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Dynamic expansion of alert responses to incoming painful stimuli following tool use

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ABSTRACT

Peripersonal space is the region closely surrounding our bodies. Within its boundaries, avoidance of threatening objects is crucial for surviving. Here we explored autonomic responses to painful stimuli with respect to the dynamic properties of the peripersonal space in healthy individuals. To this aim, in a series of experiments, we measured the Skin Conductance Response (SCR) to a noxious stimulus approaching and touching the hand, or stopping at different distances (far, near) from it. Results showed that the anticipatory response to an incoming threat is reduced if the stimulus targets a spatial position far away from the body, as compared to a near or bodily location. However, responses to far stimuli change if the boundaries of reachable space are extended further away by active tool use. Noteworthy, SCR is not influenced by a training consisting of a spatial attention task, without active tool use. This evidence sheds novel light on the adaptive role of peripersonal space, showing its importance for the coding of incoming threatening stimuli and its plasticity induced by contingent experience, such as tool use.

1. Introduction

Pain anticipation is a crucial adaptive ability of humans as well as of many living beings. It allows us to understand potentially dangerous situations, in order to carry out appropriate defensive behavior. This function is particularly relevant with respect to the coding of potentially noxious stimuli that are within, and/or rapidly moving toward, the space surrounding our body (Graziano et al., 2002; Graziano and Cooke, 2006). This sector of space, namely the peripersonal space (Rizzolatti et al., 1981a; Rizzolatti et al., 1981b), holds peculiar features due to its richness of multisensory interactions, especially with respect to body-related visual and tactile stimuli (Làdavas and Farnè, 2004; Macaluso and Maravita, 2010).

The neural substrate underlying the multisensory representation of peripersonal space comprises areas containing multisensory neurons with bimodal, visual and tactile, receptive fields (RFs) centered on body parts (Graziano and Gross, 1993, 1995). These neurons hold a tactile RF on one body part (e.g., a hand) and typically increase their firing rate when a visual stimulus approaches the tactile RF, and decrease their response when the visual stimulus moves away (Graziano and Gross, 1992). Interestingly, the visual RFs of bimodal neurons show dynamic properties. In his seminal study, Iriki et al. (1996) trained monkeys to retrieve bits of food placed in the extra-personal space, by means of a hand-wielded rake. They found that, after the training, the visual RF of parietal bimodal cells extended to the tip of the tool or to the space now reachable by the tool. This reorganization only occurred when monkeys actively used the rake, suggesting that this mechanism depends on voluntary action.

Several studies support the existence of similar mechanisms for body-related multisensory integration in humans (Maravita and Iriki, 2004; Macaluso and Maravita, 2010; Bolognini and Maravita, 2007). For instance, the investigation of right brain-damaged (RBD) patients with left tactile extinction has provided strong support to the existence of an integrated visuo-tactile representation of peripersonal space in humans. These patients can typically detect a single touch on the left or right hand in isolation, but they fail to report the contralesional, left-sided, touch when it is presented simultaneously with an ipsilesional, right-sided, stimulus of the same (Bender, 1952) or different sensory modality (di Pellegrino et al., 1997; Mattingley et al., 1997; Làdavas et al., 1998; Farnè and Làdavas, 2000). Crossmodal extinction of contralesional

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touch to the hand by an ipsilesional visual stimulus is usually more pronounced when the visual stimulus is presented close to the ipsilesional hand (Làdavas et al., 1998). However, after a brief period of training with a tool allowing to reach for objects in the space far from the body, crossmodal extinction emerges even for visual stimuli placed far from the body, but near the tip of the tool (Farnè and Làdavas, 2000; Maravita et al., 2001; Farnè et al., 2007), suggesting an expansion of crossmodal visuo-tactile interactions to the far space. Studies in healthy subjects using the Crossmodal Congruency Task (CCT) (Driver and Spence, 1998a, 1998b; Maravita et al., 2003; Spence et al., 2004b) have provided further evidence for the efficacy of tool use for expanding crossmodal responses to the far space (Maravita et al., 2002b; Holmes et al., 2004; Spence et al., 2004a; Holmes et al., 2007a; Macaluso and Maravita, 2010).

The functional meaning of having such a peculiar representation of peripersonal space is likely due to its importance for object manipulation, but also for the avoidance of incoming threats. The latter aspect, in particular, is reminiscent of the notion of "defensive flight zone", proposed in the 1950s by the Swiss zoologist Heini Hediger as the urge to protect the zone near the body as the primary goal of any creature, more important than food or sex. He defined this zone as the "flight distance", and later as "flight zone". Graziano and colleagues further corroborated Hediger' idea in non-human primates, by showing the occurrence of avoidance behaviors in response to visual stimuli rapidly approaching the body or to air puffs directed to single bodily regions (Graziano et al., 2002; Cooke and Graziano, 2003). These authors also found that the electrical stimulation of the ventral intraparietal area (VIP) and of a polysensory area in the precentral gyrus (PZ) elicits a set of defensive behaviors, such as squinting, ducking and blocking, as if the monkey was defending the portion of the body that is spatially coded by the stimulated neurons. These findings suggest that areas VIP and PZ could represent the neural substrate that coordinates defensive responses by maintaining a sort of safety barrier around the body (Graziano et al., 2002; Graziano and Cooke, 2006). A recent study in humans also supports the existence of a hand-centered coding system of the visual space in humans, where approaching objects can rapidly modulate corticospinal excitability in hand-centered coordinates (Makin et al., 2009). This mechanism may allow anticipating the impact of approaching objects as if peripersonal space acted as a protective safety barrier to incoming threats (Cardinali et al., 2009a).

Given the plasticity of peripersonal space for action, as shown in the case of tool use, the present work investigates whether also the boundaries of such a "safety barrier" may be dynamically modulated by tool use experience. Notwithstanding the critical importance of the defensive role assumed by the peripersonal space, this issue has not yet been investigated. To this aim, we first assessed the spatial organization of automatic, physiologic responses to the vision of approaching noxious stimuli by measuring the Skin Conductance Response (SCR), and then we assessed the possibility of modulating the spatial pattern of such responses following tool use.

The SCR is a measure of the electrical conductance of the skin due to sweating and represents a reliable, direct measure of sympathetic nervous system activation following psychological or physiological arousal (Mordkoff et al., 1967; Deltombe et al., 1998). When the body is threatened by an incoming dangerous stimulus, the SCR can be used as a measure of fear and pain anticipation (Armel and Ramachandran, 2003; Hägni et al., 2008; Guterstam et al., 2011). Furthermore, previous evidence has showed that SCR increases in response to affective stimuli (Armel and Ramachandran, 2003; Forgiarini et al., 2011), pain perception (Rhudy et al., 2009; Williams and Rhudy, 2009; Romano et al., 2014b) and cognitive conflict (Kobayashi et al., 2007). In particular, here we adopted a protocol recently designed to elicit reliable anticipatory responses to the vision of threatening stimuli approaching the body (Romano et al., 2014a; Romano and Maravita, 2014). Using this paradigm we explored whether SCR to incoming threatening stimuli can be modulated by the expansion of peripersonal space boundaries that follows tool use. This occurrence would be an indication that the safety region surrounding our body has not a fixed extension, but can be plastically expanded following contingent experience.

2. Experiment 1

The aim of the first experiment is to uncover whether SCR anticipatory responses to approaching threatening stimuli depend upon the distance of the stimuli from the body. Since, traditionally, studies regarding the peripersonal space were conducted considering only the horizontal, radial dimension, while the peripersonal space also extends along the vertical axis, the latter axis was also considered in the present experimental paradigm. We expect larger autonomic responses as the needle approached the hand and the nearest positions, as compared to the middle and far positions, regardless of its direction (namely, no interaction between axis and stimulus distance).

2.1. Material and methods

2.1.1. Participants

Fourteen right-handed participants took part in this experiment (4 males, mean age: 26 ± 11). All participants gave written informed consent; they were naïve to the experimental procedure and to the purpose of the study and none of them reported neurological, psychiatric, or other relevant medical problems. The protocol was carried out in accordance with the ethical standards of the Declaration of Helsinki (BMJ 1991; 302: 1194) and was approved by the ethical committee at the University of Milano-Bicocca.

2.1.2. Experimental procedure

Participants sat on a chair in a floodlit room with the experimenter sitting in front of them. Two electrodes were attached on the middle finger and ring finger of left hand (Fig. 1a) in order to record SCR, as described below. During the experiment, participants were asked to relax, and carefully fixate the approaching stimulus, namely a 4 cm long medical needle. On each trial, the experimenter manually moved the stimulus from behind the table (where it was invisible to the participant) towards the hand, in four spatial conditions: (1) touch, the needle eventually touched the right index fingertip; (2) near 1 cm, the needle placed at 1 cm from the fingertip; (3) near 5 cm: the needle placed at 5 cm-distance from the finger; and (4) far 40 cm: the needle at 40 cm from the fingertip. The reliability of noxious stimuli to be considered as painful was validated by previous studies from other groups (Cheng et al., 2007; Höfle et al., 2012), and from our lab using the same stimulus set (i.e., Romano and Maravita, 2014, Romano et al., 2014a, 2014b). Specifically we showed that when the needle was applied to the hand, the participant experienced pain, and showed reliable SCR, while control, neutral, non-painful tactile stimuli (cotton swab) do not induce pain experience nor any detectable SCR (Romano and Maravita, 2014). Hence, based on such previous evidence, here only painful stimuli, which proved to provide significant SCR, were used.[2]

[2] Additionally, in a pilot experiment (published in the Ph.D. thesis of DR) the reliability of SCR as a measure of experienced pain was assessed.

Twenty noxious stimuli were given to 21 volunteers by means of the same needle used in the present study, while recording their SCR. Participants were asked to