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Investigating the spatial characteristics of the crossmodal interaction between nociception and vision using gaze direction

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ABSTRACT

The present study investigated the influence of nociceptive stimuli on visual stimuli processing according to the relative spatial congruence between the two stimuli of different sensory modalities. Participants performed temporal order judgments on pairs of visual stimuli, one presented near the hand on which nociceptive stimuli were occasionally applied, the other one either to its left or to its right. The visual hemifield in which the stimulated hand and the near visual stimulus appeared was manipulated by changing gaze direction. The stimulated hemibody and the stimulated visual hemifield were therefore either congruent or incongruent, in terms of anatomical locations. Despite the changes in anatomical congruence, judgments were always biased in favor of the visual stimuli presented near the stimulated hand. This indicates that nociceptive-visual interaction may rely on a realignment of the respective initial anatomical representations of the somatic and retinotopic spaces toward an integrated, multimodal representation of external space.

1. Introduction

The cognitive mechanisms, and their neuronal substrates, underlying crossmodal interaction between somatic and non-somatic stimuli have been largely investigated over the last decades (see e.g. di Pellegrino & Làdavas, 2015; Holmes & Spence, 2004; Macaluso & Maravita, 2010). For such crossmodal interactions between somatic and non-somatic stimuli to be possible, one needs to be able to coordinate and to integrate the representation and the perception of the space of the body and those of its surrounding space. Conceptualized by the notion of peripersonal reference frames (Rizzolatti, Fadiga, Fogassi, & Gallese, 1997), such integrated and multisensory representations are coordinate systems for the spatial coding of both somatic and extra-somatic (e.g. visual) stimuli occurring near the body. Such systems are thought to be used as interfaces to translate the perceptual characteristics of an object near the body into a motor schema to spatially guide actions toward that object, such as grasping and dexterous manipulation (Brozzoli, Ehrsson, & Farne, 2014). It has been further hypothesized that such peripersonal representations could be used for the purpose of defensive actions against objects that threaten the physical integrity of the body (Cooke & Graziano, 2004; Graziano & Cooke, 2006). Supporting this latter hypothesis, recent studies in humans demonstrated a privileged interaction between visual stimuli occurring very close to the body, and nociceptive stimuli, that is, stimuli that selectively activate the nervous system specifically involved in coding and transmitting information about sensory events that have the potential to inflict body damage (see Legrain & Torta, 2015 for a review). Whereas the reference frames involved in tactile processing and the mechanisms underlying visuo-tactile interactions have been studied with a wide variety of tasks (e.g., di Pellegrino & Làdavas, 2015; Spence, Pavani, & Driver, 2004; Tamé, Wühle,

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Petri, Pavani, & Braun, 2017), most of the studies investigating visual-nociceptive interactions used temporal order judgment (TOJ) tasks. These tasks consist in presenting pairs of stimuli with various time delays between them, and participants have to report which of the two stimuli they perceived as having been presented first. In such tasks, the amount of time one stimulus has to follow or precede the other in order for the two stimuli to be perceived by the participant as occurring simultaneously is used as an index of attentional bias, and can be shifted to the advantage of one of the two stimuli (Spence & Parise, 2010). Indeed, according to the theory of prior entry (Titchener, 1908), paying attention to a stimulus speeds-up its processing as compared to a competing unattended stimulus. A first series of experiments in which pairs of nociceptive stimuli were used, one applied on each hand dorsum, showed that judgments about the occurrence of nociceptive stimuli were dependent on the relative position of the hands in external space (De Paepe, Crombez, & Legrain, 2015; Sambo et al., 2013). When TOJ tasks were performed with the hands crossed over the midsagittal plane of the body, judgments were much less accurate, as compared to conditions in which the task was performed with a normal, uncrossed hand posture. These results suggest that the ability of perceiving nociceptive stimuli is not only determined by the anatomical position of the stimuli on the body, but also relies on frames of reference that integrate the relative position of the stimulated limb in external space (see Smania & Aglioti, 1995). Similar effects have been reported for tactile stimuli (Shore, Spry, & Spence, 2002; Yamamoto & Kitazawa, 2001). In further experiments, the nociceptive stimuli were preceded by a visual cue presented randomly in the same side of space as one of the hands (De Paepe, Crombez, Spence, & Legrain, 2014; De Paepe et al., 2015). These studies showed that the occurrence of the visual stimulus biased judgments in favor of the perception of the nociceptive stimuli applied on the hand laying in the same side of space as the visual stimulus. The effects were shown to be stronger for the visual stimulus presented the closest to the stimulated hand (De Paepe et al., 2014), independently of the relative position of the hands and the visual stimuli according to the participant's trunk (De Paepe et al., 2015). In other words, the ability of a visual stimulus to impact the perception of a nociceptive stimulus depends on the proximity of the visual stimulus to the limb on which the nociceptive stimulus is applied and thus on the location of the stimulated hand in external space, irrespective of the fact which hand was stimulated according to an anatomical reference (De Paepe et al., 2015). Taken together, these studies suggest the existence of a peripersonal frame of reference for the localization of nociceptive stimuli, thus enabling close visual stimuli in external space to affect the perception of nociceptive stimuli applied on the body.

There are longstanding debates on the mechanisms underlying crossmodal interaction between somatic and proximal non-somatic stimuli (Macaluso, Frith, & Driver, 2001; McDonald, Teder-Sälejärvi, & Ward, 2001; Spence, McDonald, & Driver, 2004). One of the most popular theories postulates that such interactions rely on the existence of neurons able to respond to both somatic and non-somatic stimuli (see Graziano, Gross, Taylor, & Moore, 2004 for a review). More precisely, electrophysiological studies in monkeys have revealed, mostly in the ventral premotor cortex (PMv) and ventral intraparietal sulcus (VIP), the existence of neurons associating tactile and visual receptive fields (RFs). The particularity of these visual RFs is that they are often limited and anchored to the body parts which *host* their associated tactile RFs, thus following these limbs during their movements in space. In other words, the tactile and the visual RFs are aligned according to a frame of reference that takes into account external space, instead of their initial and respective anatomical frames of reference (i.e. somatotopic and retinotopic, respectively). Several studies have shown, for instance, that PMv neurons respond to both visual and tactile stimuli only when the position or the trajectory of the visual stimulus is spatially congruent with the limb that hosts the RF of the tactile stimulus, irrespective of the posture of the body and the projection of the visual stimulus onto the retina (Fogassi et al., 1992, 1996; Gentilucci, Scandolara, Pigarev, & Rizzolatti, 1983; Graziano, Hu, & Gross, 1997; Graziano, Yap, & Gross, 1994). Indeed, Graziano et al. (1997) have shown that visual stimuli were still able to activate such bimodal neurons even when the monkeys were trained to fixate their gaze at different positions. Similar effects have been observed in neuroimaging studies performed in humans (see Macaluso & Maravita, 2010). For instance, Macaluso and colleagues investigated how cortical responses to a stimulus of one sensory modality can be influenced by the proximal occurrence of a stimulus of another sensory modality (Macaluso, Frith, & Driver, 2000, 2002). In one of their studies, participants were asked to place one hand, on which tactile stimuli were applied, close to a visual stimulus, and, across conditions, to fixate their gaze either to the left or to the right of the visual stimulus and the stimulated hand (Macaluso et al., 2002). Using such a manipulation, the visual stimulus was alternately seen in different visual hemifields, while the tactile stimulus was always felt on the same hemibody. The occurrence of a tactile stimulus was shown to boost the cortical responses to the visual stimuli in the visual cortex contralateral to visual stimuli location, independently of the primary cortical projection of the tactile input to its contralateral hemisphere, and thus irrespective of the hemispheric correspondence between the visual and the tactile cortical projections (Macaluso et al., 2002).

The studies reviewed here above suggest that one of the mechanisms underlying crossmodal interaction between somatic and non-somatic stimuli relies on the ability to update the mapping coordinates from the initial anatomical reference frames of each sensory modality (i.e. somatotopic for somatosensory inputs and retinotopic for visual inputs) to an integrated mapping system using external space as main reference frame. They also suggest that such an updating takes into account the relative position of the limbs and the eyes, whatever the stimulated hemibody and hemifield. In the present study, we investigated whether nociceptive stimuli can influence the perception of visual stimuli, especially those presented close to the limb on which the nociceptive stimuli are felt. This question is of particular importance when considering that it has been suggested that chronic pain states could change how patients perceive their visual environment (see e.g. Legrain, Bultitude, De Paepe, & Rossetti, 2012). More specifically, we investigated whether such an interaction between nociceptive and visual stimuli depends on the relative spatial congruence between the location of the nociceptive stimuli (i.e. of the stimulated limb) and that of the visual stimuli, irrespective of their exact positions according to their respective sensory RFs (i.e. the congruence of their respective anatomical reference frames). To this end, we manipulated the direction of the gaze so that visual stimuli and the body part on which nociceptive stimuli were applied could be seen in different areas of the visual field, while the cortical projections of the nociceptive inputs remained constant (as it was always the same limb that was stimulated). Participants performed TOJs on pairs of visual stimuli, one centrally positioned in front of the participant and