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The visual size of one's own hand modulates pain anticipation and perception

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ABSTRACT

How to reduce pain is a fundamental clinical and experimental question. Acute pain is a complex experience which seems to emerge from the co-activation of two main processes, namely the nociceptive/discriminative analysis and the affective/cognitive evaluation of the painful stimulus.

Recently it has been found that pain threshold increases following the visual magnification of the body part targeted by the painful stimulation. This finding is compatible with the well-known notion that body representation and perceptual experience relay on complex, multisensory factors. However, the level of cognitive processing and the physiological mechanisms underlying this analgesic effect are still to be investigated.

In the present work we found that following the visual magnification of a body part, the Skin Conductance Responses (SCR), to an approaching painful stimulus increases before contact and decreases following the real stimulation, compared to the non-distorted view of the hand. By contrast, an unspecific SCR increase is found when the hand is visually shrunk. Moreover a reduction of subjective pain experience was found specifically for the magnified hand in explicit pain ratings.

These findings suggest that the visual increase of body size enhances the cognitive, anticipatory component of pain processing; such an anticipatory reaction reduces the response to the following contact with the noxious stimulus.

The present results support the idea that cognitive aspects of pain experience relay on the multisensory representation of the body, and that could be usefully exploited for inducing a significant reduction of subjective pain experience.

1. Introduction

Pain is an extremely common daily-life sensory experience. Acute pain is a complex sensation usually generated by nociceptive input (Treede, 2006) even if it is possible to feel pain in the absence of nociception (Craig, Reiman, Evans, & Bushnell, 1996; Craig, 2002; Ehrsson, Wiech, Weiskopf, Dolan, & Passingham, 2007; Lloyd, Morrison, & Roberts, 2006). As a complex sensation, pain experience seems to emerge from the co-activation of a distributed brain network, originally called neuromatrix (Melzack, 1989) and currently referred to as pain matrix (Ploghaus, 1999), which comprises brain areas related to primary discriminative-somatosensory analysis, namely S1 and S2, as well as associative multimodal areas including the posterior parietal cortex, anterior insula and anterior cingulate cortex (ACC) (Iannetti & Mouraux, 2010; Price, 2000).

Such a complex brain substrate is justified by the multicomponential nature of pain experience that includes both cognitive and sensory aspects. This is nicely shown by the experimental modulation of pain experience through a large range of experimental manipulations including crossmodal signals (Gallace, Torta, Moseley, & Iannetti, 2011; Longo, Betti, Aglioti, & Haggard, 2009; Romano, Pfeiffer, Maravita, & Blanke, 2014), emotions or meditation-induced states (Brown & Jones, 2010; Rhudy, Bartley, & Williams, 2010; Rhudy, Williams, McCabe, Russell, & Maynard, 2008; Williams & Rhudy, 2009; Zeidan et al., 2011), attention and expectations (Babiloni et al., 2008; Brown & Jones, 2008; Brown, Seymour, Boyle, El-Deredy, & Jones, 2008; Clark, Brown, Jones, & El-Deredy, 2008; Porro et al., 2002) and social factors (Avenanti, Sirigu, & Aglioti, 2010; Forgiarini, Gallucci, & Maravita, 2011).

Notably to our purpose, although nociceptive stimuli are processed through specific sensory pathways (Haggard, Iannetti, & Longo, 2013; Lenz, Casey, Jones, & Willis, 2010), pain experience has been successfully modulated through vision (Longo, Iannetti, Mancini, Driver, & Haggard, 2012; Longo et al., 2009). In particular, the distortion of the visual feedback relative to the body part affected by pain can strongly modulate painful sensations and has

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been proposed as a candidate for the reduction of pain in clinical conditions (Moseley, Parsons, & Spence, 2008; Ramachandran, Brang, & McGeoch, 2009). However the results of such a sensory distortion are not univocal. While in some reports the level of perceived pain has been increased by the magnification of the visual size of a hand targeted by the painful stimulus (Moseley et al., 2008) in other cases the same visual distortion has led to pain reduction (Mancini, Longo, Kammers, & Haggard, 2011). Furthermore, the neurophysiological underpinnings of this kind of modulation are still to be clarified.

In the current study we sought for further evidence about the effect of visual body distortion on subjective pain experience as well as its physiological correlates. The working hypothesis is that the vision of an enlarged body part may increase the preparation of the sensory system to the consequence of the incoming noxious stimulus, leading to subsequent decrease in response, once the stimulus contacts the skin. To this aim we designed an experimental paradigm where we measured the anticipatory physiological response of participants exposed to an incoming harmful stimulus, as well as the somatosensory response when the stimulus eventually touches the skin. Therefore, Skin Conductance Response (SCR) was recorded following the application of painful or harmless stimuli (Cheng et al., 2007; Romano, Gandola, Bottini, & Maravita, 2014) that touched the hand or simply approached the skin without eventually contacting it. In the former situation we expected, at baseline, a response due to the sensory processing of the nociceptive stimulation, while in the latter we expected a smaller, but still measurable response, due to the affective/cognitive anticipatory response to pain (Clark et al., 2008; Romano, Gandola, Bottini, & Maravita, 2014). Critically these measures were also taken both under real-size, or distorted vision of the participant's hand, in order to measure the effect of visual distortion on the anticipatory and sensory aspects of pain processing.

Moreover, in separate experiments, we assessed the explicit experience of pain intensity and unpleasantness under the same circumstances of visual distortion.

2. Experiment 1 (pain anticipation)

2.1. Materials and methods

2.1.1. Subjects

12 right handed, healthy participants (6 females, mean age = 24.32, s.d. = 2.1), recruited among the students attending the Università degli Studi di Milano-Bicocca took part in Experiment 1 after giving their informed consent and received course credits for their participation.

The experimental protocol was explained in detail, but the participants were blind to the purpose of the experiment. The experiment was conducted according to the principles of the Declaration of Helsinki (World Medical Organization, 1996).

2.1.2. Somatosensory stimuli

Two different kinds of stimuli were delivered: noxious (non-invasive needle with a blunt end) and neutral (cotton swab) (Cheng et al., 2007; Höfle, Hauck, Engel, & Senkowski, 2012; Romano, Gandola, Bottini, & Maravita, 2014). The stimuli could be delivered in two contact conditions: real or simulated (Factor: Contact). In the real contact condition the needle and the cotton swab were applied to the pad of the middle finger for about .5 s. In the simulated contact condition the stimuli approached the same area, but stopped at around half centimeter above the fingertip, where they were kept for about .5 s and then retracted.

Non-painful tactile stimuli were delivered in order to compute the anticipatory response to pain and to reduce SCR adaptation that typically follows repetitive stimulation (Levinson & Edelberg, 1985).

Stimuli were either applied to the right or the left hand, according to eight different experimental conditions: Painful Real Right, Painful Real Left, Painful Simulated Right, Painful Simulated Left, Neutral Real Right, Neutral Real Left, Neutral Simulated Right, Neutral Simulated Left.

2.1.3. SCR hardware and software

SCR was collected through a SC-2701 biosignal amplifier (Bioderm, UFI, Morro Bay, California) connected to a dedicated PC through a serial port. The gain parameter was set at 10 μmho/V; the signal was sampled at 10 Hz. The signal was recorded by means of two silver electrodes (1081 FG Skin Conductance Electrode) placed on the first phalanx of the index and ring fingers of the right hand for half of the participants and on the left for the other half. A saline conductive paste was applied to the electrodes in order to improve signal-to-noise ratio. Data were digitalized at 12-bit resolution using the SC-2701 dedicated software.

2.1.4. Experimental procedure

Participants sat comfortably at a table with the experimenter sitting in front of them. They were asked to put both hands, palm up on the table. Each trial started with participants gazing at the fixation point drawn at the center of a 40-cm high vertical opaque board, placed at 50 cm distance in front of them. On each trial, a trained experimenter delivered one of two somatosensory stimuli (Factor: Stimulus) to one of the two hands (Factor: Hand), by approaching it with a smooth, continuous movement eventually contacting the hand or not (Factor: Contact). The experimenter, (an undergraduate student attending at the University of Milano-Bicocca), who was running the experiment as part of her internship, was trained to deliver the stimulation as constant as possible and was blind to the specific purpose of the experiment. Neutral or painful stimuli emerged from behind the opaque board unpredictably and in random sequence, while participants were requested to gaze at them along their entire trajectory.

A total of 64 tactile and noxious stimuli were delivered to each participant in a single session, while the Skin Conductance Response (SCR) was recorded continuously.

The 64 stimuli were divided into 8 independent blocks of 8 stimuli each (1 per condition) and were delivered in random order within each block. A pause was introduced after 4 blocks, or at the end of any block when needed. The entire session lasted around 30 min.

2.1.5. Data pre-processing

The SCR peak-to-base measure (Breimhorst et al., 2011; Lykken & Venables, 1971; Rhudy et al., 2010) was computed for each trial as the difference between the maximum value detected in a 6-s post-stimulus time window and the baseline calculated as the average value of a 300-ms pre-stimulus time window (Romano, Gandola, Bottini, & Maravita, 2014).

Manual markers identifying each stimulus type were added to the SCR trace through the computer keyboard at the moment when the stimulus emerged from behind the opaque shield.

2.1.6. Data analysis

Data were analyzed with STATISTICA 6.0 (StatSoft, Italy, http://www.statsoft.it), and G*Power 3.1 (http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3/).

A General Linear Model was used on SCR data, factoring: Stimulus (painful/neutral), Contact (real/simulated) and Hand (left/right), as within subject factors. This resulted in a $2 \times 2 \times 2$ repeated-measure ANOVA design. Significant level was set at $< .05$, Fisher post-hoc tests were used when appropriate.

2.2. Results

The ANOVA showed a main effect of Stimulus ($F_{1,11} = 14.426$, $p < .01$; $\eta^2 = .567$, power = .932; painful = .17 (average) μS (microSiemens) ± .04 (St. err.), neutral = .02 μS ± .02) and a main effect of Contact ($F_{1,11} = 15.411$, $p < .01$; $\eta^2 = .584$, power = .946; real = .12 μS ± .03, simulated = .07 μS ± .03); moreover the interaction between Stimulus and Contact was significant ($F_{1,11} = 8.61$, $p \leq .01$; $\eta^2 = .439$, power = .97; painful real = .22 μS ± .06, painful simulated = .12 μS ± .04, neutral real = .02 μS ± .01, neutral simulated = .02 μS ± .02). The main effect Hand ($F_{1,11} = .116$, $p = .74$; $\eta^2 = .010$, power = .061) and the other interactions were not significant.

Post-hoc comparisons showed that painful real stimulations induced stronger SCR than all other conditions (all $p < .01$), but also that painful simulated stimuli induced larger SCR than neutral stimuli (all $p < .01$); finally neutral real and neutral simulated stimuli yielded a small, comparable SCR ($p = .93$) (Fig. 1). This pattern of results confirms that our experimental noxious stimuli evoked an anticipatory response when they approached the skin, and a subsequent somatosensory response on skin contact. Overall, the response produced by the neutral stimuli was negligible and unable to differentiate the anticipatory from the somatosensory component; for this reason neutral stimuli were not considered in the analysis of the following experiments.