization between the HM and the Digitimer constant current stimulator was performed using dedicated software programmed in C++ by R.P.G.G., linking the HM arm position and the pulse occurrence in time. All data recording and processing was performed using a commercial software package (MATLAB version, The MathWorks Inc., Natick, MA, USA, 2000).

2.3 Procedure

The experiment was conducted during a single 60-min session at the movement laboratory of Adelante Rehabilitation Centre (Hoensbroek, The Netherlands) and consisted of the following phases: Preparation, practice, calibration, acquisition and extinction. A differential conditioning paradigm was employed (see Table 1). Participants performed 10 blocks of 8 movements each, with all movements within a block either in clockwise or counterclockwise fashion. Each participant was randomly assigned to one of four possible block randomizations to control for order effects (see Supporting Information Table S1). The order of CS+ and CS− movement blocks was the same in the acquisition and extinction phase.

2.4 Preparation phase

Upon arrival in the lab, participants received detailed information about the experiment and provided informed consent and demographic information. Exclusion criteria were checked by means of self-report. No participants were excluded based on these exclusion criteria. Subsequently, the length of the participant's dominant arm was measured from the acromioclavicular joint (top of the shoulder/collar bone) to the finger tips (M = 73.25 cm; SD = 4.75; range = 63–81), in order to adjust the distance of the chair to the HM. Participants were seated on a chair in a cubicle, which was individually adjusted so that both feet were on the ground with the knees in angle of approximately 90°. The chair was positioned (and locked) such that the shoulder and elbow of the participant were in line with the centre

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Table 1 Study design (total $N = 20$).

Practice phase	Acquisition	Extinction
PRC	ACQ1-4	EXT1-4
2 blocks of 8 trials	4 blocks of 8 trials	4 blocks of 8 trials
8 × CS+	2 × 8 CS+ (with pain-US)	2 × 8 CS+
8 × CS−	2 × 8 CS−	2 × 8 CS−

CS+ and CS−, respectively, refer to the movement that is paired with the pain-US during acquisition (100% reinforcement), and the movement that is never paired with the pain-US. The suffix 'with pain-US' is used to indicate which CS+ movements were followed by a pain-US, i.e. during the acquisition phase. Block presentation was randomized within each phase.

of the circle. An elastic belt was positioned around the waist of the participant as a reminder to keep the back straight against the backrest of the chair. To help focus the participant's attention on proprioceptive information rather than on visual information, the participants were blindfolded. This allowed us to test whether pain-related fear can be acquired without any visual information.

2.5 Practice phase

During the practice phase, participants performed 2 blocks of 8 movements each (one block clockwise movements; one block counterclockwise movements; in counterbalanced order). Participants were verbally instructed to perform circular movements as accurately as possible after hearing the starting signal indicating the beginning of a trial. During this phase participants were blindfolded and no pain-USs were administered.

2.6 Calibration phase

Subsequently, the intensity of the electrocutaneous stimulus (pain-US) was individually determined. After placing the electrodes on the wrist of the dominant hand of the participant, the experimenter administered a series of electrocutaneous stimuli, starting with a low intensity and increasing stepwise. The participant rated each stimulus on an 11-point Likert scale ranging from 'I felt nothing' to 'Worst pain I can imagine'. We aimed for a stimulus with a subjective rating of '8' (mean stimulus rating ± SD = 8.30 ± 0.83; range 5.5–9), namely a stimulus that is moderately painful and demanding some effort to tolerate (mean stimulus intensity ± SD = 66.25 ± 22.8 mA; range 28–97 mA). Before the start of the acquisition phase, the experimenter informed the participants that the chosen stimulus intensity would be the maximum intensity administered during the remainder of the experiment. Note that during this phase, the participant was not blindfolded.

2.7 Acquisition phase

After the calibration phase, the participant was blindfolded again. Participants performed four blocks (2 clockwise, 2 counterclockwise) of 8 movements. The acquisition phase was identical to the practice phase, except that the pain-US was delivered at 180° (i.e. halfway through the circle) after the starting position during CS+ movements. The movement direction that was paired with the pain-US was counterbalanced across participants. After each block, participants rated their pain-related fear and their urge to avoid the movement (see Section 2.9.1).

2.8 Extinction phase

The extinction phase was identical to the acquisition phase, consisting of 4 blocks (2 clockwise, 2 counterclockwise; same order as in the acquisition phase) of 8 trials each. The only difference was that no pain-USs were administered anymore. At the end of this phase, participants were debriefed, received their compensation and were dismissed.

2.9 Primary outcomes

2.9.1 Self-report measures

After each acquisition and extinction block, participants answered two questions, which retrospectively assessed how they felt during the performance of the movements: (1) *'To what extent were you afraid that the movement was going to be painful?'* (pain-related fear) and (2) *'How strongly did you want to avoid this movement?'* (urge to avoid). Both questions were scored on an 11-point Likert scale ranging from *'not at all'* (0) to *'very much'* (10).

2.9.2 Kinematic parameters

2.9.2.1 Velocity (v, m/s). The HM logs the position of the robotic arm in x and y direction across time, with a sample frequency of 300–400 Hz, allowing for computation of movement velocity.

2.9.2.2 Acceleration (a, m/s^2). Similarly, change in velocity across time was calculated. A positive value indicates acceleration, whereas a negative value indicates deceleration.

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2.9.2.3 Force (F, N). In addition to the position, a force sensor in the HM logs the exerted force in the horizontal plane, i.e. in the *x* and *y* direction with a sample frequency of 300–400 Hz.

2.9.2.4 Angle difference (degrees, °). For each point on the movement circle, the direction of the resultant force produced in the horizontal plane was calculated from the forces in *x* and *y* direction recorded by the HM. Next, the difference between the direction of the resultant force and the 'ideal force' direction, i.e. the force perpendicular to the radius of the circle, was calculated for each point on the circle. This measure gives an indication of how *accurate* the subjects were in following the predefined circular path. Avoidance tendencies might affect the accuracy of participants' movements (e.g. accuracy would be lower if a participant tries to deviate from the predefined path).

2.10 Data preparation and statistical analyses

For the data analysis of the kinematic variables, the movement circle (see Fig. 1) was subdivided into four quadrants: Quadrant 1 (Q1, 0–90° with respect to starting location), Quadrant 2 (Q2, 90–180°), Quadrant 3 (Q3, 180–270°) and Quadrant 4 (Q4, 270–360°). Considering the anticipatory nature of fear and avoidance (Krypotos et al., 2015) and to rule out the effects of the pain-US itself on the behavioural indices, we focused our analyses on the first two quadrants of the movement circle. In order to differentiate between the initiation/beginning of the movement and the movement period just prior to the pain-US, we included quadrant as a factor in the analyses. Note that this decision was made prior to data analysis. For the sake of completeness, we report all behavioural variables also for Q3 and Q4 (see Supporting Information Table S2), even though our analyses focus on Q1 and Q2. All kinematic variables were averaged across quadrants per block.

For the self-report measures, a 2 × 2 [Movement direction (CS+/CS−) × Block (ACQ1/ACQ2)] Repeated Measures (RM) ANOVA was run to test for acquisition effects. Similarly, to test for extinction effects a 2 × 3 [Stimulus Type (CS+/CS−) × Block (ACQ2/EXT1/EXT2)] RM ANOVA was run. For the behavioural variables, a 2 × 2 × 3 [Stimulus Type (CS+/CS−), × Quadrant (Q1/Q2) × Block (PRC/ACQ1/ACQ2)] RM ANOVA was run to test for acquisition effects. To test for extinction effects, a 2 × 2 × 3 [Stimulus Type (CS+/CS−) × Quadrant (Q1/Q2) × Block (ACQ2/EXT1/EXT2)] RM ANOVA was run. Note that ACQ1 refers to the first CS+ and CS− blocks, ACQ2 refers to the second CS+ and CS− block and so forth. Based on the randomization schedule (see Supporting Information Table S1), all participants had one CS+ and one CS− block each during ACQ1, ACQ2, EXT1 and EXT2. Uncorrected degrees of freedom and corrected *p*-values are reported together with ε and the effect size indication η_p^2. 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 α at 0.05 (Holm, 1979). All statistical analyses were run using Statistica 12 (StatSoft, Inc, Tulsa, OK, USA).

3. Results

3.1 Self-report measures

3.1.1 Pain-related fear

Overall, participants reported more fear following CS+ movements than CS− movements during acquisition, Stimulus Type, $F_{(1,19)} = 5.85$, $p < 0.05$, $\eta_p^2 = 0.24$, indicating successful differential fear acquisition. Moreover, participants' fear reports increased during acquisition: Block, $F_{(1,19)} = 7.33$, $p < 0.05$, $\eta_p^2 = 0.28$. However, the difference in fear ratings between CS+ and CS− movements did not change across time: Block × Stimulus Type, $F_{(1,19)} = 3.27$, $p = 0.09$, $\eta_p^2 = 0.15$ (see Fig. 2). Since pain-related fear was assessed *after* every block, the results indicate that participants already learned the difference between CS+ and CS− movements after ACQ1.

Subsequently, we investigated extinction effects. Overall, fear ratings decreased during extinction, Block, $F_{(2,18)} = 1.36$, $p < 0.05$, $\eta_p^2 = 0.40$, but planned comparisons indicated that participants were still more afraid of CS+ movements than CS− movements at the end of extinction, $F_{(1,19)} = 6.29$, $p < 0.05$. The interaction between block and stimulus type was not significant, Block × Stimulus Type, $F_{(2,38)} = 2.02$, $p = 0.15$, $\eta_p^2 = 0.10$.

3.1.2 Urge to avoid

Overall, participants indicated more urge to avoid CS+ than CS− movements, Stimulus Type, $F_{(1,19)} = 21.83$, $p < 0.01$, $\eta_p^2 = 0.54$. Similarly, avoidance ratings increased across time, Block, $F_{(1,19)} = 4.73$, $p < 0.05$, $\eta_p^2 = 0.20$. As expected,

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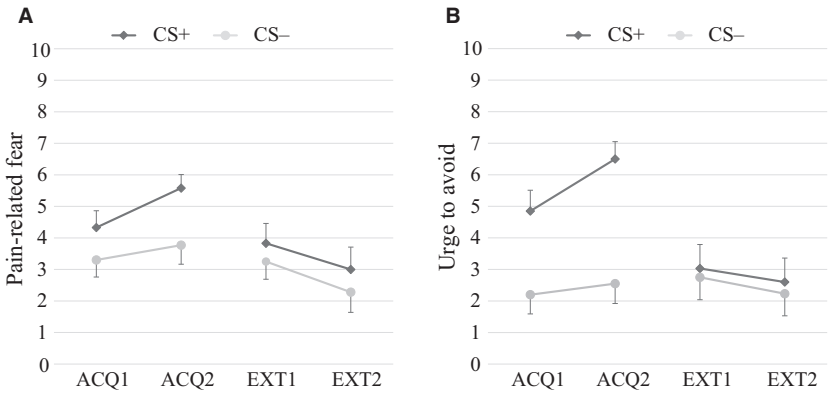

Figure 2 Self-reported mean (+SEs) pain-related fear (A) and urge to avoid the movement (B) during acquisition (ACQ1/ACQ2) and extinction (EXT1/EXT2) for movements associated with pain (CS+) and movements not associated with pain (CS−). Note: SE, standard error term based on mixed analyses estimates.

differences in the desire to avoid the CS+ and CS− movements increased during acquisition, Block × Stimulus Type, $F_{(1,19)} = 5.75$, $p < 0.05$, $\eta_p^2 = 0.23$ (see Fig. 2). In line with our hypothesis, planned comparisons indicated that participants wanted to avoid movements associated with pain more than movements not associated with pain at the end of acquisition, $F_{(1,19)} = 23.12$, $p < 0.001$.

As we expected, the difference in the desire to avoid the CS+ and CS− movements significantly decreased across extinction, Block × Stimulus Type, $F_{(2,38)} = 18{,}71$, $p < 0.001$, $\eta_p^2 = 0.50$. Planned comparisons confirm that the aforementioned differences at the end of acquisition were not present anymore at the end of extinction, $F_{(1,19)} = 2.19$, $p = 0.16$, indicating successful extinction.

3.2 Behavioural outcomes

3.2.1 Velocity

The difference in velocity between CS+ and CS− movements increased across the acquisition phase, independent of quadrant, Block × Stimulus Type, $F_{(2,18)} = 12.06$, $p < 0.001$, $\eta_p^2 = 0.57$ (see Fig. 3). Planned comparisons indicate that by the end of acquisition, CS+ movements were carried out faster than CS− movements, $F_{(1,19)} = 48.31$, $p < 0.001$. Moreover, change in velocity differed across the two quadrants, Block × Quadrant, $F_{(2,18)} = 16.21$, $p < 0.001$.

During the extinction phase, the difference in velocity between CS+ and CS− movements disappeared, Block × Stimulus Type, $F_{(2,18)} = 9.51$, $p < 0.01$, $\eta_p^2 = 0.51$. Planned comparisons indicated that at the end of the extinction phase there was no longer a difference in velocity between CS+ and CS− movements, $F < 1$.

In summary, participants performed movements associated with pain overall faster than movements not associated with pain. This difference in velocity diminished during the extinction phase.

3.2.2 Acceleration

With regard to acceleration, differential acquisition patterns differed based on movement quadrant, Block × Stimulus Type × Quadrant, $F_{(2,18)} = 9.74$, $p < 0.01$, $\eta_p^2 = 0.52$ (see Fig. 4). Consequently, we investigated differential acquisition separately per quadrant. Pairwise comparisons indicate that in Q1, CS+ movements were associated with more acceleration than CS− movements at the end of acquisition, $F_{(1,19)} = 9.44$, $p < 0.01$. In contrast, in Q2 we observe the opposite pattern: CS+ movements are associated with deceleration compared to CS− movements, $F_{(1,19)} = 4.88$, $p < 0.05$.

Consequently, also the extinction patterns differed between the two quadrants, Block × Stimulus Type × Quadrant, $F_{(2,18)} = 4.7$, $p < 0.05$, $\eta_p^2 = 0.34$. However, planned comparisons indicated that the differences between CS+ and CS− movements were eliminated by the end of extinction in both Q1, $F < 1$, and Q2, $F < 1$.

In summary, participants showed increased acceleration during the beginning (Q1) of pain-related movements but slowed down immediately before the location where the painful stimulus was delivered (Q2). These findings are only partly in line with the velocity results, which showed increased movement speed across Q1 and Q2 during movements associated with pain. So despite slowing down prior

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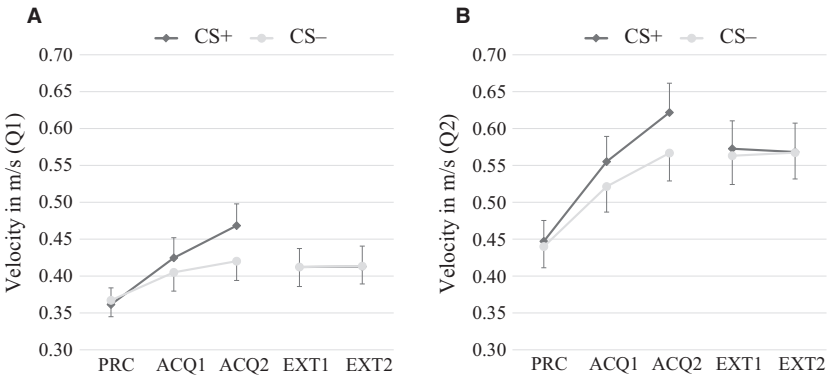

Figure 3 Mean velocity (in m/s) (+SEs) during acquisition (ACQ1/ACQ2) and extinction (EXT1/EXT2) for movements associated with pain (CS+) and movements not associated with pain (CS−), in quadrants 1 (Q1, A) and 2 (Q2, B). Note: SE, standard error term based on mixed analyses estimates.

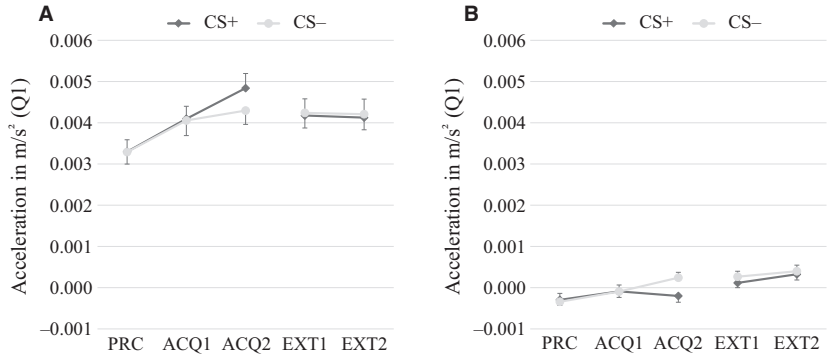

Figure 4 Mean acceleration (in m/s²) (+SEs) during acquisition (ACQ1/ACQ2) and extinction (EXT1/EXT2) for movements associated with pain (CS+) and movements not associated with pain (CS−), in quadrants 1 (Q1, A) and 2 (Q2, B). Note: SE, standard error term based on mixed analyses estimates.

to the location of the pain-US, participants still move overall faster than during the movement that was never associated with pain.

3.2.3 Force

There was no evidence for differential acquisition with regard to exerted force, Block × Stimulus Type × Quadrant, $F_{(2,18)} = 1.8$, $p = 0.19$, $\eta_p^2 = 0.17$ (see Fig. 5). We conducted planned comparisons at the end of acquisition. Here we did find evidence for differential acquisition: CS+ movements tended to be performed with more force than CS− movements, $F_{(1,19)} = 4.84$, $p < 0.05$.

In addition, force production across time differed between the two quadrants, Block × Quadrant, $F_{(2,18)} = 6.27$, $p < 0.01$, $\eta_p^2 = 0.41$. Consequently, analyses were run for each quadrant separately. There were no significant main or interaction effects in Q1 (all $F < 1$), but overall force production increases across time in Q2, Block, $F_{(2,18)} = 6.69$, $p < 0.01$, $\eta_p^2 = 0.43$.

Following the evidence for differential acquisition, we also investigated extinction. We observed successful extinction, Block × Stimulus Type, $F_{(2,18)} = 4.02$, $p < 0.05$, $\eta_p^2 = 0.31$. Planned comparisons indicate that there were no longer differences in exerted force between CS+ and CS− movements by the end of extinction, $F_{(1,19)} = 0.35$, $p = 0.56$.

In summary, these findings are in line with the velocity results, indicating that movements associated with pain are performed with more force than movements that are not associated with pain and that this difference disappears during the extinction phase.

3.2.4 Angle difference

With regard to angle difference, the difference between CS+ and CS− movements seems to depend

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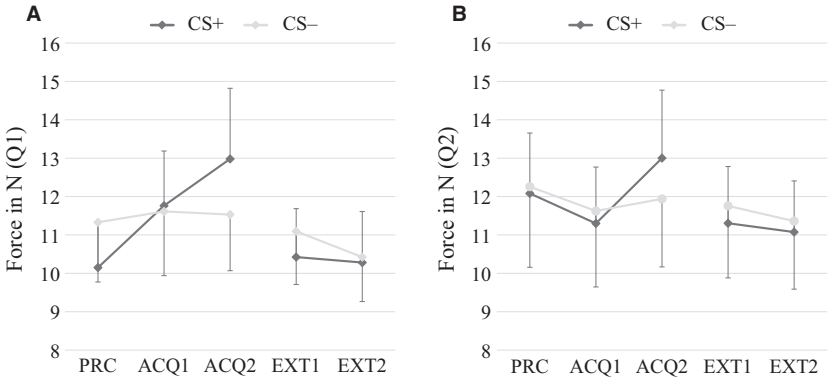

Figure 5 Mean force (in Newton) (+SEs) during acquisition (ACQ1/ACQ2) and extinction (EXT1/EXT2) for movements associated with pain (CS+) and movements not associated with pain (CS−), in quadrants 1 (Q1, A) and 2 (Q2, B). Note: SE, standard error term based on mixed analyses estimates.

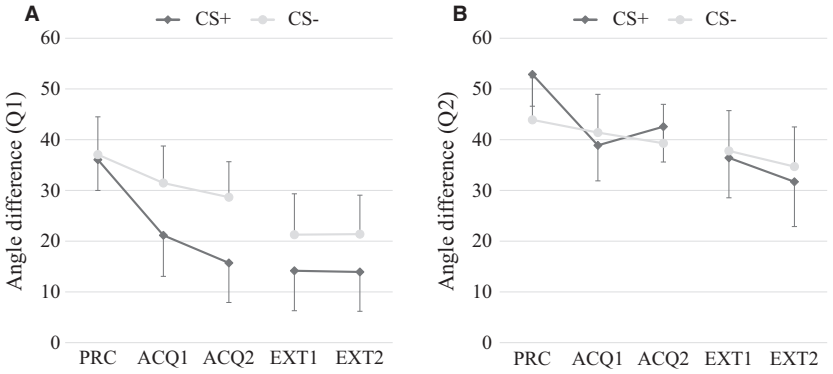

Figure 6 Mean angle difference (in degrees) (+SEs) during acquisition (ACQ1/ACQ2) and extinction (EXT1/EXT2) for movements associated with pain (CS+) and movements not associated with pain (CS−), in quadrants 1 (Q1, A) and 2 (Q2, B). Note: SE, standard error term based on mixed analyses estimates.

on the quadrant, Quadrant × Stimulus Type, $F_{(1,19)} = 4.72$, $p < 0.05$, $\eta_p^2 = 0.20$ (see Fig. 6). In Q1, planned comparisons indicated that by the end of acquisition CS+ movements were associated with a smaller angle difference than CS− movements, $F_{(1,19)} = 5.07$, $p < 0.05$, although this effect is no longer statistically significant when Holm-Boferroni correction is applied. In Q2, there was no difference between CS− and CS+ movements at the end of acquisition, $F_{(1,19)} < 1$, $p = 0.48$.

Overall, angle difference decreased during extinction, Block, $F_{(2,18)} = 3.75$, $p < 0.05$, $\eta_p^2 = 0.29$, and angle difference was larger in Q2 compared to Q1, Quadrant, $F_{(1,19)} = 13.69$, $p < 0.01$, $\eta_p^2 = 0.42$.

In conclusion, the start of movements associated with pain (Q1) was performed more accurately (i.e. smaller angle difference) than movements that were not associated with pain, whereas there was no difference in performance between these movements immediately prior to the point where the painful stimulus was administered (Q2).

4. Discussion

The current study introduced a novel paradigm using the HapticMaster (HM), a force feedback robotic arm, to study changes in motor behaviour following the acquisition of pain-related fear using a fear conditioning paradigm. We hypothesized that pairing a movement (CS+) with pain would lead to (1) the acquisition of pain-related fear, (2) the acquisition of avoidance tendencies and, (3) changes in motor behaviour, specifically in velocity, acceleration, exerted force and force direction. In addition, we hypothesized that (4) these differences would diminish when the movement is no longer paired with the pain-US.

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We found support for *hypothesis 1*: Participants reported increased pain-related fear in response to movements that were paired with a painful electrocutaneous stimulus compared to movements that were never paired with such a stimulus. This extends the findings by Meulders et al. (2011) by showing that fear of movement-related pain can be acquired via associative learning pathways, even when participants could not rely on visual feedback.

We also found support for *hypothesis 2* and *hypothesis 4*: Participants reported a higher urge to avoid movements associated with pain than movements not associated with pain. In addition, we showed complete extinction for the urge to avoid but only partial extinction for pain-related fear, when the CS+ movement was no longer paired with a painful stimulus. In other words, although the desire to avoid movements associated with pain fully extinguished when the movement was no longer paired with pain, participants still indicated higher fear for formerly painful movements. Consequently, it might be worthwhile to include avoidance ratings in future research investigating differential fear acquisition, in order to distinguish between beliefs about the threat value of movements versus the behavioural intentions regarding these movements.

Third and most importantly, we were interested if the acquisition of pain-related fear would lead to changes in motor behaviour. To this end we assessed velocity, acceleration, exerted force and force direction. We found support for *hypothesis 3*: Movements that had been paired with pain were performed differently than movements that had never been associated with pain. Specifically, movements associated with pain were performed faster, more forcefully and more accurately than movements not associated with pain.

This finding is noteworthy for several reasons: We demonstrated changes in motor behaviour, despite the fact that pain in this study was unavoidable and inescapable. That is, even though participants could not actually avoid pain, they still adapted their movement pattern following fear acquisition. This finding fits with the current idea that emotions such as fear are primarily action tendencies (Krypotos et al., 2013). In this case, a feared CS per definition also produces avoidance tendencies, even if the threatening US cannot be avoided or be escaped from (Krypotos et al., 2013, 2015; Volders et al., 2015). Krypotos et al. (2013) have shown previously that such tendencies can be acquired by mere associative learning and are sensitive to Pavlovian extinction. Our current findings support this notion.

Alternatively, it could be speculated that, because participants had no option to actually avoid the pain-US, they employed a *'get it over and done with'* logic and completed the movement as quickly and accurately as possible. In the context of threat-imminence and defense-cascade models (Hagenaars et al., 2014; Krypotos et al., 2015), this behaviour could be conceptualized as *escape* behaviour intended to minimize the harmful event (i.e. the painful movement) (Low et al., 2015). According to these models, an ongoing threat (e.g. performing a painful movement) would elicit an *escape/flight* response, whereas the anticipation of an imminent threat (e.g. anticipation of a painful movement) would elicit avoidance behaviour.

However, technically speaking, the behaviour displayed here cannot be described as genuine escape behaviour, because the behaviour cannot terminate an ongoing noxious stimulus (pain-US). Rather, it minimizes the duration of the painful, aversive movement (CS+). Moreover, it should be stressed that we tested the response of pain-free participants to an acute pain stimulus. In this sense, changes in motor behaviour might be adaptive and whether they are indicative for clinically relevant escape or avoidance behaviour in the context of chronic pain remains to be seen.

Similarly, our findings differ from previous research investigating changes in motor behaviour in clinical samples (Thomas et al., 2008a,b). Whereas other studies showed that patients with low back pain perform feared movements slower, possibly to avoid harm, we found the opposite pattern: Pain-free participants performed movements associated with pain faster, more forcefully and more accurately than movements not associated with pain. This difference might indicate a more adaptive change in motor behaviour in response to pain in pain-free participants compared to a clinical sample.

Similarly, and in support of *hypothesis 4*, we found that these changes in motor behaviour are sensitive to extinction, indicating a flexible, adaptive response to painful movements: When movements that were formerly associated with pain were no longer paired with the pain-US, differences in motor behaviour diminished as well. In this sense, a flexible adjustment of movement based on experiences with pain might be adaptive, whereas a prolonged and inflexible change in motor behaviour might aid in the development and maintenance of chronic pain and associated disability (Vlaeyen and Linton, 2000; Thomas et al., 2008a). However, since the current study focused on pain-free participants and their response to phasic experimental pain, this is speculative.

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There are a few important strengths about the current experiment and the paradigm itself. *First and foremost,* we have demonstrated that the acquisition of pain-related fear in pain-free participants leads to changes in motor behaviour and that these changes diminish when a movement is no longer associated with pain. *Second*, we have shown that the HM can be used to experimentally study the acquisition and extinction of pain-related fear. We showed that pain-related fear can be acquired based on haptic feedback alone, representing a cross-paradigm replication of earlier studies (Meulders et al., 2011).

Third, the use of the HM allows the combination of self-report with relevant behavioural measures and possibly physiological measures, allowing us to scrutinize the dynamic interplay of behavioural and psychophysiological protective responses related to pain-related fear. To our knowledge, this was one of the first studies to directly assess changes in motor behaviour following acquisition of pain-related fear. In the future, the HM could be used to measure and quantify clinically relevant indicators of protective behaviour such as guarding (van der Hulst et al., 2010), safety seeking behaviour (Tang et al., 2007) or avoidance/escape behaviour (Dannecker and George, 2009).

Fourth, the presented paradigm has the unique potential to create ecologically valid experimental manipulations. For instance, the HM allows for movements in three-dimensional space and it can be combined with virtual reality in order to create (clinically) meaningful and immersive environments and settings (e.g. reaching for or lifting virtual objects). This has already been done in the context of rehabilitation (Houtsma and Van Houten, 2006; Timmermans et al., 2014), demonstrating the clinical utility of the HM. The possibility to precisely capture numerous behavioural variables also demonstrates the usefulness of the HM in experimental pain research or treatment outcome research. The present study is a first step in this direction.

Some limitations of the present study should be considered as well. *First*, the movements in the current study were limited to the horizontal plane and participants were not able to deviate from a predefined, circular path and to actually avoid the pain-US. While this might limit ecological validity, it allowed us to test whether there is a change in motor behaviour following fear acquisition independent of instrumental reinforcement (e.g. fear reduction), which indeed turned out to be the case. Future studies could remedy this by increasing the degrees of freedom during the movements (e.g. three-dimensional space without a predefined path) (see also Meulders et al., 2016). *Third*, since there was very little prior research on changes in motor behaviour following fear acquisition in the context of pain, the analyses in the present study are explorative and interpretations are speculative, with the aim to inform future research. In addition, the sample size was relatively small, meaning that the results presented here should be replicated and interpreted with caution. *Fourth*, it should be noted that in the present study, trial type was blocked. That is, a single block only consisted of either CS+ or CS− trials. As a consequence, one might expect that learning rates differ in comparison to studies which used an intermixed trial procedure, such as in Meulders et al. (2011). Even though differential learning of pain-related fear at the end of blocks was similar to studies using an intermixed trial procedure, the underlying learning process itself might differ (López et al., 1998). Unfortunately, since the present study did not include any online measurements during blocks, we cannot directly investigate these differences.

In summary, the present study shows promising evidence for a new method to study pain-related fear and associated changes in motor behaviour. We successfully employed the HM in a pain-relevant fear conditioning paradigm, investigating the acquisition and extinction of pain-related fear and associated changes in motor behaviour using self-report and behavioural outcome measures. Movements that were associated with pain were also associated with increased levels of self-reported fear and desire to avoid and interestingly, changes in motor behaviour such as increased speed, exerted force and accuracy.

Future studies could adapt this paradigm to study generalization of pain-related fear (Meulders et al., 2013), add physiological outcome measures (e.g. eye blink startle), study clinical populations and increase the ecological validity of the paradigm by means of virtual reality and using the three-dimensional movement space. Especially, considering the lack of valid experimental paradigms to study changes of motor behaviour in the context of pain, the use of robot-generated force feedback seems a promising new avenue to investigate the effect of acute and chronic pain on several behavioural variables in an ecologically valid and clinically relevant setting.

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Author contributions

All the authors discussed the results and commented on the manuscript.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. The four possible block-randomization schemes.

Table S2. Kinematic data in the four quadrants.

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