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Pain relativity in motor control

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Abstract

Motivational theories of pain highlight its role in people's choices of actions that avoid bodily damage. By contrast, little is known how pain influences action *implementation*. To explore this less-understood area, we conducted a study in which participants had to rapidly point to a target area to win money while avoiding an overlapping penalty area that would cause pain in their contralateral hand. We found that pain intensity and target-penalty proximity repelled participants' movement away from pain and that motor execution was influenced not by absolute pain magnitude but by relative pain differences. Our results indicate that the magnitude and probability of pain have a precise role in guiding motor control and that representations of pain that guide action are, at least in part, relative rather than absolute. Additionally, our study shows that the implicit monetary valuation of pain, like many explicit valuations (e.g. patients' use of rating scales in medical contexts), is unstable, a finding that has implications for pain treatment in clinical contexts.

Keywords

relative coding; pain perception; motor control

Pain plays a dominant role in shaping behaviour in health and disease. As the body's primary aversive stimulus, pain signals imminent or actual physical harm, evokes a feeling of unpleasantness, and constitutes a potent learning signal that helps to shape future behaviour toward minimising injury (Craig, 2003, Fields, 2004;). Traditional studies of motivational aspects of pain have concentrated on either subjective rating of unpleasantness (in humans), or on aversive classical and instrumental conditioning (primarily in other species;(Dayan & Seymour, 2008; Price, 2000;). Although these approaches have yielded considerable insight into how pain influences action *choice*, few studies have investigated

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how pain influences action *implementation*. Both action choice and action implementation are central themes in theories of optimal control: action choice is formalised, for example, by reinforcement learning theory (Seymour et al., 2004), and action implementation is formalised by theories of motor control. To see how both factors operate, imagine that you burn your arm while removing bread from the oven. The ensuing pain might influence both your decision to use the oven in the future and the movements you will make when reaching into the oven again. Pain's influence on action implementation, although ubiquitous in ecological contexts, remains poorly understood.

From a functional point of view, pain is often viewed as helping to guide behaviour in an effort to balance an agent's long-term interests and immediate goals. Conventional ideas about the motivational role of pain are based on the assumption that pain provides a signal of an approximate but absolute quantity of ascending nocioceptive input (leaving aside descending modulatory influences that arise in specific circumstances (Fields, 2004)). Optimality requires that pain signals provide an absolute measure of potential bodily damage. For example, from an evolutionary or economic and nutritional standpoint, people should stop gathering or eating a food at exactly the point when the risk of bodily damage outweighs the food's calorific value. Successfully making this type of trade-off via the proxy of experienced pain requires that instances or predictions of bodily damage map consistently onto subjective pain—that is, such ideas assume that pain is absolute, rather than relative.

However, recent studies on explicit decision making when pain is a factor have produced striking results that call into question this assumption about the absolute nature of pain. For example, when people bid money to avoid painful electrical stimuli in an auction paradigm, the financial value they were willing to pay for pain relief was influenced by the amount of a different pain they had recently experienced (Vlaev, Seymour, Dolan, & Chater, 2009). This finding supports theories about relative judgement in explicit affective valuation, as well as theories in perceptual domains such as vision and audition (Laming, 1984; Laming, 1997; Garner, 1954). However, it remains possible that these results reflect a relativistic process related to the construction of explicit valuations, rather than a more fundamental property of pain perception itself. This possibility motivated our experimental approach in the present study, in which we exploited a motor task that obviates the need for explicit judgments (Maloney, Trommershäuser, & Landy, 2007) but nevertheless provides a metric of sensitivity to pain intensity.

In recent motor-control experiments, participants making rapid pointing movements in situations involving risk choose visuomotor strategies that maximized gain (Trommershäuser, Maloney, & Landy, 2008; Trommershäuser, Landy, & Maloney, 2006; Trommershäuser, Maloney, & Landy, 2003a; Trommershäuser, Maloney, & Landy, 2003b). In these studies, participants pointed at configurations similar to the ones shown in Fig. 1b. If participants hit the target area they won a small monetary reward, but if they hit an overlapping or abutting penalty circle, they incurred a small monetary loss. Results showed that participants optimized their mean pointing response according to changes in penalty value. The distance by which participants avoided the penalty region was indicative of how 'bad' they rated the monetary loss. Participants chose pointing strategies maximizing expected gain.

Extending this approach, one can estimate how aversive a shock would be to participants in terms of monetary units by presenting two overlapping regions, one carrying monetary gain, and one carrying immediate shock and measuring how far participants' finger points are repelled from the shock region. A region that carries a higher shock level should repel finger pointing further than a region that carries a milder shock level. This approach provides an

ideal system in which to study the role of pain as a disincentive in motor planning and to test the hypothesis that relative coding of pain intensity is a core property of pain representation.

Method

Participants

Seventeen volunteers (9 males and 8 females, mean age 24 (SD = .74)) were recruited through the participant pool of University College London. All were right-handed or ambidextrous. They gave written consent to participate in the study, were paid between £20 and £32 (depending on performance), and were debriefed after the experiment. The study was approved by the local university ethics committee.

Apparatus and materials

The experiment was conducted using Matlab 6.5 (Math-Works, Natick, MA) and Psychophysics Toolbox Version 2.54 (Brainard, 1997; Pelli 1997) software programs on a computer running Microsoft Windows. Participants sat 70 cm from a 25-in touch screen (Keytec, Inc., Garland, TX). Electrical pain stimuli were delivered and controlled by three DS7 Stimulators (Digitimer, Hertfordshire, United Kingdom), which have been fully approved for clinical use. These apparatuses have been used for various pain experiments (Vlaev et al., 2009; Mobbs et al., 2007). Electrical pain stimulates a broader range of a nocioceptive and non-nocioceptive afferents than, for example, laser or thermal noxious stimulation. Electrical pain offers researchers an advantage over other forms of stimuli because it is largely free of the confounding effects of stimulus habituation or sensitization (McMahon & Koltzenburg, 2005)

General task description

We trained participants to rapidly touch (within 650 ms) a small target area on a computer screen (Trommershäuser, Gepshtein, Maloney, Landy, & Banks, 2005; Gepshtein, Seydell, & Trommershäuser, 2007). Participants earned money by hitting the target area, which carried a fixed known reward of approximately 6 pence per hit (paid at the end of the experiment). Hitting the penalty area resulted in immediate administration of a shock (low, medium, or high level). Participants received both money and a shock if they hit the overlapping region of the target and penalty areas (see Figure 1a). The magnitude of pain varied between trial blocks, and participants learned the magnitude in each block only when they hit the penalty region. Participants received no money or shock if they did not respond within 650 ms. These late responses were indicated by the message "too late" on the screen.

We manipulated the target-penalty distance (near: 6.6 mm; far: 10.56 mm), and the shock level associated with each penalty (low, medium, and high pain). End-point shift-the distance between the center of the target circle and the end point of a pointing movement (see Figure 1c)- was the critical dependent variable. The idea behind the experiment was that penalties should have the effect of repelling a participant's end points away from the penalty region to a degree dependent on the movement inaccuracy for that individual participant. Specifically, we believed that a near penalty region and a higher pain level would be more aversive that a far penalty region (Trommershäuser et al., 2006) and a lower pain level, and would therefore result in larger end-point shifts.

To test for absolute versus relative pain encoding, we presented two shock strengths during each trial block (low-medium, medium-high, and low-high). On each trial, the relative intensity of the shock was indicated by the colour of the penalty area. That is, participants were told that the color of the penalty area indicated whether the higher or lower shock

intensity *in that block* was in effect, but experience alone informed them of the actual intensity.

We assumed that each response would not reflect a summarised coding of two pain intensities within the block. Rather, we assumed that participants' motor system would distinguish the two pain intensities consistently, such that a higher pain level would always be avoided by a greater distance than its lower-level counterpart. The crucial distinction between an absolute and relative model of pain is that this higher-versus-lower pain response pattern applies only within blocks in the case of relative coding, but applies both within and across blocks in the case of absolute coding.

Put differently, according to an absolute-coding model, end-point shifts should depend purely on the absolute pain intensity presented at each trial, and should be independent of the other shock intensity presented in that block. In contrast, according to a relative-coding model, end-point shifts should vary according to a pain's intensity relative to the other pain stimulus occurring in the same block. For instance, a medium intensity stimulus should repel end points to a greater degree if it is the higher of the two intensities in a block (i.e. in a low-medium block) than if it is the lower of two intensities (i.e. in a medium-high block). Figure 2a illustrates the predictions of these hypothesised absolute and relative models.

Stimuli

The visual stimulus presented on each trial consisted of a target and a penalty circle, each of which had a 9.24 mm radius. The target was always an open yellow circle. The penalty was always a filled circle.

Each of the three experimental blocks had two shock levels, which were indicated visually by different colors; different colors were also used in different blocks. For each participant, we randomly chose six penalty colors from among seven colors (excluding four color pairs that could not be visually discriminated easily). This variability in colour coding was made clear to participants; they were able to visually distinguish the target circle from the penalty circle and expected two penalty colours representing different shock levels in each block. Colour coding allowed participants to identify which penalties had a higher pain level within an experimental block; this use of color coding also ensured that the color-pain association did not carry over to other blocks. For example, a blue circle might represent low pain throughout the first block, but in the next block, low pain would be associated with a different color, such as pink. Penalty colors in practice blocks were different from the penalty colors in experimental blocks.

At the start of each trial, a cross $(8mm \times 8 mm)$ appeared at the center of the screen. When participants touched the cross, the stimulus appeared for 650 ms; its location was randomly selected to be 9.9 cm to the left of, to the right of, above, or below the cross.

Procedure

Appropriate shock levels for each participant were calibrated in advance of the trials. Two silver chloride electrodes were placed on the back of the left hand, through which a brief current was delivered to cause a transitory aversive sensation, which feels increasingly painful as the current is increased. We administered shocks, starting at extremely low intensities, and ascending in small steps, until participants reached their maximum tolerance. No shocks above a participant's stated tolerance level were administered. Participants rated each shock on a visual analog score from 0, no pain at all, to 10, the worst possible pain. Their ratings allowed us to determine the appropriate range of current amplitudes to use during the actual experiment and to assign pain levels (low, medium, and high) that were subjectively comparable across participants.

Once their maximum tolerance was reached, participants received 14 random subtolerance shocks that removed expectancy effects created by the incremental procedures. We statistically fitted a Weibull (sigmoid) function to participants' rating for the 14 shocks and estimated the intensities of current that related to three levels of pain (mild: 4, moderate: 6, strong: 8); these intensities were used for the three shock levels (low, medium, and high) in the experiment. Participants were unaware that only three specific amplitudes of current were used during the experimental task. The participants rated the same set of 14 subtolerance shocks in a random order at the end of experiment. A one sample t-test showed that the sum of difference between participants' first and second ratings was not significantly different from zero, t(16) = 1.25, p = .22, which suggests that there was no systematic change between participant' first and second ratings.

To investigate the possibility of adaptation more precisely, we compared the second ratings made by participants who completed the low-medium, medium-high, or low-high block, as their final block in the experiment. If participants had adapted after their final block, ratings made by participants whose final block included low intensities (e.g., the low-medium block) should have been higher than ratings made by participants whose final block included high intensities (e.g., the medium-high block). A Kruskal Wallis (nonparametric) test showed no evidence of such adaptation: The mean rating differences were the same among participants who had just completed the low-medium, medium-high, or low-high blocks; $\chi^2(2 \text{ N} = 17) = .40$, p = .81. These results suggest that there was no significant habituation or sensitization during the experiment.

Participants completed three practice phases and three experimental blocks. During the first practice phase, which had 64 trials (eight repeats of eight stimulus locations), participants learned to point within 650 ms. The penalty area appeared randomly at a 'middle' distance (9.24 mm) to the left or right of the target's center point. Participants then completed the second phase, which was the same as the first phase except that there were 72 trials and participants received a mild shock when they hit the penalty area. In the third phase, the penalty circle was randomly presented either 'near' (6.6 mm) or 'far' (10.56 mm) from the target (Figure 1b). Participants completed 112 trials (seven repeats of 16 stimulus locations). The shock level was the same in Phases 2 and 3, but this level was different from the shock levels in the experimental blocks. Because of the time limit for responding, the task was difficult, and these three practice phases allowed participants to achieve adequate accuracy rates without learning the pain magnitudes to which they would be exposed in the experimental blocks.

There were 128 trials (four repeats of 16 stimulus locations and two pain levels) in each of the three experimental blocks. The order of the experimental blocks was determined randomly for each participant. The experimental blocks represent three pairs of pain magnitudes which allowed us to test whether finger-pointing shifts reflected relativistic or absolute coding of pain magnitudes.

Data analysis

We conducted repeated measures analyses of variance (ANOVAs) with three independent variables: distance (near or far), block (low-medium, medium-high, or low-high), and relative pain (lower or higher within each block). The dependent variables were average end-point shifts from the center of the target (Figure 1c) and reaction times (RTs). F values were calculated under the assumption of sphericity, and we report Greenhouse-Geisser F values when sphericity was violated. Responses on 14% (SD = 2%) of the trials were late (equally distributed across blocks) and these trials were excluded from all analyses. (Data on late trials can be found in Additional Results in the Supplemental Material available online).

All trials during which participants responded within 650 ms (including those with endpoints outside the circles) were included in the analyses.

In principle, stimulus intensity (measured in milliamps) could have been added into the general linear model, although any significant association between stimulus intensity and end-point shifts would vary widely according to factors such as skin temperature, sweating, hydration, sex, skin thickness. Therefore, in line with normal practice in the pain literature, it was not included.

To determine trade-offs between reward and pain, we compared the shifts we observed in participants' response to changes in pain intensity with the strategies of an optimal movement planner maximizing gain. The only free parameter in this comparison was alpha, which represented the pain-pence exchange rate for each shock level. This comparison yielded an estimate for the monetary value of the penalty that corresponded to the movement shift we observed in response to changes in pain intensity. The method for computing this equivalent monetary value is described in Methodological Details in the Supplemental Material available on-line.

Results

As Figure 3 shows, participants hit the target-only area significantly more often than they hit the penalty-only area or the overlapping region, R(1,17.46) = 171.65, p < .00001, $\eta_p^2 = .91$.

We tested whether participants adjusted their end-points according to pain intensity and target-penalty proximity. To do this, we computed pooled-participant mean end-point shifts by calculating the median horizontal end-point shift for each participant in each condition and then averaging these median values across all participants. This value served as an index of how far participants deviated from optimal pointing (Trommershäuser et al., 2005).

An ANOVA revealed that participants displaced their end-point much farther from when the penalty was near the target than when it was far from the target (Figure 2b), R(1,14) = 66.60, p < .00001, $\eta_p^2 = .82$. This finding is consistent with the hypothesis (Trommershäuser et al., 2008) that movement execution incorporates information relating to judged movement variability (noise).

Displacement from target's center also depended on relative pain magnitudes; that is, end-point shift was larger when pain was stronger than when pain was milder, R(1,14) = 4.84, p = .045, η_p^2 .25. End-point shift was not affected by absolute pain intensities. The Block × Relative Pain interaction was not significant; the difference between lower and higher pain was similar across the three experimental blocks (Figure 2c). These results suggest that end-point shift was influenced by *relative* pain intensities. Other effects on end-point shifts were non-significant, $F_8(2, 13) < 3.59$, ps > .057, and R(1, 14) < 2.46, p > 0.13.

We also examined participants' RTs (calculated from when they touched the fixation cross to when they touched the stimulus compound). Participants responded more slowly when the penalty circle was near than when it was far, (see Figure 4b). R(1,14) = 12.32, p = .003, $\eta_p^2 = .46$. RT's were also influenced by block, R(2,28) = 5.2, p = 0.012, $\eta_p^2 = .27$. (see Fig 4a). RT's in the low-high block were significantly slower than RT's in other blocks-low-medium t(14) = 2.7, p = 0.017; medium-high block: t(15) = 2.23, p = 0.041. Participants responded with equal quickness in the low-medium and medium-high conditions, (p > .05). Although Figure 4b suggests that there may be a trend for an interaction, all interaction effects were non-significant, Fs < 0.12, ps > .80. (Further ANOVA data on end-point shifts and RTs in each block can be found in Additional Results in the Supplemental Material available online).

Under the assumption that our end-point displacements corresponded to an optimal pointing strategy that maximised gain (Trommershäuser et al., 2005), we estimated the equivalent monetary value of each shock level to assess participants' trade-offs between reward and pain. Overall, participants consistently experienced higher shocks to be more painful/unpleasant than lower shocks. When converted into a hypothetical equivalent monetary value of pain for an optimal movement planner maximizing gain, the shift in mean motor response to higher shocks corresponded to higher equivalent monetary values than the shift in mean motor response to lower shocks did. (Details about the computation of the monetary values of pain can be found in the Methodological Details in the Supplemental Material available on-line). These results demonstrate that pain can be measured in equivalent monetary values. The results for this implicit measure correspond with those for our explicit measure (pain avoidance in end-point shifts) which suggests that pain is encoded relatively in guiding motor movement. Figure 2d depicts context-dependency of the estimated equivalent monetary values of pain.

Discussion

The data show how previous painful outcomes exert a pervasive influence on future movement control. First, we have shown that higher intensity pain generally has a stronger influence on biasing future movement in a direction away from pain. Second, we have shown that the likelihood of pain, inferred by the proximity of pain to goal target, biases movement in a similar way. This suggests that movement execution incorporates the consideration of both the magnitude and the probability of pain, as predicted by an optimal account of motor control. This helps build a richer picture of the motivational dimension of pain because it shows that pain not only influences decisions about whether or not to perform an action (i.e., escape and avoidance behaviour), but also informs the actual execution of that action.

Our results indicate that the influence of pain is more relative than absolute. That is, relatively intense pain that has been recently experienced has a greater effect on movement control than *relatively* mild pain that has been recently experienced. In addition, these findings suggest that noxious events are represented in relative terms at the level of basic motor control, which is putatively much more fundamental index of the mental representation of such events than subjective ratings are. Our results correspond nicely with the relativistic valuation of pain we (Vlaev et al2009) demonstrated in an economic bidding game (borrowed from behavioural economics). The correspondence between explicit and implicit pain valuation in our study also resembles the correspondence between risk perception as assessed via a classical economic decision-making task and risk perception as assessed via an equivalent motor task (Wu, Delgado, & Maloney, 2009).

Our implicit analysis of monetary values of pain implies that its context effect on movement control could be explained by differential economic values of pain. It is conceivable that people will trade off the amount of pain they will choose to suffer against the amount of money they are willing to pay to relieve that pain (Vlaev et al., 2009). Thus, the relative endpoint shifts we found in this study could partially be explained by the fact that participants' monetary valuation of pain was sensitive to the relative context of that pain.

Two caveats should be noted in relation to the interpretation of our findings. First, it is difficult to rule out the possibility that short-term habituation to pain might have contributed to the relative coding we observed. Although we did not find evidence for habituation over the course of the experiment, it is possible that higher-intensity stimuli cause a relative diminution of pain through habituation effects that operated over the course of each block. Second, according to some accounts of relativity effects, participants use recent experiences

to inform prior expectancies about forthcoming pain (Seymour & McClure, 2008). That is, participants infer distributions of anticipated pain and incorporate these distributions as priors in representational inference about inherently uncertain ascending afferent inputs. Thus, apparent relative effects might emerge not because of a fundamental limitation in people's ability to encode intensity, but because of uncertainty in the ascending input.

Our results have implications for pain in clinical environments. A number of conditions and disorders cause pain that is exacerbated by movement; examples include arising out of peripheral injury (e.g., post-trauma), neuropathic conditions (e.g., complex regional pain syndrome) and central nervous system disorders (e.g., post-stroke pain). Behaviours such as limb guarding (protecting a limb after recent trauma) are pervasive during recuperation and are essentially 'physiological'. In other clinical situations, pain acts as a barrier to optimal functional recovery for the affected limb. Accordingly, an understanding of the exact ways in which pain modulates movement planning and execution can inform therapeutic strategies, particularly in poorly understood (but critically important) areas such as upperlimb physiotherapy. Furthermore, the existence of relative coding might inspire strategies that exploit context effects to improve movement recovery where pain experience is a recognised obstacle.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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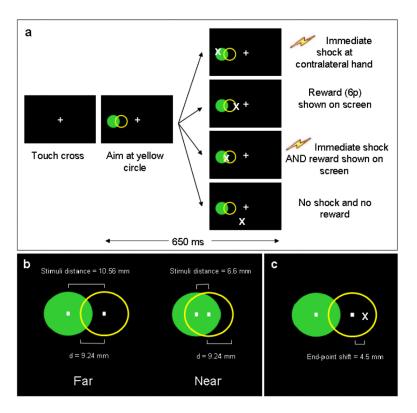


Figure 1. Illustrations of the experimental stimuli, sequence of events in a trial, and main dependent variable. The stimulus compound consisted of an open yellow circle (the target circle) and a filled colored circle (the penalty circle, shown here in green). The hand images indicate the end points of participants' pointing movements, and white squares highlight the centers of the circles. As shown in (a), participants had to touch a central cross to make the stimulus compound appear, after which they had 650 ms to respond to the stimulus. If participants touched the penalty region, they received an electric shock. If they touched the target region, a monetary reward was shown on the screen. Participants received both pain and reward if they touched the overlapping region, and they received neither pain nor reward if they touched the screen outside the target and penalty regions. The illustrations in (b) show the stimulus configurations in the far and near conditions. The measured end-point shift for a given trial (c) was the horizontal distance between the end point of the participant's response and the center of the target region. The illustrations are not to scale.

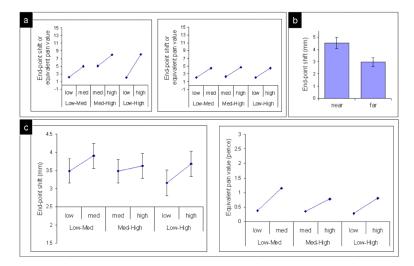


Figure 2.

Context-dependency in motor control for pain avoidance. The graphs in (a) illustrate the end-point shift predicted in the three experimental blocks according to an absolute-coding model (left) and a relative-coding model (right). Increases in end-point shift would be expected to reflect increases in pain magnitude in the absolute-coding model, but in the relative-coding model, increases in end-point shift would be expected to remain identical across experimental blocks. The observed pooled-participant mean end-point shifts are shown as a function of (b) target-penalty distance and (c) pain intensity in the low-medium, medium-high, and low-high blocks. Error bars represent standard errors of the mean. The graph in (d) shows estimated equivalent monetary value of low, medium, and high pain within the low-medium, medium-high, and low-high blocks.

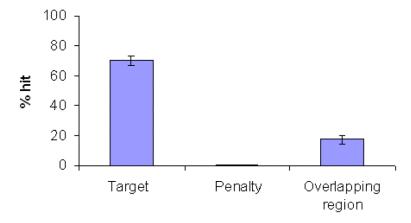


Figure 3. Mean percentages of participants' end points that hit the target-only area, penalty-only area, and overlapping region of the target and penalty areas. Error bars represent standard errors of the mean.

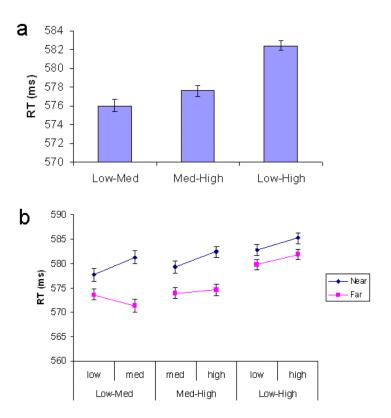


Figure 4.

Reaction times (RTs) The graph in (a) shows pooled-participant mean RT for each of the three experimental blocks (low-medium, medium-high and low-high) and the graph in (b) shows pooled-participant mean RT as a function of target-penalty distance (near vs. far) and pain intensity within each experimental block. Error bars represent standard errors of the mean.