Motor action changes pain perception: a sensory attenuation paradigm in the context of pain

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Total number of pages: 35

Number of figures: 5

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Abstract

A large body of evidence indicates how pain affects motor control, yet the way the motor system influences pain perception remains unclear. We present two experiments that investigated sensory attenuation of pain implementing a two-alternative forced choice paradigm. Particularly, healthy participants received painful stimuli on a moving and nonmoving hand during the execution or the preparation of reaching motor actions. At the end of each trial they indicated on which hand they perceived the stimulus stronger. The Point of Subjective Equality was obtained to measure sensory attenuation. The intensity (experiment 1) and the threat value (experiment 2) of the pain stimuli were manipulated between-subjects to examine their impact on sensory attenuation. Results of experiment 1 (N=68) revealed that executing a motor action attenuates pain processing in the moving hand. Sensory attenuation during motor preparation only occurred with stronger stimulus intensities. Sensory attenuation was not affected by the intensity of the pain stimuli. Results of experiment 2 (N=79) replicated the phenomenon of sensory attenuation of pain during motor action execution. However, sensory attenuation was not affected by the threat value of pain. Together these findings indicate that executing, but not preparing, a motor action affects pain processing in that body part. No significant associations were found between sensory attenuation indices and inhibitory control abilities or pain catastrophizing, vigilance and rumination. These results provide insight in the inhibitory effects of motor actions on pain processing, suggesting that pain perception is a dynamic experience susceptible to individuals' actions in the environment.

1. Introduction

There is abundant evidence that pain affects multiple levels of motor control from motoneuron discharge, muscle recruitment and mechanical/kinematic output [31,32,46] to complex behaviors like avoidance of specific motor actions [17,67]. Less is known, however,

about the effect of motor action on pain. Understanding how motor actions interact with pain perception is important as individuals often face real life situations in which motor actions are required despite pain. In this context, it is well known that the processing of innocuous somatosensory inputs is inhibited by motor actions, a phenomenon referred to as sensory attenuation [2,11]. This has been described as a filtering mechanism optimizing the extraction of sensory information required for motor control [5]. It depends on the dispatch of feedforward motor commands and on the reafferent sensations caused by the body movement, together masking sensory inputs [7,69], and is reflected in slower detection and reduced intensity ratings of somatic stimuli [30,38,68,71,73–75]. There is anecdotic evidence of sensory attenuation with pain stimuli, but experiments are scarce and limited to stereotypical (i.e. simple and repetitive) finger-lifting movements [10,49] that are not representative for common daily life actions (such as reaching). Furthermore, although nociception is a sub-modality of the somatosensory system, pain might be less susceptible to sensory attenuation because it signals potential bodily threat and therefore captures attention [26]. Studies using innocuous tactile stimuli have shown that sensory attenuation is reduced when attention is focused on stimuli in the moving body part, suggesting that attention might counteract sensory attenuation [34,38]. It has been theorized that attentional processing of pain is influenced by various dispositional and situational bottom-up and top down factors [43,53]. Pain intensity is considered an important bottom-up facilitator, with high-intense stimuli more easily capturing attention [14,26,50,56]. Top-down facilitators include dispositional factors such as catastrophizing [19,61], vigilance [4,58,70] and rumination [8,41], as well as situational factors such as a threatening context, known to enhance pain processing [3,15,33,72]. On the contrary, inhibitory control is positively associated with the ability to focus on a task despite pain and a decrease in pain intensity and sensitivity [6,39,48,66]. To which extent these factors modulate sensory attenuation of pain by motor action is, however, unknown. The current studies aimed,

firstly, to examine how pain processing is affected during different phases of motor actions. Secondly, they aimed to examine the role of potential moderators of sensory attenuation. In two experiments, participants were administered simultaneous pairs of painful stimuli to both hands during preparation or execution of motor actions. Participants indicated on which hand the stimulus was felt stronger to obtain sensory attenuation indices. We hypothesized sensory attenuation of pain stimuli on the hand preparing for and executing motor actions. Furthermore, we expected facilitators of pain-related attention (pain intensity [experiment 1], threatening context [experiment 2], rumination, pain catastrophizing and vigilance) to enhance pain processing and attenuate sensory attenuation. Finally, we expected inhibitory control to facilitate focus on the movement and to attenuate pain processing, resulting in stronger sensory attenuation.

2. Experiment 1

2.1 Participants

97 right-handed participants (67 women) gave their informed consent before taking part in the experiment. Sample size calculation was performed with GPower software (G*power 3.1; [28]). Particularly, to obtain 80% of power for a medium effect size, a total sample size of at least 77 participants was needed. A final sample size of 97 participants was recruited and tested to account for potential dropout. Participants were recruited via an online research participation system (Sona) within the Ghent University network and via social media. Exclusion criteria were having articulation problems affecting the motor system, pregnancy, presence of clinical electronic devices, color-blindness, neurological or psychiatric diagnosis (current or previous), epilepsy, chronic pain condition, or being left-handed. Participants were compensated with a monetary incentive (15 Euros) or with course credits. They were not aware of the aim of the study until the end of the experiment. Participants were informed about the potential discomfort of pain stimuli before signing the informed consent. Both studies were conducted in accordance with the principle of the Declaration of Helsinki and the protocol was approved by the local ethical committee (number 2017/102). The research protocol was pre-registered before the start of data collection on Open Science Framework (<u>osf.io/3huas</u>). Three participants were excluded in the analysis because of technical problems and one because of left-handedness.

2.2 Materials

2.2.1 Painful stimuli

Painful stimuli consisted of electrocutaneous stimuli (ES bipolar, frequency 50Hz, 500 ms). A constant current stimulator (DS5; Digitimer Ltd, Hertfordshire, United Kingdom) and four lubricated Medcat Ag/ClAg surface electrodes (1 cm diameter; Antwerp, Belgium) were used to administer the painful stimuli. The electrodes were attached to the skin of the participant next to the ulnar styloid bone of both the hands using double-sided taper rings [22,54]. The intensities for the pain stimuli were determined following a three-steps calibration procedure. First, each participant's tolerance to the stimuli was measured with a manual staircase procedure. The experimenter first gave oral instructions and subsequently started administering manually stimuli at 0.5 mA (as an initial familiarization with the type of stimulation used in the experiment) and then at 1mA. Subsequently, the intensity was increased each time by 1mA until the participant verbally reported his/her tolerance. Tolerance was explained and defined as the intensity that was as painful as possible, but that the participant was still willing to tolerate. Secondly, a calibration procedure was conducted for each participant. With this procedure, 20 random stimuli were administered at a random intensity between 0.25 mA and the tolerance of each participant, using INQUISIT Millisecond software package (Version 5). After each stimulation, participants gave a rating from 0 to 100, answering the question "How painful was this stimulus?" (0 = "not painful at all") and 100 =

"very painful"). Given that participants were aware that the most intense stimuli they could receive during the experiment were stimuli within the range of their pain tolerance intensity, they were asked to base their ratings on that range. From these ratings, 10 intensities (in mA) that corresponded to a scale of subjective pain intensities were estimated per participant using a linear trend line starting from dependent y-values (ratings) and independent x-values (mA), returning a given number of values along the trend line (subjective 1-10 scale) [47]. All these procedures were performed on the right hand. Third, a staircase procedure was implemented to make the pain stimulus intensity of the right hand equal to that of the left hand. During this procedure, the right hand and it was used as reference to find the threshold intensity at which the pain on the left hand was reported to be the same as the pain on the right hand. With this purpose, intensities on the left hand were increased/decreased by 0.5 mA first and then by 0.1 mA, until the matching self-reported threshold was found.

2.2.2. Sensory attenuation task

The stimuli and the main tasks were presented on a laptop (DELL, Windows 10, 34 * 27 cm). The motor task was programmed in INQUISIT Millisecond software package (Version 5). During the task, participants comfortably sat in front of a computer screen. Participants were instructed to use their right, dominant hand to reach a point indicated on the desk (white cross). The movement was performed after a visual cue was presented. The visual cue consisted of a bar (10 x 1 cm) presented horizontally in the central bottom of the screen (screen coordinates 50, 75). If a green bar was shown, participants were instructed to perform the reaching movement as soon as the green bar disappeared from the screen. If a red bar was presented, participants were instructed not to move and remain in the starting position. The visual cue was presented on the screen for 5000 ms. During the task, the left hand (reference hand), remained at rest during the entire procedure and the movement was always performed

with the right hand. During each trial, two painful stimuli were administered simultaneously, one to the left and one to the right hand. The stimuli were administered either at the exact moment the bar disappeared (motor preparation phase and rest) or when the movement was initiated (motor execution phase). To do so, an optical sensor box was used to monitor a) that at the beginning of each trial participants hands were in the correct starting position, and b) to detect movement onset in order to administer the stimuli during the execution of the movement. If participants' hands were not in the correct position at the beginning of the trial, a message appeared on the screen inviting them to replace their hands in the correct starting position. If participants moved too fast (before the bar disappeared), a message saying "too soon" was presented and they had to perform the trial again after re-placing their hands in the correct position. During the task, a total of 150 trials were presented, randomized across three withinsubjects experimental conditions (50 trials per movement phase: motor execution, motor preparation, and 50 for rest). Furthermore, 6 practice trials (2 per each condition) were included at the beginning of the task.

Sensory attenuation of pain was measured using a two-alternative forced choice (2AFC) paradigm, which has been previously implemented to investigate attenuation of vibrotactile somatosensory stimuli [68,69]. In the 2AFC paradigm participants are given two options and they have to choose one of them based on a perceptual criterion. In this study, participants are asked to indicate on which hand the painful stimulation was perceived stronger using the right or the left arrow on the keyboard. As the stimuli of the left hand were used as reference stimuli, the stimuli administered on the left hand were set at a fixed intensity, while the intensity of the stimuli on the right hand (test hand) was randomly varied from trial to trial. Five different stimulus intensities were applied to the right hand using the constant stimuli trials' placement method (i.e. the 5 stimulus levels were preset before the experiment). Intensities in the test hand could be lower, higher or equal to the intensities on the reference hand. With this paradigm, the Point of Subjective Equality (PSE) is computed to extract indices of sensory attenuation (for a detail description of the computation of the sensory attenuation indices, see *"2.4. Outcomes"* section).

In experiment 1, the experimental design also included a between-subjects manipulation: participants were randomly assigned to either the low pain intensity group or to the high pain intensity group. In the low pain intensity group, the levels of painful intensity used in the task were 2, 3, 4, 5 and 6 in the right hand and 4 in the left hand. In the high pain intensity group, the levels of painful intensity used in the task were 4, 5, 6, 7 and 8 in the right hand and 6 in the left hand. The paradigm and the experimental set-up are visually represented in *Figure 1*.

****Figure 1****

2.2.3. Psychological trait questionnaires

After the experiment, participants filled in the Dutch version of the following questionnaires. Pain vigilance was assessed with the *Pain Vigilance Awareness Questionnaire* (PVAQ; McCracken, 1997). This is a measure of awareness, consciousness and vigilance to pain (Cronbach's alpha r= 0.86 and test–retest reliability r= 0.80, [51]). The PVAQ consists of 16 items rated on a 6-point scale with anchors ranging from 'never' to 'always'. Participants are asked to answer considering their behavior over the last 2 weeks. Ruminative style of thinking was measured with the *Perseverative thinking questionnaire* (PTQ; [27]). It assesses dysfunctional aspects of Repetitive Negative Thinking (RNT, Cronbach's $\alpha = 0.95/0.94$; [27]). RNT as relevant to emotional problems is a style of thinking about one's problems (current, past, or future) or negative experiences (past or anticipated) that is experienced repetitive, intrusive, and difficult to disengage from. In this questionnaire participants are asked to rate each item on a scale ranging from '0' (never) to '4' (almost always). Pain catastrophizing (or pain-related worrying [18]) was measured with the *Pain Catastrophizing Scale* (PCS; [60]),

participants are asked to refer to recent painful experiences and report the intensity of painrelated thoughts and feelings on a 5-point scale. The PCS consists of 13 items and evaluates 3 subscales associated with pain (magnification, rumination, and helplessness; Cronbach's alpha = 0.85; [16]).

2.2.4. Inhibitory control assessments

Inhibitory control abilities were assessed using the Stop Signal task [44] and the colorword Stroop test [59]. In the Stop Signal Task [65], participants look at a fixation circle, subsequently, an arrow (5x5cm, presented in the center of the screen) that points either left (half of the trials) or right (half of the trials) is shown. The task consists of pressing the left or the right response key (D or K key on an AZERTY keyboard), depending on the direction of the arrow. In case an auditory beep is presented after the arrow, participants have to inhibit the response. Participants are required to respond to the stimulus as fast and accurately as possible and they can respond until the next trial starts. The delay between presentation of arrow and signal beep is first set at 250 ms. Subsequently, it is adjusted up or down (by 50 ms) depending on performance accuracy. In case of successful performance, the delay gets longer (+1150 ms). On the contrary, it gets smaller if the previous signal stop was not successful (-50ms). The total duration of the trial is 2000 ms (stimulus onset asynchrony; SOA). The practice block consists of 32 trials (8 signal trials and 24 no signal trials). Three test blocks include 64 trials each (16 signal trials and 48 no signal trials).

In the color-word Stroop test, participants are asked to indicate the font color of the words/rectangles presented on the screen. The size of the words presented is 1.5-3cm x 1cm and they are presented in the middle of the screen. Rectangles are 2.5 x 1.5 cm and they are presented in the middle of the screen. The font color can be congruent or incongruent with the meaning of the word. Each block includes 4 possible colors (red, green, blue, black) x 3 color-stimulus congruency (congruent, incongruent, control) x 7 repetitions (resulting in 84 total

trials per 3 block). Trials are randomly sampled. Participants respond by pressing the key (D = red, F = green, J = blue, K = black) corresponding to each color as fast and accurate as they can. Stimuli remain on-screen until participants have responded. Reaction time is measured from onset of the stimuli. The intertrial-interval is set at 200 ms and the error feedback is presented for 400 ms.

2.3 Procedure

After arriving in the lab, participants were first given time to read the information sheet and, they were told that they could ask questions regarding the upcoming procedure. After they provided informed consent, the experimenter started cleaning the surface of the skin adjacent to the electrode site with a scrub gel (Skin Pure; Nihon Kohden). Subsequently, the electrodes were placed after applying an electroconductive gel (Signagel, Parker Laboratories, Inc.). Then, calibration of the painful stimuli was conducted as described above. The experimental procedure consisted of the following steps: the sensory attenuation task, assessments of inhibitory control, psychological trait questionnaires, payment and oral debriefing. The entire experiment lasted approximately 75 minutes.

2.4 Outcomes

The 2AFC paradigm allows the calculation of a psychophysical index named *Point of Subjective Equality (PSE)*. The PSE corresponds to the virtual intensity at which the pain administered to the test hand is perceived as equal as the one on the reference hand. In other words, the PSE is found at the intensity that corresponds to the 50% probability of reporting to perceive the pain on the right hand as equally painful as on the left hand. The assumption behind it is that if participants do not know which stimulus is stronger (when they feel no difference between both stimuli), they tend to answer randomly (therefore with a 50% probability for each choice). The sensory attenuation index (SAI) was defined and computed as a PSE percentage increase above the rest level in the motor preparation and execution phases. SAIs were calculated using the formula ([PSE execution/preparation – PSE rest]/PSE rest)*100 [69]. The SAI represents how larger the pain stimuli administered on the moving hand (during motor preparation and motor execution compared to rest) have to be in order to be perceived as equally painful as the reference stimuli administered to the non-moving hand.

The Stroop interference score was computed on the reaction times (RT) for correct trials as RT difference for incongruent minus control trials [13].

The average stop delay (i.e., the estimated time at which the stopping process finishes) was scored as the main outcome for the Stop Signal task. It is defined as the estimation of the covert *stop signal reaction time* in ms (SSRT). Generally, slower SSRTs represent difficulties to stop the go-process and the faster SSRTs represent ease to stop the go-process (measure of inhibitory control; [65]).

2.5 Data pre-processing

Data pre-processing was performed in R [52]. In particular, participants' responses (left or right perceived stronger) were fitted according to a maximum-likelihood procedure with logistic regression (using the general linear model, *GLM* function in R). Subsequently, the stimulus intensity that corresponded to the 50% probability of responding "right-hand stimulus perceived stronger" was estimated in order to obtain the PSE (defined as the intensity of a stimulus to the right hand which would feel as strong as the reference stimulus to the left hand; [69]). A mean PSE was computed for each within-subjects experimental condition (rest, motor execution and motor preparation) in both experimental groups. In addition to the PSE, also the just noticeable difference (JND) was computed as a secondary outcome. The JND refers to the slope of the psychometric function and indicates the interval needed to achieve 75% accuracy. This index represents perceptual sensitivity in detecting changes in the stimuli and reflects the variability of responses given by the participant. The JND has been used in psychophysical studies on the tactile domain as well as in sensory attenuation experiments [9,23,25,35]. Practice trials were excluded from both the analysis.

17 participants were excluded as their pain tolerance was 1mA (or lower). This was done because, when participants' tolerance was 1mA (or lower), the range of stimuli that could be administered during the calibration procedure was limited since the minimal intensity difference possible in our set-up was 0.1mA. Consequently, when applying the trend formula to calculate the scale of subjective pain intensities, the same stimulus intensity (in mA) would be estimated for different levels of subjective pain intensity. To calculate the PSE, it is crucial that the stimulus intensities in each level are distinct from each other, otherwise equal stimuli would be administered during the task making the estimation of the non-discrimination threshold (PSE) problematic. Furthermore, outlier analysis was also conducted in R. Participants' whose PSE was higher than the upper and lower boxplot limits were excluded from the analysis. The lower limit was calculated with the formula: [Q1 (first quartile) - 1.5 * IQR (inter quartile range = Q3 - Q1)]. The upper limit was calculated with the formula: [Q3 (third percentile) + 1.5 * IQR]. In these cases, participants consistently gave the same response at the task (i.e. either "left/right hand stronger"), as a result of which the PSE was estimated as extremely low or high. In Figure 2 the individual values of PSEs are shown. The same outlier procedure used for the PSE data, was implemented for the computation of the JNDs. Similarly, Stroop outlier RT per condition (congruent, incongruent and control) and per subject exceeding the limits of [1.5 * interquartile range (IQR)] were removed from the analyses.

****Figure 2****

2.6 Data analysis

Statistical analysis was performed using JASP Computer Software (2020 Version 0.13.1; [36]). To test if sensory attenuation for pain stimuli occurred, we tested whether the SAIs differed from 0 during motor preparation and execution separately for the high pain and

low pain intensity groups, using the non-parametric one sample Wilcoxon t-test (one tailed; test value = 0). A mixed Repeated Measures (RM) ANOVA was used to test whether the SAIs were significantly different during motor execution vs. motor preparation and between pain intensity groups (high vs. low pain). As a secondary analysis, a mixed RM ANOVA with pain intensity (high vs. low) and movement phase (rest, preparation, execution) was performed on the JND data (no specific hypothesis was pre-registered regarding the JND results and it is reported here as a secondary outcome). Note that, for the JND analysis, the factor "movement phase" includes 3 levels (rest, preparation and execution). However, for the SAI analysis the factor "movement phase" consists of 2 levels, since rest is used for the computation of the SAI (i.e. PSE percentage increase above rest condition during motor execution and preparation). Cohen's d or partial eta squared is reported to calculate effect size (respectively for the t-tests and ANOVAs). For the non-parametric Wilcoxon and Mann-Whitney test, effect size is given by the matched rank biserial correlation. Multiple linear regression analyses were used to test whether pain catastrophizing, rumination and pain vigilance negatively predict the magnitude of the SAIs (for motor executing and preparation) in both groups (pain intensity was included as a factor in the model). Similarly, linear regression analyses were used to test whether scores at the Stroop task and Stop the Signal task could predict the magnitude of the SAI in both groups (pain intensity was included as factor in the model).

2.7 Results experiment 1

2.7.1 Sensory attenuation

After outlier analysis (as described in the data pre-processing session), the finale SAI analysis was conducted on a sample of 68 participants (42 women; M age 21 years; range 18-46). Results from the one sample Wilcoxon test showed that the SAI was significantly larger than 0 in the high pain intensity group during motor execution (M = 23.74%, SD = 27.86, $W_{(32)} = 528.000$, p = .000, $r_{rb} = .882$), and motor preparation (M = 9.59%, SD = 23.31, $W_{(32)} =$

399.000, p = .017, $r_{rb} = .422$), indicating the presence of sensory attenuation of pain during motor execution and preparation (*Figure 3*). In the low pain intensity group, the SAI was significantly larger than 0 during motor execution (M = 21.34%, SD = 33.67, $W_{(34)} = 519.000$, p < .001, $r_{rb} = .648$), but not during motor preparation (M = 5.85%, SD = 28.74, $W_{(34)} =$ 372.000, p = .103, $r_{rb} = .250$). Furthermore, the 2x2 RM ANOVA (pain intensity [high vs. low] x movement phase [preparation, execution]) showed no main effect of pain intensity ($F_{(1,66)} =$.216, p = .644, $\eta_p^2 = .003$; *Figure 3*). Yet, a significant main effect of movement phase emerged, showing that the SAI was higher during movement execution than during movement preparation ($F_{(1,66)} = 44.69$, p = .000, $\eta_p^2 = .404$). No significant pain intensity x movement phase interaction was found ($F_{(1,66)} = .091$, p = .763, $\eta_p^2 = .001$).

****Figure 3****

2.7.2. Just-noticeable difference

JND analysis was computed as a secondary outcome on a sample of 63 participants (after outlier removal). Results from the mixed RM ANOVA revealed a main effect of movement phase ($F_{(2, 61)} = 3.344$, p = .039, $\eta_p^2 = .052$) and a main effect of the pain intensity ($F_{(1, 61)} = 4.246$, p = .044, $\eta_p^2 = .065$) with higher JND in the high pain intensity group (M = 0.925, SD = .407) compared to the low pain intensity (M = 0.758, SD = .466). Post hoc analysis showed that the JND was larger during motor preparation (M = .920, SD = 0.489) compared to rest (M = 0.765, SD = 0.371).

2.7.3. Predictors of sensory attenuation

Hierarchical multiple linear regressions were used to predict sensory attenuation indices during motor preparation and motor execution based on pain catastrophizing (M =18.162, SD = 8.072), pain vigilance (M = 35.915, SD = 10.569), and rumination (M = 27.794, SD = 11.173) scores. First, the predictor variables were centered. Secondly, an interaction variable was created from the product between the dummy-coded group variable and the centered predictors. The regression model was built entering first the centered predictors together with the dummy-coded group variable. The cross-products were entered in the second block of the hierarchical regression. The results showed that these variables did not predict the magnitude of the SAI during motor execution ($F_{(7,67)} = .792$, p = .597, $R^2 = .085$), nor during motor preparation ($F_{(7,67)} = 1.174$, p = .331, $R^2 = .121$). Except for the PCS and SAI during motor preparation ($\beta = -.428$, p = .023), indicating that only catastrophizing negatively predicted sensory attenuation during motor preparation. Similarly, inhibitory control abilities ($M_{Stroop} = 84.003$, $SD_{Stroop} = 82.047$; $M_{ssrt} = 240.302$, $SD_{ssrt} = 44.302$) did not predict the magnitude of the SAIs during motor preparation ($F_{(5,67)} = .858$, p = .514, $R^2 = .065$) nor execution ($F_{(5,67)} = .864$, p = .510, $R^2 = .065$).

2. Experiment 2

3.1 Participants

92 right-handed healthy volunteers gave their informed consent. However, one session could not be completed because of technical problems. Therefore, 91 participants were tested successfully. Participants were compensated with a monetary incentive (15 Euros). Recruitment was similar as experiment 1. The research protocol was pre-registered before the start of data collection as an addendum on Open Science Framework (<u>osf.io/uag62</u>).

3.2 Materials

For this study, again five levels of intensity obtained after the calibration. These intensities matched with subjective pain ratings of 2, 3.5, 5, 6.5, 8. Note that larger intervals were used between the intensities compared with the first experiment. This choice was made because, in the previous experiment, when participants had a low tolerance to pain, it was not possible to compute 5 different intensities due to the small range of possible values.

Calibration of painful stimuli and the sensory attenuation task in this experiment were identical to experiment 1. The main difference regarded the addition of the pictures of a bogus

"skin sensitivity meter" used for the threat manipulation (see *3.3 Threat manipulation* paragraph). In this version of the task the color of the visual motor cues were changed (the green/red bars were replaced by +/- bars in order to avoid confusion with the color used in the meter showed on the screen during the task). Participants were instructed to prepare a motor action after the bar with a + sign was presented and to not prepare any motor action in case of a bar with a – sign was shown. Similarly to experiment 1, during the task, 150 trials were presented for rest, motor preparation and motor execution. Three blocks of 50 counterbalanced trials were used. Furthermore, the same questionnaires and inhibitory control tasks as the first experiment were used with the same procedure.

3.3 Threat manipulation

We included a between-subjects threat manipulation. Participants were randomly assigned to a low-threat (in which the painful stimulation is explained in a neutral way) or a high-threat group (in which the painful stimulation is presented as potentially harmful). To serve this purpose, two additional sham electrodes were attached on the left hand in proximity of the electrodes administrating pain stimuli. Participants were told these extra electrodes would continuously measure the skin sensitivity to the painful stimulations during the experiment. The sensitivity was defined as the skin resistance to electrocutaneous stimuli. This was explained with standardized instructions that the experimenter gave at the beginning of the sensory attenuation task. The instructions were based on a previous study [33]. The content of the instruction differed depending on the experimental group. Participants in the high-threat group were told that their skin was relatively vulnerable to the stimuli and that this could lead to more discomfort and potentially negative consequences caused by repeated stimulation (reddening of the skin, increased discomfort, pain, and rarely blisters). In contrast, in the low-threat group participants were told that their skin showed normal reactions and that it would be likely that with repeated stimulation the skin would habituate to the stimulations. In reality, the

sham electrodes - and the device they were attached to - did not measure any bio-signal. They were used to increase the credibility of the experimental manipulation. Participants from both groups were also told that during the motor task it would have been possible to monitor the trend in their skin sensitivity online by monitoring a visual scale on the bottom right part of the screen. Inside the visual meter, a dynamic pointer was programmed to move either in the green zone (low-threat group) or in the orange zone (high-threat group). In the low-threat group the pointer progressively moved from a light green zone towards a bright green zone. In the high-threat group the pointer started from the middle (light orange zone) and then moved progressively towards a dark orange zone during each type of trial presented (rest, motor preparation and execution).

3.4 Manipulation check

The outcomes computed in this experiment are the same as experiment 1. However, a set of questions was added as a manipulation check. After each block 7, questions were presented to measure: (1) the fear of sensitivity increase as it was shown by the meter (0 = not afraid at all; 10 = very afraid); (2) whether they were attending potential negative effect of the stimuli on their skin (0 = never; 10 = always); (3) to what extent they were monitoring the meter (0 = not attending at all; 10 = very focused on the meter); (4) to what extent they expected the meter to increase (0 = not at all; 10 = very strong); (5) how afraid they were of the stimuli (0 = not afraid at all; 10 = very afraid); (6) how distracting the pain stimuli were during the task (0 = not distracting at all; 10 = very distracting); (7) how sure they were about their responses at the 2AFC task (0 = not sure at all; 10 = very sure). Participants answered using a 0-10 Likert digital scale presented on the computer screen. The full text used for the verbatim instructions and the exact formulation of the questions used for the manipulation check can be found in the protocol addendum at the pre-registration link: <u>osf.io/uag62</u>.

3.5 Data analysis

The computation of the PSE and JND as well as the SAIs was obtained with the same method as experiment 1. Similarly to experiment 1, JNDs were obtained for secondary analysis. The same outlier removal formula of experiment 1 was used in this experiment. SAIs were obtained for motor execution and preparation for both the groups (high vs. low threat). Similar to experiment 1, to examine whether sensory attenuation occurred, the non-parametric one sample Wilcoxon test was used (one tailed; test value = 0) to test if the SAIs differed from 0 in both movement phases (i.e., motor preparation and execution), and groups (high vs. low threat). A 2 (motor preparation and execution) x 2 (high vs. low threat) RM ANOVA was used to test whether the SAIs were significantly different during motor execution and motor preparation and between threat groups. Multiple linear regressions were used to test whether pain catastrophizing, vigilance, and rumination negatively predict the magnitude of the SAIs (for motor preparation and motor execution) in the two groups. Similarly, multiple linear regressions were used to test whether inhibitory control abilities positively predict the magnitude of the SAIs in the two groups (threat was included as a factor in the model).

3.6 Results experiment 2

3.6.1 Sensory attenuation

After using the outlier exclusion formula in R (same as experiment 1), 12 participants were excluded from the analysis. The final data analysis was performed on a final sample of 79 participants (61 women; M age 23 years; range 18-52). Individual values of PSEs are shown in *Figure 4*.

****Figure 4****

Results showed that the SAI was significantly larger than 0 in the low-threat group during motor execution (M = 23.757%, SD = 29.273, $W_{(37)} = 677.000$, p < .001, $r_{rb} = .827$) but not during motor preparation (M = 5.337%, SD = 27.407), $W_{(37)} = 469.000$, p = .078, $r_{rb} = .266$).

Similarly, the SAI was significantly larger than 0 in the high-threat group during motor execution (M = 14,85%, SD = 40.21, $W_{(40)} = 653.000$, p = .022, $r_{rb} = .517$) but not during motor preparation (M = 6.32%, SD = 45,91, $W_{(40)} = 502.000$, p = .181, $r_{rb} = .166$).

The ANOVA showed no main effect of threat ($F_{(1,77)} = .261$, p = .611, $\eta_p^2 = .003$), however there was a main effect of movement phase as the SAI was higher during motor execution than during motor preparation ($F_{(1,64)} = 21.394$, p = .000, $\eta_p^2 = .217$). No significant threat x movement phase interaction was found ($F_{(1,64)} = 2.885$, p = .093, $\eta_p^2 = .036$; *Figure 5*).

****Figure 5****

3.6.2 Manipulation check

One-tailed non-parametric Mann–Whitney U test were used to test whether the scores at the 7 items of the manipulation were significantly higher in the high-threat group relative to the neutral. This choice was made because the scores at all the items except *meter monitoring* were not normally distributed (Shapiro-Wilk p < .05). The Mann-Whitney U test showed that *fear of increase in sensitivity* was higher in the high-threat group (M = 3.321, SD = 2.068) than the low-threat group (M = 1.886, SD = 1.648; W = 462.000, p = < .001, $r_{rb} = -.407$). Moreover, *expectancy of increase in sensitivity* was higher in the high-threat group (M = 5.679, SD = 2.387) than the low-threat group (M = 3.728, SD = 2.166; W = 431.500, p < .001, $r_{rb} = -.446$). *Meter monitoring* was significantly higher in the high-threat group (M = 4.980, SD = 2.423) than in the low-threat group (M = 3.816, SD = 1.895; W = 553.000, p = .013, $r_{rb} = -0.290$). *Attention to negative effects* was higher in the high-threat group (M = 4.248, SD = 2.716) than in the low-threat group (M = 3.254, SD = 2.518; W = 609.500, p = .048, $r_{rb} = -0.218$). Differences between threat groups in *fear of stimuli, distraction* and *certainty at the 2AFC task* were not significant (p > 0.05).

3.6.3 Just-noticeable difference

After outliers were removed, the JND analysis was performed on a sample of 72 participants. Results from the RM mixed ANOVA revealed a main effect of movement phase

 $(F_{(2,70)} = 12.066, p < .001, \eta_p^2 = .147)$, but no main effect of threat $(F_{(1,77)} = .034, p = .853, \eta_p^2 = .00004)$. Post-hoc analysis showed that the JND was larger during motor execution (M = 1.136, SD = .743) and during motor preparation (M = 1.145, SD = .588) compared to rest (M = ..896, SD = .611).

3.6.4 Predictors of sensory attenuation

Multiple linear regressions were used to test whether pain catastrophizing (M = 17.244, SD = 8.132), pain vigilance (M = 29.410, SD = 10.567), and rumination (M = 36, SD = 8.204) could predict the magnitude of the SAIs in the two groups. The method used to build the model was equivalent to that of study 1. These variables did not predict the magnitude of the SAIs during motor preparation ($F_{(7,77)} = 1.152$, p = .342, $R^2 = .103$) nor during motor execution ($F_{(7,77)} = .663$, p = .702, $R^2 = .062$). Also inhibitory control abilities ($M_{Stroop} = 93.072$, $SD_{Stroop} = 205.723$; $M_{ssrt} = 242.022$, $SD_{Ssrt} = 44.072$) did not predict the magnitude of the SAIs during motor preparation ($F_{(5,77)} = .552$, p = .736, $R^2 = .037$) or motor execution ($F_{(5,77)} = .825$, p = .536, $R^2 = .054$).

4. General Discussion

The aim of this study was to investigate whether sensory attenuation extends to the domain of pain. As hypothesized, both the experiments show evidence for sensory attenuation of pain during motor action execution. These findings are in line with previous studies showing that performing a voluntary action produces attenuation of neural activity in sensory areas and reduces levels of conscious sensation of innocuous afferent inputs [11,30]. However, our results regarding the occurrence of sensory attenuation during the motor preparation phase are inconsistent. We did not find sensory attenuation for motor preparation in experiment 2 nor in the in the low intensity pain group of experiment 1. We expected sensory attenuation during motor preparation since previous studies found a first significant decrease of somatosensory processing of innocuous tactile stimuli 120 ms before movement onset and 70 ms before the

onset of EMG activity [19]. Furthermore, it is known that the expectation to move induces attenuation of somatosensory inputs occurring during motor preparation [69]. While sensory attenuation during action execution is supported by a combination of efferent and afferent processes, attenuation in preparation of the movement is mainly attributed to the effect of the generation of the motor command (i.e., the efference copy). One can speculate that pain expectancy might be more pronounced during movement preparation, in which the motor command generation is still at an early stage, leaving therefore more "room" for pain processing. Perhaps the mere preparation of the movement did not compete enough with the natural attentional prioritization of pain, therefore resulting in a less robust attenuation effect. In line with this, we found significantly stronger SAIs during motor execution than during motor preparation in both the experiments. However, the reason why we found sensory attenuation during the preparation window in the high intensity pain group but not in the low intensity pain group (experiment 1) remains still unclear since stronger pain intensity was expected to promote pain prioritization [26]. Similarly, JND results revealed that participants in the high intensity group were less accurate during motor preparation compared to motor execution and rest. The presence of attenuation for motor preparation only in the high pain intensity group might be explained in terms of decreased ability in detecting changes in high intensity stimuli. In line with this, JND results of experiment 1 showed a main effect of pain intensity, with higher JNDs in the high pain intensity group.

In contrast with our hypotheses, stronger painful stimulus intensity did not decrease the magnitude of sensory attenuation as an effect of the increased attentional responses elicited by more intense pain [15]. A possible methodological explanation for the absence of the effect of pain intensity is that perhaps the ranges of intensities implemented in the task were not sufficiently different, as there was a partial overlap. Alternatively, the higher intensity was not appraised as threatening enough to elicit stronger attentional responses and increase the

processing of pain (therefore leading to a weaker attenuation effect). However, higher threat did not modulate sensory attenuation in the second experiment either. We assumed that, by manipulating the threatening value of the painful stimuli, the processing of pain would have been prioritized in the high-threat group since attentional disruption by pain is often enhanced when pain is appraised as threatening [15,20]. This lack of effect might depend on the effectiveness of the threat manipulation in inducing pain-related attentional prioritization, as suggested by the mixed findings at the manipulation check items. In fact, *distraction* and *fear of stimuli* were not higher in the high-threat group and, overall effect sizes did not reveal strong effects. Crucially, the sample of these experiments is largely composed by students whose familiarity with these experiments, together with the presentation of the experimental procedure as safe in the Informed Consent, might have affected the effectiveness of the between group manipulations in inducing threat.

Moreover, in both experiments no association emerged between inhibitory control and sensory attenuation. It was previously found that individuals with higher inhibitory control perform better in a pain distraction task, indicating that inhibition might be important in focusing on a task despite the pain [66], suppressing automatic processes [6] and decreasing pain sensitivity [47]. In line with this, we expected people with better response inhibition (stopsignal task) and interference control (Stroop task) abilities [24] to have a stronger top-down control on pain that would result in greater sensory attenuation (i.e. suppressing the automatic response of orienting the attention to pain in order to maintain the ongoing motor task). Nevertheless, we did not find evidence for the hypothesized relationship. A possible aspect to consider is that general inhibitory control was assessed not using a pain-related task. Investigating inhibitory control in the context of pain may be a more sensitive alternative to detect associations with pain sensory attenuation. Furthermore, the motor task implemented in this experiment was simple and repetitive. The cognitive load of the task might have been too low and not demanding enough to require an engagement of strong voluntary top-down control aimed to maintain the execution of the movement despite the distraction caused by the pain. The absence of this relationship can be interpreted in terms of load theories of pain [64], which suggest that attentional effects on sensory processing depend on the interaction between task difficulty and stimuli features [42].

Similarly, no associations were found between dispositional facilitators of pain-related attention and sensory attenuation. However, these questionnaires measure dispositional features and their items often refer to daily experiences. In other words, they do not measure pain catastrophizing, vigilance, or rumination in relation to the specific experience occurring in the lab. We believe that the lack of relationship can be explained in terms of poor capability of these questionnaires to assess situational effects [1], such as experimentally induced pain.

Overall, the absence of relationship between dispositional facilitators and inhibitors of pain-related attention and sensory attenuation seems to suggest that sensory attenuation of pain (as it is measured by this paradigm) is poorly modulated by pain-related attention modulators. A limitation of this study could be that the motor action required in the task, as it is conceived now, is still stereotypical and therefore the paradigm seems more suitable to detect only the pure physiological effect of motor actions on pain processing. Crucially, pain models suggest that the attentional modulation of pain needs to be framed in the context of affective/motivational theories [3,12] and that pain must be considered in the context of goal pursuit [21,53,55]. It is possible that the motivational significance of pursuing this particular motor action was not strong enough to prepare the ground for top-down influence on sensory attenuation. In other words, participants might not have been particularly motivated to execute the movement well as no motor output was measured and no strong attentive volitional focus was required to carry out the task. It may well be that by manipulating the functional value of the movement (for instance by adding a reward for a good performance), top-down voluntary

control aimed at shielding the ongoing task has a stronger impact on sensory attenuation of pain. We believe future studies should increase the ecological validity of the paradigm, whereby the motor action is more demanding and functional to achieve a valued goal. Integrating the study of sensory attenuation of pain with more instrumental motor actions might shed further light upon individuating associations with psychological and cognitive variables.

There are important limitations to consider in these studies. Primarily, the high number of participants excluded. However, our decision is partially attributable to the ethical limit of administering stimuli within the pain tolerance range and to the challenge of adopting a psychophysical method to study pain perception. Furthermore, we were unable to extract from our data whether 150 trials induced pain habituation and if that affected our outcomes. We believe this is an important aspect to consider when designing future studies on sensory attenuation of pain. Moreover, previous research indicated that seeing the hand produces analgesic effects on infrared laser-induced pain [45]. However, we did not investigate to what extent seeing the moving hand influenced sensory attenuation. Future studies might benefit from considering potential synergetic analgesic effects of movement and vision on pain, perhaps with eye-tracking procedures. Finally, both samples were mainly composed by women. Considering the differences in pain perception between men and women [40], future research could consider the role of gender in sensory attenuation of pain.

In conclusion, this study provides a first insight into the changes in pain perception that occur during the execution of motor actions. Our findings support the idea that the activation of the motor system might have an inhibitory effect on nociceptive processing [29,37,57,62]. These studies showed that pain perception is a dynamic phenomenon, susceptible to individuals' interaction with the environment. These studies emphasizes the importance of studying pain adopting an embodied approach [63]. This account suggests that the body is a

core part of human cognition and that pain experiences are shaped in a dynamic context on which individuals act driven by complex goals.

5. Acknowledgments

These studies were funded by the FWO grant (no. G000518N) awarded to SVD, AM and DT. EP and SVD designed the studies. DVR programmed the studies. EP and AC conducted data collection. EP performed the analyses and wrote the manuscript. All the authors contributed with valuable feedbacks on the manuscript. The authors have no conflict of interest to declare.

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Figures

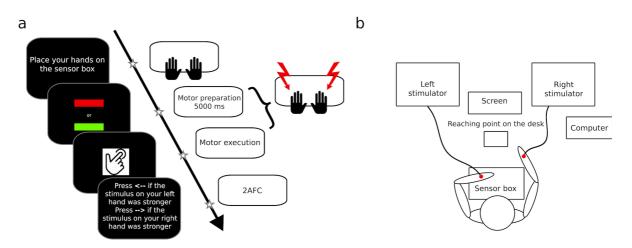


Figure 1. Graphic representation of the paradigm (a) and the set-up (b) of experiment 1. Each trial started when the hands were correctly placed on the sensor box. Subsequently the visual cue (green or red bar) was presented for 5000 ms. Participants were instructed to prepare the right-hand reaching motor action when the bar was green (no motor action was required for a red bar). The two painful stimuli could be administered either at 5000 ms (i.e. when the visual cue disappeared - for rest or motor preparation) or once the movement was initiated and detected by the sensor box (for motor execution). Therefore, three within subjects experimental conditions are motor execution, motor preparation and rest phase. At the end of each trial participants indicated their judgments about on which hand the stimulus felt more intense.

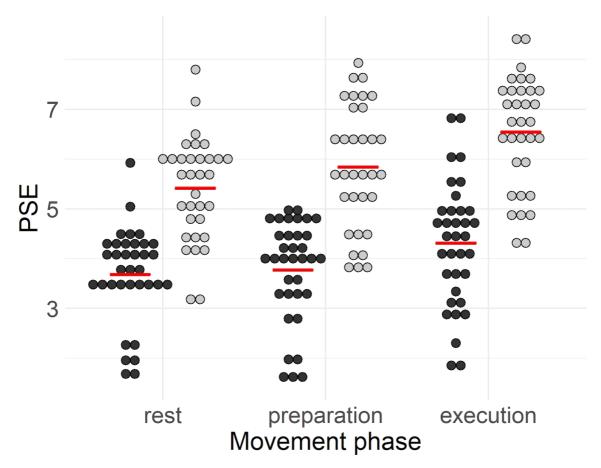


Figure 2. Overview PSEs. Point of subjective equality (PSE) values are shown for each subject across experimental conditions. The means are marked with a red line. PSE values from the low pain intensity group are presented in black and PSE values from the high intensity pain group in grey. Higher PSEs in the movement and preparation phases compared to rest indicate that a higher stimulus intensity needs to be applied on the moving hand in order to perceive the same pain intensity as the non-moving hand.

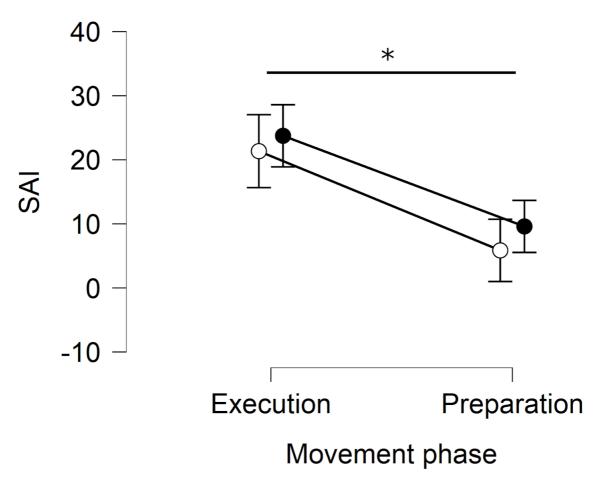


Figure 3. Sensory attenuation indices (SAIs). Mean (+SE) indices of sensory attenuation (i.e. PSE % percentage increase above rest condition) for motor preparation and execution phase for the high (black dots) and low pain intensity (white dots) group separately.

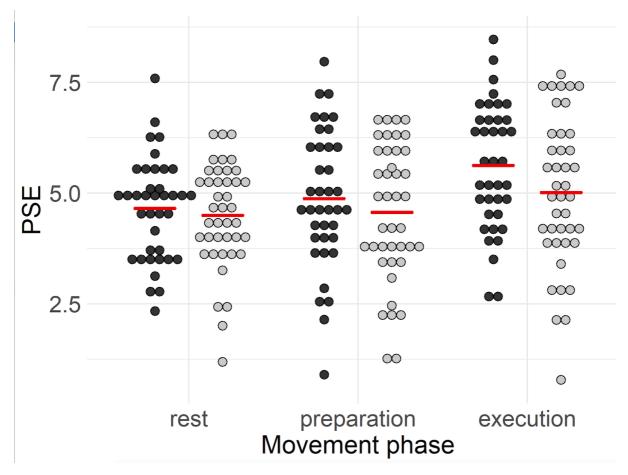


Figure 4. Individual PSEs across conditions experiment 2. In black individual PSE values from the low threat group and in grey PSE values from the high threat group for the different movement phases. The means are marked with a red line.

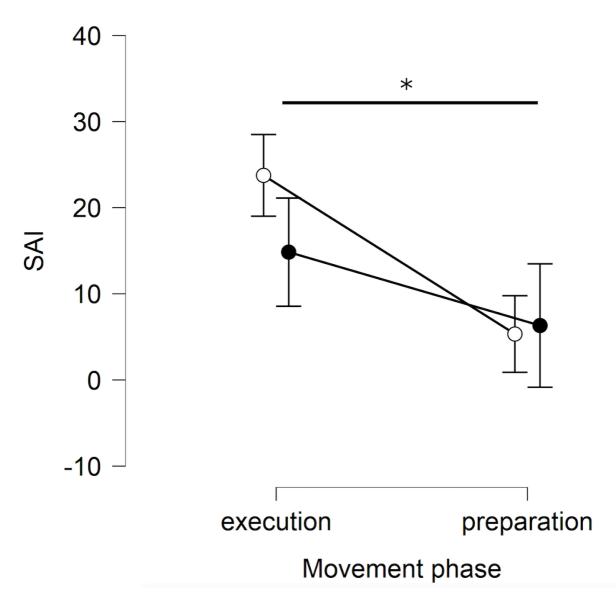


Figure 5. Sensory attenuation indices (SAIs) experiment 2. Mean (+SE) of the indices of sensory attenuation (i.e. PSE % percentage increase above rest condition) for motor execution and motor preparation in the high (black) and low threat (white) groups.