PAIN IN CONTEXT: CUES PREDICTING A REWARD DECREASE FEAR OF MOVEMENT RELATED PAIN AND AVOIDANCE BEHAVIOR

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Abstract

Previous research shows that goal-directed behavior might be modulated by cues that predict (dis)similar outcomes. However, the literature investigating this modulation with pain outcomes is scarce. Therefore, this experiment investigated whether environmental cues predicting pain or reward modulate defensive pain responding. Forty-eight healthy participants completed a joystick movement task with two different movement orientations. Performing one movement was associated with a painful stimulus, whereas performance of another movement was associated with reward, i.e. lottery tickets. In a subsequent task, participants learned to associate three different cues with pain, reward, or neither of the two. Next, these cues were integrated in the movement task. This study demonstrates that in general, aversive cues enhance and appetitive cues reduce pain-related fear. Furthermore, we found that incongruence between the outcomes predicted by the movement and the cue results in more oscillatory behavior, i.e., participants were more willing to perform a painful movement when a cue predicting reward was simultaneously presented, and vice versa. Similarly, when given a choice, participants preferred to perform the reward movement, unless there was an incongruence between the outcomes predicted by the movements and cues. Taken together, these results provide experimental evidence that environmental cues are capable of modulating pain-related fear and avoidance behavior.

Keywords*:* Fear; pain; classical conditioning; instrumental learning

Introduction

Being goal-directed, and simultaneously pursuing multiple goals is a characteristic of human life (Emmons, 1986). Recently, theorists have argued in favor of a motivational approach which considers pain and suffering in the context of multiple demands (Eccleston & Crombez, 1999; Van Damme, Crombez, & Eccleston, 2008; Vlaeyen & Linton, 2012). Indeed, evidence is accumulating that attention to pain, pain-related fear and pain avoidance are not static, but profoundly affected by the presence of other, competing goals (Claes, Crombez, & Vlaeyen, 2015; Claes, Karos, Meulders, Crombez, & Vlaeyen, 2014; Schrooten & Vlaeyen, 2010; Van Damme, Van Ryckeghem, Wyffels, Van Hulle, & Crombez, 2012). In a context with multiple goals, concurrent goals might conflict with each other, and the presence of a competing goal may impede the pursuit of another goal (Boudreaux & Ozer, 2012; Shah, Friedman, & Kruglanski, 2002). Pain is considered to be a salient and biologically relevant aversive stimulus that most individuals want to avoid, reduce or limit its impact when present (den Hollander et al., 2010; Eccleston & Crombez, 1999; Vlaeyen, 2015). One of the most debilitating consequences of experiencing pain is the withdrawal from other, valued activities. For instance, a recent study demonstrated that introducing an aversive painful stimulus concurrent with a reward, decreases the motivation to put effort in obtaining the reward (Gandhi, Becker, & Schweinhardt, 2013) and that pain or the attention demanded by pain is indeed capable of interfering with other, valued activities (Notebaert et al., 2011). Conversely, engaging in other tasks reduces attention to pain (Schrooten et al., 2012), and even is capable of reducing the experience of pain (Verhoeven et al., 2010), indicating that pleasurable activities can be potent motivators as well. Take for example an individual with a wish to increase muscle tone might persist in exercising, despite the physical distress they experience.

Not only is our behavior characterized by goal-directedness, but it can also be modulated by environmental cues (Doya, 2008). Although previous studies demonstrate the context-dependent nature of attention, fear and avoidance, it is largely unknown how situational factors influence the decision to avoid further harm or to pursue pleasurable activities. One intriguing mechanism that has demonstrated the cue-controllability of behavior is Pavlovian-to-Instrumental Transfer (PIT). PIT refers to the capacity of

Pavlovian cues (conditioned stimuli; CSs) to modulate the vigor of instrumental actions. Two types of PIT can be discerned: When cues predict a similar outcome as one of the instrumental responses, instrumental responding that is associated with that outcome increases, is called specific PIT; whereas a non-selective increase in instrumental responding motivated by a conditioned cue is termed general PIT (Cohen-Hatton, Haddon, George, & Honey, 2013; Holmes, Marchand, & Coutureau, 2010; Talmi, Seymour, Dayan, & Dolan, 2008). The PIT effect is well established in non-human animals (Balleine & Ostlund, 2007; Dickinson & Balleine, 2002; Estes, 1943; Lovibond, 1983; Rescorla & Solomon, 1967), and has also been documented in humans (Bray, Rangel, Shimojo, Balleine, & O'Doherty, 2008; Geurts, Huys, den Ouden, & Cools, 2013; Huys et al., 2011; Staats & Warren, 1961; Talmi et al., 2008), but largely in a context of approach behavior. To date, there is only a limited number of studies investigated the impact of *aversive* stimuli on behavior (Geurts et al., 2013; Huys et al., 2011). Despite accumulating evidence for the importance of environmental influences on behavior, there is a need for more research to further our understanding about the maintenance of dysfunctional avoidance behavior (Lewis, Niznikiewicz, Delamater, & Delgado, 2013; van Meurs, Wiggert, Wicker, & Lissek, 2014).

Therefore, the current experiment was set up to investigate the impact of environmental cues on pain-related responding. For this purpose, we created an experimental set-up following a similar structure as a PIT-procedure, containing an instrumental learning phase, a Pavlovian learning phase, and a subsequent test phase in which the cues were integrated in the instrumental task. Our design is however also conceptually different from a typical PIT procedure. First, we incorporated both pain and reward (lottery tickets) as outcomes associated with the movements. This is relatively novel, as most studies only incorporate appetitive outcomes, and allows us to uncover whether cues predicting pain selectively enhance fear and avoidance of painful movements—resembling a specific PIT effect—, or reduce pleasure and approach for appetitive actions—reflecting a general PIT effect. Second, we included three cues, associated with either pain, reward, or neither of the two, allowing for a direct comparison between different types of stimuli. Non-presentation of a CS serves as a baseline. Furthermore, this design allows creating different types of movement-cue pairings, each possibly producing different types of competition between the outcome predicted by the movement and the outcome predicted by the cue. Previous work in our lab has demonstrated that especially avoidance-avoidance competition—being presented with two negative outcomes—increases fear and avoidance (Claes, Crombez, Meulders, & Vlaeyen, 2015). Third, and most importantly, our main dependent variables are acquired fear responding and avoidance behavior operationalized as choices and response latencies, rather than focusing on free operant responding as is common in PIT-studies. We expected that presenting a cue predicting a painful outcome would generally increase pain-related fear and avoidance, whereas cues predicting reward would generally decrease pain-related fear and avoidance as compared to neutral cues or the absence of cues. Furthermore, we expected that presenting an incongruent cue—that is, presenting a reward cue with the painful movement or a pain cue with the reward movement—would result in more hesitant behavior, as it may bring about both approach and avoidance tendencies (Claes, Crombez, Meulders, et al., 2015).

Methods

Participants

Forty-eight healthy individuals (35 female; mean age 21.42 years [SD = 4.58]) took part in order to earn € 8 or to fulfill course requirements. Exclusion criteria during the recruitment were: insufficient knowledge of the Dutch language, cardiovascular diseases, lung diseases, neurological diseases (e.g. epilepsy), other serious medical conditions, chronic pain, currently experiencing (acute) pain of the wrist or related body regions, being asked to avoid stressful situations by a general practitioner, presence of electronic medical devices (e.g. pace-maker), pregnancy, hearing problems and impaired vision that is not corrected (including color blindness). Some further participants were excluded for a priori stated criteria. One participant was unable to handle the joystick correctly. Another participant failed to learn the necessary contingencies. Two participants indicated that both pain-avoidance and earning tickets were unimportant to them. All participants provided informed consent. The experimenter (female; N.C., L.M.) emphasized that participants could refrain from participating at any time. The Ethical Committee of the Faculty of

Psychology and Educational Sciences of the KU Leuven (Belgium) approved the experimental protocol. The final sample consisted of 44 participants, of which 33 were female (M_{age} = 20.73, SD_{age} = 2.76).

Apparatus

A Windows XP computer (Dell OptiPlex 755, Dell, Round Rock, TX) with 2 GB Random-access memory (RAM) and an Intel Core2 Duo processor (Intel, Santa Clara, CA) at 2.33 GHz and an ATI Radeon 2400 graphics card (Advanced Micro Devices, Sunnyvale, CA) with 256 MB of video RAM was used to run the experiment, which was programmed in Affect, version 4.0. (Spruyt, Clarysse, Vansteenwegen, Baeyens, & Hermans, 2010)

Procedures and Stimuli

We employed a procedure that followed a similar structure as studies on Pavlovian-to-instrumental transfer (Cohen-Hatton et al., 2013; Talmi et al., 2008), which comprises of two different experimental tasks, namely an instrumental joystick movement task (Meulders & Vlaeyen, 2013) and a Pavlovian learning procedure. For an overview of the procedure, see Figure 1/Video 1.

In the *instrumental joystick movement task*, an arrow in the middle of the screen pointing either towards the left or towards the right served as a discriminative stimulus (SD). Participants carried out movements (Response, R) with their dominant hand using a Paccus Hawk Joystick (Paccus Interfaces BV, Almere, The Netherlands). The outcome associated with the movements was either a painful electrocutaneous stimulus (painful outcome; O_p) or lottery tickets (reward outcome; O_r). The painful stimulus (painful outcome; Op) was a 1500 ms Electrocutaneous Stimulus (ECS), consisting of trains of 30 ms sinusoid pulses, administrated on the wrist of the dominant hand through surface SensoryMedics electrodes (1 cm diameter; SensorMedics Corp, San Diego, CA) filled with K-Y gel (Johnson & Johnson, New Brunswick, NJ). The ECS was delivered by an Isolated Bipolar Current Stimulator (DS5; Digitimer ltd, Welwyn Garden City, England). The intensity of the ECS was individually determined during a calibration procedure (see Preparation phase). The reward outcome (Or) always comprised of two lottery tickets with which participants could win a prize worth approximately € 100 that was chosen by the participant out of a list of possible prizes. At the end of the experiment, one participant was selected as the winner of his/her chosen prize. A movement in one direction (e.g., left) resulted in the administration of the O_p, whereas a movement in the other direction (e.g., right) resulted in receiving the O_r.

In the *Pavlovian learning procedure*, circles in three different colors (yellow, pink, and orange) served as conditioned stimuli (CSs). These CSs were presented in the middle of the screen. Each stimulus was followed by an unconditioned stimulus. The unconditioned stimuli (USs) were identical to the O_p and O_r from the joystick movement task. Therefore, we refer to the USs as O_p and O_r. Similarly, the O_p followed one circle (e.g., pink), the O_r another (e.g., yellow), and the last circle was not associated with either of the outcomes (e.g., orange).

In the test phases of the experiment, the CSs were integrated in the instrumental joystick task. For this purpose, we created 6 new SD-CS configurations, namely left-pink, left-orange, left-yellow, right-pink, right-orange, and right-yellow (for an example, see Fig.1 'choice phase'). During choice trials of the transfer phase, participants were presented with juxtaposed SDs, which were either presented without a CS, or accompanied by the pain CS, the reward CS, the neutral CS, with a congruent cue, i.e. the pain-SD with the pain-CS and the reward-SD with the reward-CS, or 3) with an incongruent cue, i.e. the pain-SD with the reward-CS and the reward-SD with the pain-CS (for an example, see Fig.1, 'transfer phase').

-INSERT FIGURE 1/VIDEO 1 ABOUT HERE-

Measures

Self-reported measures

Rating electrocutaneous stimulus. Participants rated the pain intensity ("pain intensity"), unpleasantness ("pain unpleasantness"), and tolerance ("pain tolerance") of the selected ECS using an 11-

point Likert-scale ranging from 0 (not at all) to 10 (very much) immediately after calibrating the stimulus. Pain intensity was also assessed using a verbal rating scale: participants had to select one of four words that matched their experience (“light”-“medium”-“serious”-“enormous”).

Rating lottery ticket. Participants reported how valuable (“ticket value”) and how pleasant (“ticket pleasantness”) they found the tickets using a 11-point Likert-scale ranging from 0 (not at all) to 10 (very much).

Goal measures. Participants a priori indicated how important it was to avoid pain (pain importance), as well as how important it was to earn tickets (ticket importance) on a scale from 0 (not important at all) to 10 (very important). Additionally, participants indicated whether they preferred to avoid pain, to obtain tickets, or considered both equally important.

Manipulation check: pain and ticket expectancy. Participants retrospectively indicated to what extent they expected painful electrocutaneous stimulation (“pain expectancy”) and lottery tickets (“ticket expectancy”) for each SD type and CS type using an 11-point Likert scale ranging from 0 (not at all) to 10 (very much). For this purpose, the SD and/or CS was presented visually, along with the presentation of the question on top of the screen and a rating scale at the bottom of the screen participants could click.

Pain-related fear and eagerness. Participants reported how afraid (“pain-related fear”) and how eager they were to perform the movement (“eagerness”) for each SD type using an 11 point Likert scale ranging from 0 (‘not at all’) to 10 (‘very much’).

Decision making behavior. Participants verbally reported whether or not they wanted to perform the depicted movement in a later phase of the experiment. Participants could either select ‘yes’ or ‘no’ as an answer. ‘Yes’ was coded as 1, whereas ‘no’ was coded as 0. Per block and per SD type and SD-CS configuration, the number of times participants were willing to perform the depicted movement was summated.

Behavioral responses

Decision latency. Decision latency was operationalized as the time from stimulus presentation (SD or SD-CS configuration) until participants indicated whether they would perform the presented movement in a later phase of the experiment.

Choice behavior. On choice trials, participants were given the possibility to perform only one of the movements represented. As an index of choice behavior, the number of times the reward movement was chosen was summated per block and per type of choice trial.

Choice latency. Choice latency was recorded for every choice, and was defined as the time between presentation of both symbols and the performance of the selected movement.

Procedure

The experimenter informed participants that the experiment consisted of 7 phases and lasted about 60 minutes.

Preparation phase. First, the intensity level of the electrocutaneous stimulus was individually determined. The experimenter instructed participants to select a stimulus that was painful and required some effort to tolerate. They were also informed that painful electrocutaneous stimuli of increasing intensity would be administered repeatedly. Participants could indicate when they no longer wanted to increase stimulus intensity, and agreed upon receiving painful stimuli of maximally the selected intensity during the remainder of the experiment. Participants assessed pain intensity, unpleasantness and tolerance of the selected stimulus. Subsequently, participants were informed that they could earn lottery tickets for a lottery during the experiment. With this lottery, they had a chance of winning a prize of their choice, selected out of a list of possible prizes. Participants were informed that the more tickets they earned, the more chances they had to win the lottery. In reality, all participants had an equal chance (2%) of winning the lottery; and only one participant won his/her selected prize. Additionally, participants rated ticket value and ticket pleasantness.

Instrumental acquisition phase. Participants were instructed to perform the movements as indicated by the arrow (SD) as soon as the arrow appeared in the middle of the screen. Prior to the acquisition phase, participants practiced the joystick movements, without the pain and reward outcome. There was one block of 2 left movements, and 2 right movements. Next, participants were informed that one movement (painful movement, M_p) would be paired with a painful outcome of maximally 75% of the selected stimulus intensity, whereas another movement (reward movement, M_r) resulted in receiving lottery tickets. In reality, participants always received the same stimulus intensity, that is, 75% of the selected stimulus intensity. Movements were reinforced in 67% of the trials. This phase consisted of 2 blocks of 3 movements in each movement direction, i.e. 2 (3 M_r, 3 M_p). Upon completion of these blocks, a contingency check was administered. More specifically, participants were presented with each of the SDs, and had to indicate what this movement predicted: pain, reward or nothing. If participants did not learn the associations, participants could perform a maximum of 4 additional blocks. When acquisition was successful, participants assessed pain-related fear and eagerness for both movements. A trial comprised of a 1 s-presentation of the fixation cross, followed by the presentation of the SD, upon which participants performed the depicted movement. Depending on participant's movement speed, movement completion varied in length. Inter Trial Intervals (ITI) were 5s in duration.

Pavlovian acquisition phase. Participants were instructed to look at the middle of the screen, where circles of three different colors would appear. Participants were told that one color would be associated with an electrocutaneous stimulus of maximally 75% of the selected stimulus intensity (CS_p), another color with the lottery tickets (CS_r), and yet another color would not be paired with either of the two ($CS_{neutral}$). Reinforcement rate was 67%. Similar to the previous phase, participants completed 2 blocks of 3 presentations of each CS, that is, 2 (3 CS_p, 3 CS_r, 3 $CS_{neutral}$). Participants could complete up to 4 additional blocks until the contingencies were successfully learned—that is, successfully identified what each of the CSs predicted—or were otherwise excluded from the experiment. Lastly, participants reported pain-related fear for each of the CSs. A trial consisted of a 1 s-presentation of the fixation cross, followed by the presentation of the CS, and a 5s-ITI.

Choice phase. The experimenter informed participants that in this phase, the CSs would be integrated in the movement task. As such, the cues provided a context for their decision behavior. The experimenter requested that participants chose whether or not they would perform the depicted movement in a later phase of the experiment, in which they could receive painful electrocutaneous stimuli of maximally the selected intensity (100%), as well as lottery tickets. However, participants were informed that they would not receive any electrocutaneous stimulation nor lottery tickets when making their choice during this phase. Participants completed 3 blocks of one presentation of both SDs presented alone, as well as all SD-CS configurations. Note that two SDs or two CSs were never presented together. For every trial, decision making behavior and decision latency were recorded.

Acquisition reminder. To avoid extinction of the contingencies, participants completed 1 reinforced trial of each SD movement and each CS.

Transfer phase. The same 8 symbol presentations—both SDs and all SD-CS configurations—as in the choice phase were used. Participants were again requested to perform the movements as indicated on screen. The experimenter emphasized that in this phase participants would be presented with the outcomes again. More specifically, participants were informed that now the painful electrocutaneous stimulus could be their maximally selected intensity, as well that they could earn more lottery tickets. Two different types of trials were presented. First, *standard trials*, in which participants were presented with one symbol presentation and had to perform the depicted movement. For some of the trials, pain-related fear and eagerness were assessed just prior to performing the movement. Second, *choice trials*, in which participants were presented with both movements, presented with or without a CS, and participants had to choose and perform one of both movements (see 2.3 Procedures and Stimuli). In total, participants completed 3 blocks of 2 standard trials per symbol presentation (16 trials), and 1 choice trial per two juxtaposed symbol-presentations (6 trials). During all choice trials, choice behavior and choice latencies were recorded.

Debriefing. Participants were informed about the course of the lottery and were debriefed about the objective of the experiment. Participants could leave their contact information to be contacted if they had won the prize and/or if they wished to be informed about the results of the current study. A winner was selected at random by the computer.

Results

Data processing and statistical analyses

To test our hypotheses, Repeated Measures ANOVAs were carried out for the choice and transfer phase, and when appropriate, were followed up with planned comparisons using a Bonferroni correction. All statistical analysis were run with SPSS 22.0(IBM Corp, 2013). Whenever necessary, Greenhouse Geisser corrections were reported. As a measure of effect size, generalized eta squared (η_G^2) was calculated (Bakeman, 2005; Lakens, 2013; Olejnik & Algina, 2003).

Descriptive statistics

The average intensity of the painful electrocutaneous stimulus was 11.61 mA (*SD* = 5.34). The mean pain intensity was 8.43 (*SD* = 1.07), mean pain unpleasantness 8.5 (*SD* = 1.11), and the mean pain tolerance 8.05 (*SD* = 1.14). The mean ticket value was 6.46 (*SD* = 2.14), and the mean ticket pleasantness 7.52 (*SD* = 1.92). The painful stimulus was considered as more unpleasant than the ticket was considered pleasant, $t(43) = -3.03$, $p = .004$. Similarly, the painful stimulus was considered as more painful than the ticket was considered valuable, $t(43) = 5.56$, $p < .001$. The pain intensity and ticket value were both most often classified as ‘serious’ on a scale ranging from ‘light’ – ‘medium’ – ‘serious’ – ‘enormous’, and no differences in classification for both measurements could be discerned, $\chi^2 = 4.815$, $p = .568$. Additionally, no difference was found between the importance of pain avoidance and winning tickets: 6.91 (SD = 2.31), and 7.18 (SD = 1.77), respectively, $t(43) = -.67$, $p = .507$. Furthermore, 17 participants (38.6 %) considered both goals equally important, 12 (27.3 %) considered pain avoidance more important, whereas the remaining 15 participants (34.1 %) considered obtaining the lottery tickets as more important. As there were no differences between groups, we did not include them in the main analysis.

Manipulation check: pain and ticket expectancy

2 (SD type [reward/pain] × 4 (CS type [reward/pain/neutral/none]) Repeated Measures ANOVAs revealed that participants expected the painful stimulus more for the SD associated with the painful outcome than during the SD associated with the reward outcome, main effect SD type, F (1,43) = 227.63, p < .001, η_G^2= .515. A main effect of CS type, F (3,43) = 41.5, p < .001, η_G^2= .244, was also found, indicating that participants expected the painful stimulus more when the CS_p was presented, compared to one of the other CSs. The SD type × CS type interaction was also significant, F (3,43) = 19.42, p < .001, η_G^2= .082, indicating that a pain CS is associated with a further increase in pain expectancy for both painful and rewarding movements. Similar results were found for ticket expectancy: a significant main effect of both SD type, F (1,43) = 189.84, p < .001, η_G^2= .428, and CS type, F (3,43) = 67.13, p < .001, η_G^2= .309, was found, indicating that participants also successfully learned which SD and which CS predicted the lottery tickets. There was again a significant interaction between SD and CS type, F(3,43) = 15.79, p < .001, η_G^2= .07, showing that when a reward CS was presented, participants expect the reward more for both the painful and the reward movement.

Pain-related fear and eagerness

Figure 2 presents the results for pain-related fear and eagerness. A 2 × 4 × 3 (SD type × CS type × Block) Repeated Measures ANOVAs for *pain-related fear* yielded a main effect of SD type, F (1,43) = 295.13, p < .001, η_G^2= .556, indicating that participants overall were more afraid to perform the painful movement than the reward movement. A main effect of CS type, F (3,43) = 183.05, p < .001, η_G^2=.326, and a main effect of block, F (2,43) = 15.78, p < .001, η_G^2= .033, were found. The interaction between SD and CS type was also significant, F (3,43) = 63.21, p < .001, η_G^2=.121, as was the interaction between SD type and block, F (2,43) = 7.3, p < .001,η_G^2= .009 (See Fig.2, top plane). None of the other interactions were significant. Analysis revealed that participants were most afraid of a painful movement when combined with the CS_p, compared to when the CS is absent, t(43) = 3.14, p < .001, which in turn elicited more fear than when accompanied by the $CS_{neutral}$, t(43) = -3.20, p < .001; the latter did not differ from the CS_r, t(43) = -1.98, p = .054. Similarly, for the reward movement, results showed that when it was combined with the CS_p, participants were more afraid compared to when there was no CS presented, $t(43) = 14$, $p < .001$. There was no difference in reported pain-related fear between presenting the reward movement with a $CS_{neutral}$, CS_r or without a CS, $t < 1$.

Furthermore, the results showed that participants were more *eager* to perform the reward movement than the painful movement, main effect of SD type, $F(1,43) = 289.91$, $p < .001$, $\eta_G^2 = .525$. There was also a main effect of CS type, $F(3,43) = 121.14$, $p < .001$, $\eta_G^2 = .284$. The main effect of block however was not significant, $F(2,43) = 1.67$, $p = .2$, $\eta_G^2 = .003$. There was an SD type × CS type interaction, $F(3,43) = 28.67$, $p < .001$, $\eta_G^2 = = .085$ (see Fig.2, bottom plane), an SD type × block interaction, $F(2,43) = 7.84$, $p < .001$, $\eta_G^2 = .012$, and an interaction between CS type and block, $F(6,43) = 4.62$, $p = .001$, $\eta_G^2 = .009$. The SD type × CS type × block interaction did not reach significance, $F(6,43) = 1.52$, $p = .186$, $\eta_G^2 = .003$. Further analyses revealed that participants were the least eager to perform the *painful movement* when accompanied with a CS_p compared to when there was no CS presented, $t(43) = -9.08$, $p < .001$, which elicited more fear thana $CS_{neutral}$, $t(43) = 4.07$, $p < .001$, which in turn elicited less eagerness than a CS_r was presented , $t(43) = 4.83$, $p < .001$. Participants were the least eager to perform the *rewarding movement* when it was accompanied with the CS_p compared to when there was a $CS_{neutral}$ presented, $t(43) = -9.9$, $p < .001$, which in turn elicited less eagerness than a presentation without a CS, $t(43) = -2.34$, $p < .001$, which did not differ from eagerness reported for the reward movement with the CS_r, $t(43) = 1.02$, $p = .315$.

-INSERT FIGURE 2 ABOUT HERE-

(Avoidant) Decision making behavior

For decision making behavior, 2 × 4 × 3 (SD type [reward/pain] × CS type [reward/pain/neutral/none] × Block [1/2/3]) Repeated Measures ANOVAs showed that there was a main effect of SD type, $F(1,43) = 111.08$, $p < .001$, $\eta_G^2 = .424$, indicating that participants chose to perform the reward movement more often than the painful movement. Furthermore, there was a main effect of CS type, F (3,43) = 70.85, $p < .001$, η_G^2= .2, and an interaction between these variables, F (3,43) = 11.24, $p < .001$, η_G^2= .06. The main and interaction effects with the variable Block were all non-significant. Further analysis that there was no significant difference in the number of times participants indicated wanting to perform the *painful movement* in a later phase when a CS_p was presented compared to the absence of a CS, $t(43) = -1.43$, $p = .16$, which in turn did not differ from the presentation of a $CS_{neutral}$, $t(43) = 1.35$, $p = .183$. Participants however indicated that they wanted to perform the painful movement in a later phase more often when a CS_r was presented, compared to a CS_p: $t(43) = -6.03$, $p < .001$; a $CS_{neutral}$: $t(43) = 5.5$, $p < .001$, no CS: $t(43) = 5.2$, $p < .001$. For the *reward movement*, participants less often indicated that they would perform the movement in a later phase when a CS_p was presented, compared to no CS, $t(43) = -4.48$, $p < .001$, a $CS_{neutral}$, $t(43) = -4.48$, $p < .001$, and a CS_r, $t(43) = -5.2$, $p < .001$. There was no significant difference between the latter three CS types, all $p > .183$. In Table 1, the number of participants (in both frequencies and percentages) choosing to perform the depicted movement in a later phase is presented per SD, CS, and block.

-INSERT TABLE 1 ABOUT HERE-

Decision latency

Repeated measures ANOVAs showed that there was no main effect of SD type, F (1,43) = 1.16, $p = .287$, η_G^2= .001, on the time participants took to make a decision. There was however a main effect of CS type, F (3,43) = 8.46, $p < .001$, η_G^2= .021, and a main effect of block, F (2,43) = 39.1, $p < .001$, η_G^2=.054. We also found an SD × CS type interaction, F (3,43) = 9.22, $p = .001$, η_G^2=.03 (See Fig.3). The other interactions were non-significant.

Planned contrasts revealed that participants were initially (block 1) slower in making a decision when the movement was accompanied with an *incongruent* CS, or in other words, when competition between the pain and reward outcome was introduced into the trial (for the *painful* movement: CS_r vs. CS_p: $t(43) = -3.73$, $p = .001$, vs. $CS_{neutral}$: $t(43) = 3.24$, $p = .002$, and vs. no CS: $t(43) = 3.83$, $p < .001$; for the *reward* movement: CS_p vs. CS_r: $t(43) = 2.06$, $p = .005$, vs. $CS_{neutral}$: $t(43) = 2.18$, $p = .035$, and vs. no CS: $t(43) = 3.49$, $p = .001$). These effects however disappeared over time (cf. block 3).

-INSERT FIGURE 3 ABOUT HERE-

Choice behavior

6 [cue(pain CS/ reward CS/ neutral CS/ without CS/ congruent CS/ incongruent CS)] × 3 (block) Repeated Measures ANOVAs showed that participants chose to perform the reward movement less often when both SDs were presented with their incongruent CS, compared to all other contextual cues, main effect of cue, F (5,43) = 15.43, $p < .001$, η_G^2=.098. There were no significant effects with the block variable, all : $F < 1$. Planned comparisons further corroborated this finding: when comparing the SDs presented with their incongruent CSs to all other pairings, participants chose the reward movement less often, all $p < .001$. Table 2 presents the number (frequencies) and percentage of participants choosing to perform the reward movement per context cue and block.

-INSERT TABLE 2 ABOUT HERE-

Choice latency

RM ANOVAs conducted for choice latency showed a significant main effect of cue, F (5,43) = 10.12, $p < .001$, η_G^2= = .055, a significant main effect of block, F (2,43) = 27.69, $p < .001$, η_G^2=.056, as well as a significant interaction block × cue, F (10,43) = 2.24, $p = .042$, η_G^2=.019. The results for choice latency are presented in Table 3. Moreover, planned contrasts indicate that participants were initially (block 1) slower in deciding which movement to perform when presented with an incongruent cue compared to all other contexts, all $p < .05$.

- INSERT TABLE 3 ABOUT HERE-

Discussion

The current study investigated whether acquired movement-related fear and avoidance behavior increase in the presence of cues that predict a painful outcome, and decrease in the presence of cues predicting a reward. Participants first performed an instrumental joystick movement task, with arrows indicating the to-be-performed movement (SDs). One movement was painful, whereas another was associated with a reward. Thereafter, participants completed a Pavlovian task, in which three different CSs were associated with either the painful outcome, the rewarding outcome or neither of them. Subsequently, these cues were integrated in the instrumental joystick movement task. Participants were presented with the movements, which were presented alone or with one of the CSs. Of particular interest to this study was whether these cues modulate the outcome of instrumental responding in terms of pain-related fear, avoidant decision-making behavior and avoidant choice behavior. Results relating to these questions can be readily summarized. As hypothesized, reported anticipatory pain-related fear for the to-be-performed movement was generally enhanced in the presence of a cue predicting a painful outcome, and in general decreased when accompanied with a cue predicting a rewarding outcome. Regarding avoidant decision-making, participants were overall not willing to perform a painful movement, unless it was accompanied with a cue associated with the reward. However, participants were almost always willing to perform the reward movement, except when a cue associated with pain was presented, indicating that participants show more oscillatory behavior when the outcome predicted by the movement and the outcome predicted by the cue are incongruent. Similarly, when given the choice between performing the painful movement and the reward movement in the presence of cues, participants mostly chose to perform the rewarding movement and thus avoid the painful one. Only when incongruent cues were presented—that is, when the reward cue was paired with the painful movement and the pain cue with the reward movement—participants tended to switch more between performing the painful and reward movement.

Although individuals are confronted with different cues in the environment representing different, sometimes competing demands (Boudreaux & Ozer, 2012), the impact of contextual cues has received little to no attention in the context of pain. The current study is one of the first to help closing the gap in literature on the study of cue-controlled “avoidance” behavior. The findings of the present study provide preliminary evidence that Pavlovian cues indeed influence pain-related fear, thereby further extending existing literature that not only instrumental behavior (Cohen-Hatton et al., 2013; Talmi et al., 2008), but also fear responding and decision making behavior (Balleine & Ostlund, 2007; Bray et al., 2008; Huys et al., 2011) can be cue-controlled. We not only explored the possible detrimental effects of aversive and appetitive cues on responding to aversive movements, but also focused on the possible interference or facilitation of environmental cues with appetitive movements (Karoly & Ruehlman, 1996). The results suggest that not only aversive cues are capable of increasing fear of a painful or rewarding movement, but that they also decrease the positive experience of performing a rewarding movement. These findings extend existing literature and show that that cues associated with pain are capable of interfering with pleasurable activities (Gandhi et al., 2013; Notebaert et al., 2011). Taken together, fear responding and avoidant decision making may dynamically depend on the contextual cues representing different goals, rather than stable responses (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012; Hasenbring, Hallner, & Rusu, 2009; Hasenbring & Verbunt, 2010; Leeuw et al., 2007; Vlaeyen, Crombez, & Linton, 2009). Furthermore, the study provides evidence that when there is a mismatch between the outcome predicted by the cue and the outcome predicted by the response, people hesitate more, and display more oscillatory behavior (Claes, Crombez, Meulders, et al., 2015; Diederich, 2003; Miller, 1944).

Although our findings are in line with literature showing that actions are governed by value—that is, decreased by pain, and increased by reward—as indicated by expectancy-value models and the hedonic principle, alternative explanations might be possible (Higgins, 1997). First, it is possible that there is a difference in the salience and the valence of the outcomes. Indeed, our results indicate a difference in the valence of the painful and reward outcome. Although there is no difference in the importance to obtain the reward versus to avoid pain, strength of valence—equality in desirability—is a key factor to take into account when studying decision making behaviour (Vlaev, Chater, Stewart, & Brown, 2011). Related, we employed primary and secondary reinforcers, rather than reinforcers specific to the task at hand as is common in PIT-research. It might be that pain—which is a primary reinforcer—had a more potent effect than our lottery tickets (being secondary reinforcers). However, previous research in fear and pain conditioning has shown that secondary reinforcers such as monetary rewards can be as effective as primary ones as they both draw their strength from the anticipation of an outcome, rather than from the experience of pain/pleasure (Delgado, Laboulière, & Phelps, 2006; Higgins, 1997), although their effects might differ dependent on the context. Furthermore, although there seems to be an inconsistency in the timing between the administration of pain and the lottery prize, this operationalization closely mimics patients' experiences, as they also often have to choose between short term pain relief and long term goals, such as returning to work (Karoly, 2015). Future studies might benefit from more explicitly studying the differential impact of the valence of the outcomes, for example by installing variation by means of re-evaluation (inflation or devaluation) of the outcomes (e.g., Baeyens, Eelen, Van Den Bergh, & Crombez, 1992).These findings may have some clinical implications, although caution is warranted in generalizing the results to the general or a clinical population. It may be useful to target the motivational context in order to reduce pain-related fear and dysfunctional behavior (Crombez et al., 2012; Van Damme et al., 2008; Vlaeyen & Linton, 2012). More specifically, increasing rewarding activities may also be a factor in inhibiting avoidance behaviors and improving functioning (Gatzounis, Schrooten, Crombez, & Vlaeyen, 2012; Schrooten & Vlaeyen, 2010). Identifying contextual cues affecting pain-related behavior as well as possible underlying mechanisms contributing to differences in behavior warrant further scientific inquiry. An interesting avenue to explore is studying the impact of differences in cue value (Vlaev, Seymour, Dolan, & Chater, 2009). Furthermore, the results of the current study corroborate the use of cognitive-behavioral treatments for chronic pain problems that explore benefits and costs of both pain control and other life tasks to strive towards a resolution of patients' ambivalence and a more flexible goal pursuit (Schrooten, Vlaeyen, &

Morley, 2012). In particular, this study provides experimental evidence for Contextual Cognitive-Behavioral treatments and Acceptance and Commitment Therapy, as these treatment strategies focus on contextual factors, as well as values an individual patient considers important (Schrooten, Vlaeyen, et al., 2012; Vowles & McCracken, 2008).

There are several limitations to this study. First, the sample of the current study comprised of healthy participants, mostly students. Therefore, generalizability of the results to a clinical population or clinical reality may be limited. Second, the current study employed a short electrocutaneous stimulus, and lottery tickets. For chronic (musculoskeletal) pain patients however, pain is often present for long periods of time, and the outcome associated with performing a movement is usually more pain than usual. Similarly, although lottery tickets have been shown efficient reinforcers in laboratory situations (Talmi, Dayan, Kiebel, Frith, & Dolan, 2009; Verhoeven et al., 2010; Vlaev et al., 2009), real life behavior may be influenced by other rewards. Third, although (pain-related) fear is considered to comprise of three different response systems, being verbal responding, escape/avoidance behavior, and physiological responding (Lang, 1968), the latter was not included in current study. Future research would benefit from incorporating a psychophysiological marker of fear in the experimental design, such as the eye blink startle reflex (Lang & McTeague, 2009; Meulders, Vansteenwegen, & Vlaeyen, 2011) and pupil dilatation (Anderson & Yantis, 2012). Lastly, although the procedure is quite similar to Pavlovian-to-Instrumental Transfer (Holmes et al., 2010; Talmi et al., 2008), we focus on the impact of (Pavlovian) cues on responses to signaled painful and rewarding movements, and little on the capacity of these cues to affect free operant responding. Given the possible detrimental impact of avoidance behavior on patients' daily life and pain experience, future studies would merit from further scrutinizing the impact of cues predicting (increases in) pain and reward on avoidance behavior in a context of pain.

Conflict of interest statement

The authors report no conflict of interest.

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Figures

Fig.1. Overview of the procedure. A movie clip of the experimental procedure is available in the online version of this paper by clicking the Figure.

Fig.2. Mean self-reported pain-related fear (top) and eagerness (bottom). Mean scores (± SDs) for both the painful and reward movement per CS type (pain/reward/neutral/none) and per block during the transfer/test phase are presented.

Fig.3. Decision latencies. Average time (± SDs) needed to choose whether or not to perform the depicted movement (in ms) for both SD types (painful/reward movement), all CS types (pain/reward/neutral/none) and per block during the choice phase.

Table 1

Number and percentage of participants that chose to perform the depicted movement per SD, CS, and block during the choice phase

		block 1		block 2		block 3	
SD	CS	Freq	%	Freq	%	Freq	%
Pain	Pain	3	6.8	2	4.5	3	6.8
	Reward	25	56.8	24	54.5	26	59.1
	Neutral	8	18.2	5	11.4	6	13.6
	None	5	11.4	5	11.4	5	11.4
Reward	Pain	25	56.8	21	47.7	20	45.5
	Reward	42	95.5	43	97.7	44	100
	Neutral	39	88.6	40	90.9	39	88.6
	None	39	88.6	40	90.9	41	93.2

Note. Freq = Frequency, number of participants; SD = discriminative stimulus; CS = Pavlovian conditioned stimulus. 44 participants were included in the analyses. The percentage is calculated based on the total number of participants, per SD-CS configuration per block.

Table 2

Number and percentage of participants that chose to perform the reward movement during choice trials of the transfer phase

		block 1		block 2		block 3	
CS1	CS2	Freq	%	Freq	%	Freq	%
Pain	Pain	39	88.6	40	90.9	40	90.9
Reward	Reward	41	93.2	41	93.2	40	90.9
Neutral	Neutral	39	88.6	40	90.9	38	86.4
None	None	43	97.7	43	97.7	42	95.5
Pain	Reward (congruent)	40	90.9	39	88.6	42	95.5
Reward	Pain (incongruent)	27	61.4	28	63.6	31	70.5

Note. Freq = Frequency, number of participants; SD = discriminative stimulus; CS = Pavlovian conditioned stimulus. CS1 refers to CS presented with the pain SD; and CS2 to the CS presented with the reward SD. Forty-four participants were included in the analyses. The percentage is calculated based on the total number of participants, per SD-CS configuration per block.

Table 3

Mean and standard deviations and t-values of planned comparisons for choice time during the first block of choice trials of the transfer phase

		descriptives		Planned comparisons (*t*)				
	Context	M	SD	2	3	4	5	6
1	no CS	922	550					
2	pain	1116	777	1.35				
3	reward	1206	682	2.16*	-0.59			
4	neutral	1200	746	2.09*	-0.56	0.04		
5	congruent	1036	653	0.88	0.64	-1.22	-1.07	
6	incongruent	1760	1316	4.15**	-3.3*	2.52*	2.6*	-3.92**

Note. CS = Pavlovian conditioned stimulus. Congruent refers to the choice trial in which the painful movement was presented with the CS_p and the reward movement with the CS_r; Incongruent refers to the choice trial in which the painful movement was presented with the CS_r and the reward movement with the CS_p. Forty-four participants were included in the analyses.

*$p < 0.05$

** $p < 0.01$

Figure 1

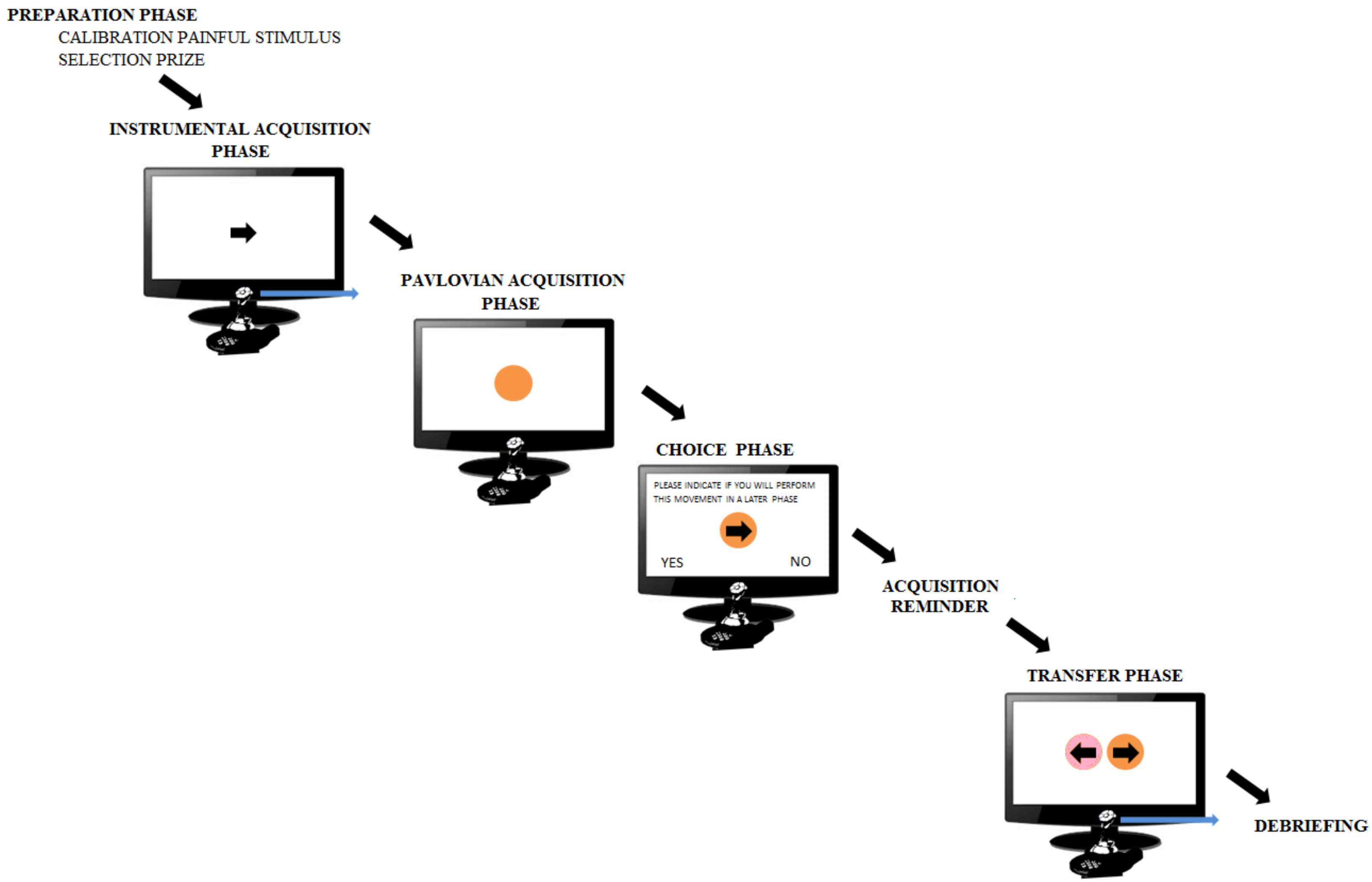

PREPARATION PHASE
CALIBRATION PAINFUL STIMULUS
SELECTION PRIZE
INSTRUMENTAL ACQUISITION PHASE
PAVLOVIAN ACQUISITION PHASE
CHOICE PHASE
PLEASE INDICATE IF YOU WILL PERFORM THIS MOVEMENT IN A LATER PHASE
YES
NO
ACQUISITION REMINDER
TRANSFER PHASE
DEBRIEFING

Figure 2

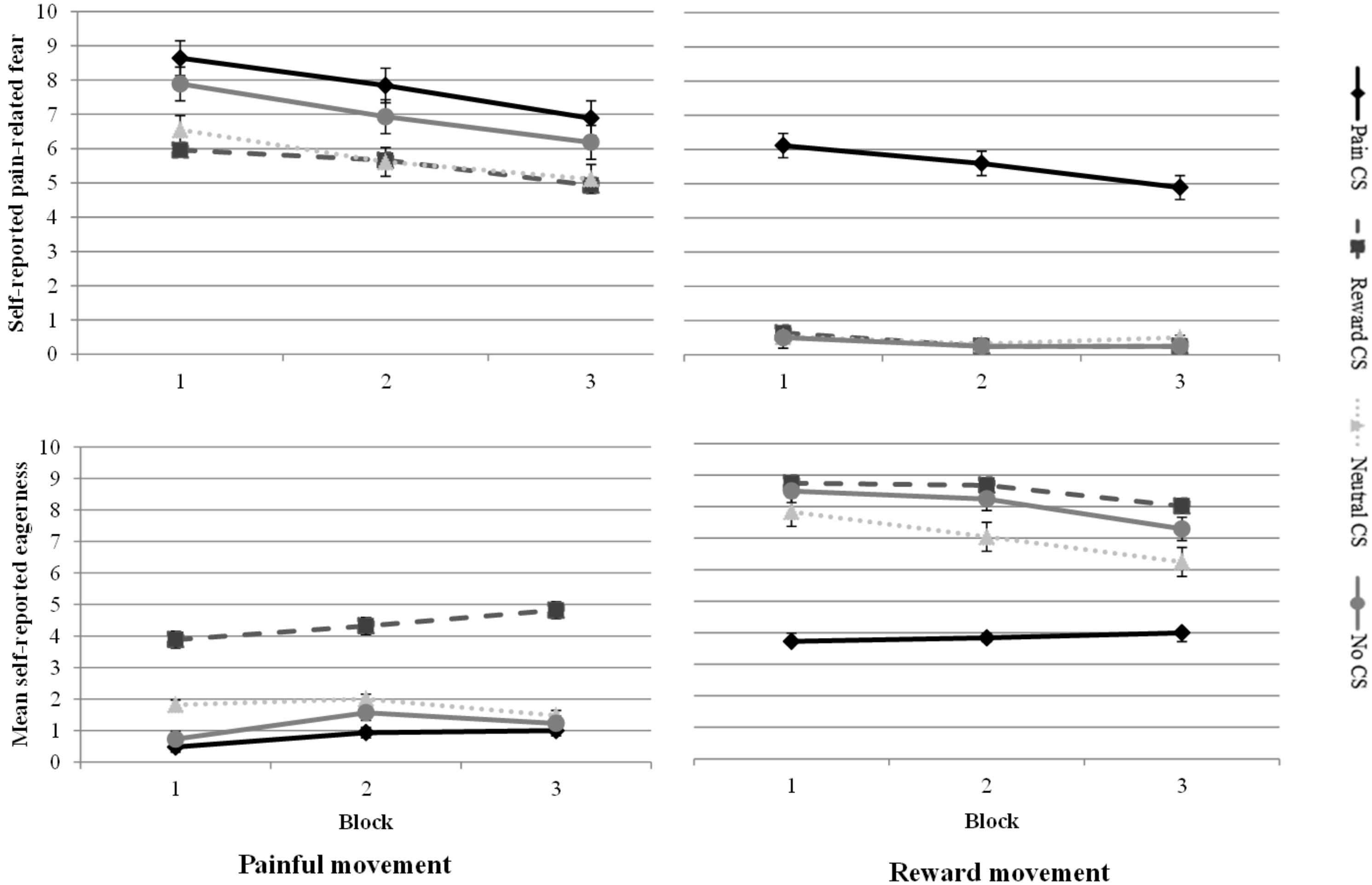
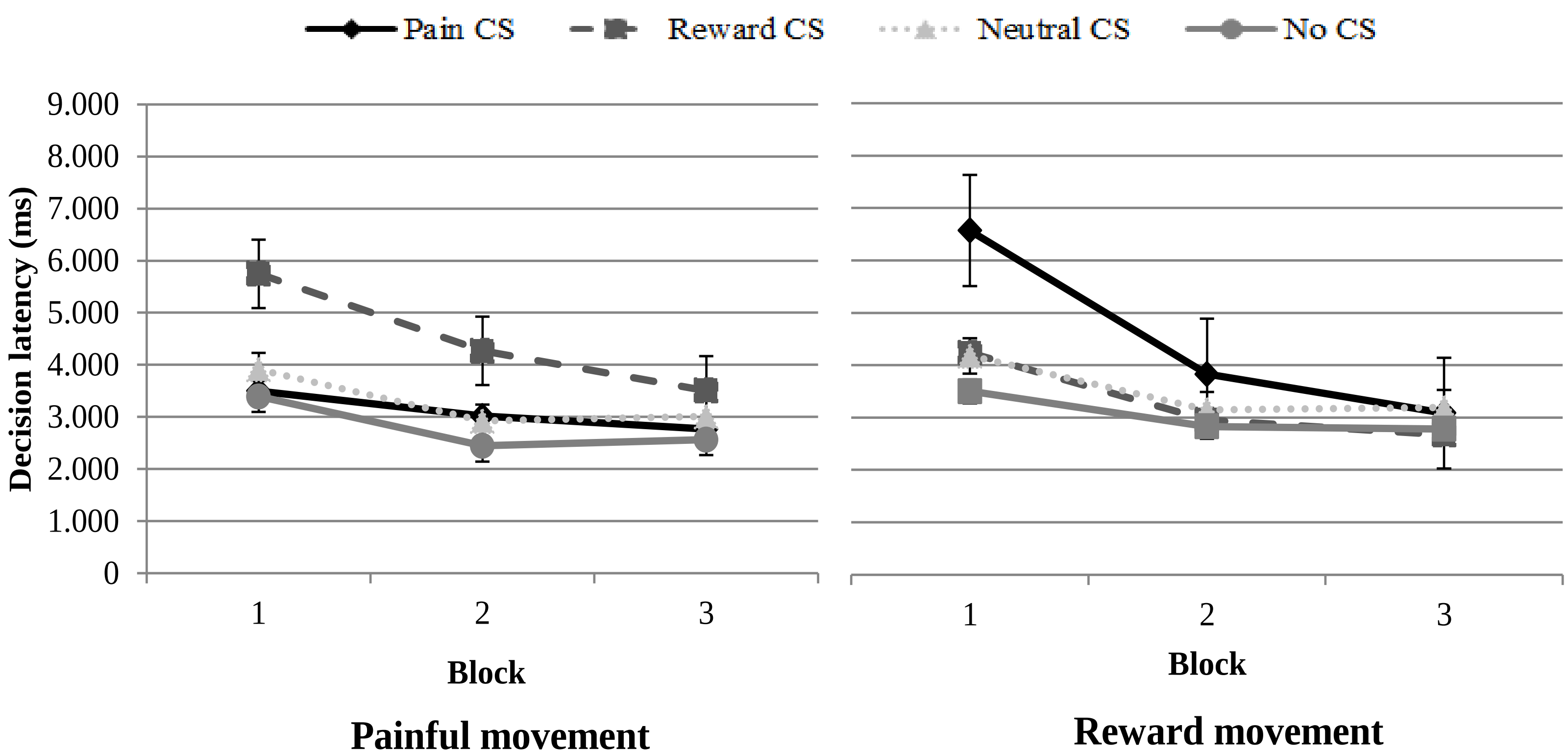

Self-reported pain-related fear
Mean self-reported eagerness
Block
Block
Painful movement
Reward movement
Pain CS
Reward CS
Neutral CS
No CS

Figure 3


Pain CS
Reward CS
Neutral CS
No CS
Decision latency (ms)
9.000
8.000
7.000
6.000
5.000
4.000
3.000
2.000
1.000
0
1
2
3
Block
Painful movement
1
2
3
Block
Reward movement