Chapter 1
Cognitive Psychology and Neuropsychology of Nociception and Pain

Valery Legrain and Diana M. Torta

Abstract For a long time, pain research has focused on understanding the mechanisms underlying the unpleasant experience generated by a nociceptive stimulus. Cognitive theories emphasize the functional aspects of nociception by defining it as a warning process. Nociceptive inputs are processed in a multisensory processing system that prioritizes stimuli that are meaningful for the integrity of the body and integrates them into multi-frame representations of the body and the proximal space. The ultimate purpose of this multisensory system is to guide defensive behaviors. Recent experimental evidence supports the role that cognitive functions such as selective attention, spatial perception, and motor preparation play in nociceptive processing. In addition, the cognitive approach of pain offers new clinical perspectives by providing a framework for the treatment of chronic pain based on neuropsychological rehabilitation.

1.1 Introduction

Cognitive psychology is a theoretical and methodological framework which aims to study the architecture of mental processes (Neisser 1967). Unlike behaviorist psychology which focuses only on observable behaviors, cognitive psychology tries to infer knowledge about mental states from the observation of behavior. More specifically, cognitive psychologists are interested in the description of the processing steps through which sensory inputs are transformed into thoughts and actions. Research in cognitive psychology generally consists in observing the behavior of participants when they are involved in specific tasks such as perception, attention, memory, or language tasks. Most often, participants have to respond to the occurrence of stimuli. Their response depends on variations of the stimulus parameters and the experimental instruction, and these variations are systematically controlled by the experimenter. Experimental manipulation is aimed at disclosing the succession of

V. Legrain (✉) • D.M. Torta
Institute of Neuroscience, Université catholique de Louvain,
Avenue Mounier 53, bte B1.53.04, Brussels 1200, Belgium
e-mail: valery.legrain@uclouvain.be; diana.torta@uclouvain.be

operations from the processing of the incoming input to the computation of the output response during the task. Cognitive psychology mostly uses the experimental method, in the sense that variations of stimulus parameters and task instructions are deducted from theoretical hypotheses. The cognitive psychology method is based therefore on a principle: only one parameter of the task is changed at a time in order to measure its effect on participants' behavior. Cognitive psychology also tries to understand how cognitive processes are implemented in their material support, that is, the brain. Neuropsychology is a long-lived and yet still contemporary approach which aims to localize mental processing in regions of the brain, by inferring normal processes from brain lesions (among other methods). Neuropsychologists try to characterize the cognitive dysfunction produced by a lesion of a cortical area, with the aim to establish a link between a specific function and that cortical area. The underlying hypothesis is the following: *the way how the cognitive system is deconstructed is related to its structure and rules of normal functioning* (Seron 1994). The neuropsychologist is therefore especially interested in the knowledge of normal function that can be derived from the description of a pathological state. This classic top-down neuropsychological approach tries to characterize how cortical lesions, and the supposed changes in cognitive organization, affect the processing of sensory information. An alternative bottom-up approach can be used to understand how peripheral deficits such as impaired sensory transmission modify cognition due to maladaptive neuronal plasticity (e.g., Crollen and Collignon 2012; Jacquin-Courtois et al. 2012; Ramachandran et al. 1992).

1.2   Cognitive Psychology in Pain Research

Regarding nociception and pain, one of the first cognitive models was proposed by Leventhal and Everhart in 1979. The model describes four processing steps between the stimulus input, that is, the nociceptive stimulus, and the perceptual output, that is, the conscious experience of pain: (1) stimulus encoding, (2) motor elaboration and memory encoding, (3) perceptual elaboration, and (4) attentional amplification. These steps operate in two parallel pathways, one that elaborates sensory-discriminative aspects generating the perceptual knowledge about the stimulus features, and a second that codes the emotional aspects generating the experience of unpleasantness. The model predicts that the degree of pain experienced by an individual would depend on how much attention is paid to the nociceptive stimulus. However, because the model dissociates the sensorial and the affective aspects of pain (see Melzack and Casey 1968), both aspects are susceptible to be modified by attention in isolation. Conversely, the model developed later by Price and Harkins (1992) proposes an architecture of nociceptive processing during which sensorial and affective components are sequentially organized. Therefore, attentional control over the sensory-discriminative aspects of pain also modifies the processing of the emotional distress generated by the experience of pain. The two models predict a close interaction between attention and nociceptive processing. This has led to the

general idea that paying attention to pain makes it worse. It was then assumed that reducing the attention allocated to the experience of pain by modifying the focus of attention towards cognitive activities unrelated to pain would alter the salience of the experience and promote better coping with pain (see Van Damme et al. 2010). For instance, according to McCaul and Malott (1984), the elaboration of pain is made in a capacity-limited system in which selection is operated to reduce processing overload (see Broadbent 1958). As nociceptive processing is an effortful and subject-regulated processing mode (Shiffrin and Schneider 1977), the reduction of attention will affect the ability to transform sensory inputs into pain. Discarding attention from nociceptive stimulus can be used as a strategy to decrease pain, if pain does not draw too much attentional resources and if the distracting task also involves controlled processing components (McCaul and Malott 1984).

Other cognitive models highlighting the functional role of pain were recently put forward (e.g., Legrain et al. 2011, 2012b; Van Damme et al. 2010). Indeed, most of the current research on pain focuses on discovering brain mechanisms underlying the generation of the pain sensation and on characterizing the mechanisms involved in the descending modulatory control of nociceptive transmission. However, besides the unpleasant sensory experience associated with the noxious stimulation, pain can also be described as a warning signal allowing detection, localization, and reaction against a stimulus potentially meaningful for the physical integrity of the body. This definition proposes an important role in nociception for three cognitive processes, respectively: (1) selective attention to prioritize the processing of stimuli that are the most significant, (2) spatial perception to map their accurate position in space, and (3) action selection to prepare the most appropriate motor action in response to the nociceptive stimuli (Legrain et al. 2012b). It is worth noting that, despite the fact that these processes are not specifically involved in nociception (meaning they are not exclusively involved in the generation of pain in the brain), they are inherently involved in the elaboration of motivationally driven behaviors towards meaningful stimuli, such as physical threats. As nociception can be seen as an epiphenomenon of warning processes, the description of how selective attention, spatial perception, and action selection are involved in the processing of nociceptive inputs is of primary importance to understand how the brain adapts to meaningful changes and defends the body against potential harmful stimuli. In this perspective, the study of the sensation of pain can sometimes appear secondary to other responses such reaction times or perceptual judgments. In addition, the importance of these cognitive processes is emphasized by the fact that impairment of any one of them can be relevant for the understanding of clinical pain states (Moseley et al. 2012b; Haggard et al. 2013).

1.3 Salience Detection and Selective Attention

The role of selective attention is to prioritize the processing of some inputs at the expense of other inputs. Selective attention can be indeed defined as a *restricted focus of consciousness on one out of several objects physically present in the*

environment or one out of several mental representations of objects or ideas (James 1890). Such a selective prioritizing of perceptual, decisional, and, even, motor activity can be dissociated from phasic alertness, a general activation determining an unspecific state of readiness to external sensory events, and from alerting attention, a tonic alertness or readiness induced by the sensory events (Boisacq-Schepens and Crommelinck 1996). The concept of selective attention is grounded by the assumption that perception and action abilities are restricted, and, therefore, information flow has to be filtered in order to avoid processing overload (Broadbent 1958). However, this classic view of attention was challenged by theories that recognize the finality of attention is to prioritize and facilitate the perception of the information that enables one to select, among many possibilities, the most efficient action (Allport 1987; Hommel 2010; Rizzolatti and Craighero 1998). The selection of the meaningful stimulus and, consequently, the guidance of the appropriate action are based on the individual's aims and on the environmental context. Indeed, information processing is filtered based on a stimulus-driven (or bottom-up) selection and on a goal-directed (or top-down) selection (Egeth and Yantis 1997; Knudsen 2007). According to the first mode of selection, attention is captured by the stimuli themselves according to their salience, that is, their ability to stand out relatively to surrounding or preceding stimuli. This involuntary capture of attention allows the modification of processing priorities and cognitive goals to adapt behaviors to sudden changes in the environment or to tune to high-order motivational functions such as escape from a danger. According to the second mode of selection, the selection of information is voluntarily regulated by the relevance of the stimuli when compared to cognitive objectives and motivations.

The ability of a painful stimulus to involuntarily capture attention was firstly observed in studies showing that the performance in auditory discrimination tasks was impaired (increased reaction times) by the concomitant occurrence of a painful stimulus even completely irrelevant to the task goal (Crombez et al. 1994). This suggests that attention was transiently displaced from the auditory target to the painful distracter (see Eccleston and Crombez 1999). These studies showed that the ability of a nociceptive stimulus to attract attention and interrupt ongoing cognitive activities was more dependent on the context than on the perceived pain (Crombez et al. 1994, 1996, 1997). One can wonder how the salience of a stimulus can be established before the stimulus receives attention. Salience detection is supposed to rely on the existence of neurons particularly sensitive to contrasts and changes. In other words, those neurons would be activated by the occurrence of stimuli particularly contrasting relative to other surrounding stimuli (Itti and Koch 2001) or by the detection of transient changes in the afferent sensory flow (Näätänen 1992). Salience detectors, by responding more strongly and in a more sustained way to these kinds of stimuli, would give to salient sensory inputs greater cortical resources to ensure them a more complete processing (Desimone and Duncan 1995). Regarding nociceptive processing, it was suggested that responses of the cingulate cortex to nociceptive inputs play a pivotal role in the attentional selection by biasing the cortical activity to nociceptive stimuli (Bantick et al. 2002; Legrain et al. 2002; Peyron et al. 1999). More recent studies have demonstrated that most of the cortical responses to

nociceptive stimuli are sensitive to their salience, independent of the intensity of the perceived pain (Downar et al. 2003; Iannetti et al. 2008; Legrain et al. 2009a). For instance, Legrain et al. (2009a) showed that unexpected novel nociceptive stimuli, that is, stimuli irregularly presented, elicited event-related brain potentials (ERPs) of greater magnitude as compared to the ERPs elicited by nociceptive stimuli of the same intensity but presented more regularly and monotonously. Importantly, all components of the nociceptive ERPs were increased by stimulus novelty, including the earliest one supposed to be generated in somatosensory areas. In this experiment, nociceptive stimuli were made task irrelevant and participants were instructed to perform a task on visual stimuli that followed each nociceptive stimulus. Performance in the visual task was impaired by the occurrence of novel nociceptive stimuli. Iannetti et al. (2008) showed that the loss of novelty induced by the repetition of the stimuli at a constant rate decreased the magnitude of the elicited ERPs, whereas the perception of pain remained unchanged. Hu et al. (2013) identified in the ERPs elicited by nociceptive stimuli a component that could be interpreted as a neuronal change detector for nociception. In their experiment, they used a similar paradigm as Legrain et al. (2009a) during which nociceptive stimuli were delivered at a constant rate on a specific area of one hand (e.g., the lateral section). After a random repetition of stimuli, the area onto which the stimuli were then applied was switched to another section of the hand (e.g., the median section). Unexpected occasional changes in stimulus location induced increased ERP responses to nociceptive stimuli mostly around the ipsi- and the contralateral parts of the scalp, even when nociceptive stimuli were completely unattended by the participants. Conversely, a similar electrocortical activity was identified at the top of the scalp and was shown to be increased in magnitude when the nociceptive stimuli were actively attended. This seems to confirm that the median part of the cortical network activated by nociceptive stimuli (e.g., the mid-cingulate area) can be more consistently interpreted as reflecting the effective orienting of attention towards nociceptive stimuli (Legrain et al. 2002, 2009a).

In order to promote survival, evolution has naturally prompted individuals to escape from physical threats. Pain has then the potential to change cognitive goal and to override the effort to disregard attention from nociceptive information (Van Damme et al. 2010). However, since it was evidenced that the experience of pain is largely influenced by the attention paid to the nociceptive stimulation, both in experimental settings (e.g., Honoré et al. 1995; Miron et al. 1989; Van Ryckeghem et al. 2011, 2013) and in clinical situations (e.g., Hadjistavropoulos et al. 2000; Harvey and McGuire 2000; Johnson and Petrie 1997; Rode et al. 2001), the manipulation of attention, such as distraction, was proposed as a potential therapeutic strategy to alleviate pain (See Eccleston and Crombez 1999; Morley 2011). One may wonder how it is possible to direct attention away to a stimulus that has inherently the ability to capture attention. Legrain et al. (2009b) proposed that the capture of attention by nociceptive stimuli can be inhibited by three main ways (Fig. 1.1). First, attention should be focused to stimulus features that match task requests. Conversely, features of the unattended irrelevant distracter should be excluded from the selection and the searching set mode (attentional set hypothesis; Van Ryckeghem
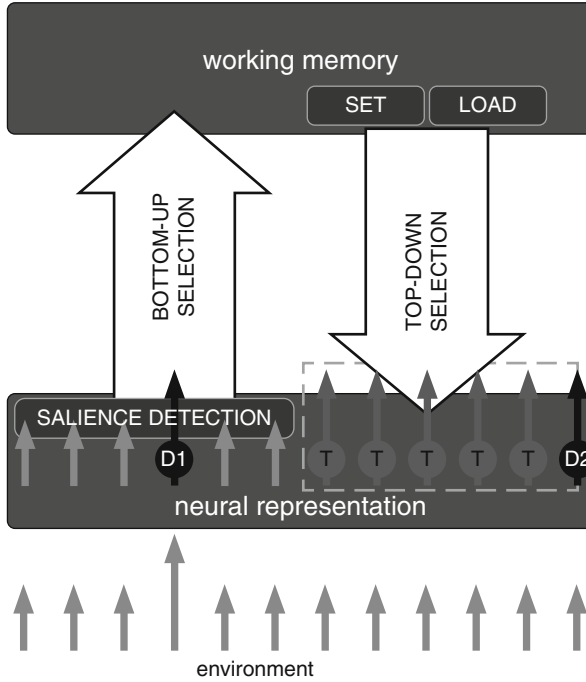
Fig. 1.1 Components of attention. Physical features of the information from the environment are *represented*, that is, encoded, into particular patterns of neural activations. The representations with the highest signal strength will be selected for further processing and access to working memory that holds active the representations of the information which are significant for ongoing cognitive processing. The selection is based on the salience of the sensory stimuli, that is, their ability to stand out relative to neighboring stimuli or relative to recent past events, or their relevance, that is, their pertinence for current cognitive and behavioral aims or for motivation. At the first level, information flow is filtered by salience detectors. These detectors weight the neural representations of sensory inputs relative to the representations of the sensory inputs from neighboring stimuli. These detectors modify the weight of the neural representations of sensory inputs relative to the representations of the sensory inputs from neighboring stimuli (Itti and Koch 2001). The stimuli that are the more distinctive receive then stronger representation signals (spatial salience detection). Other detectors increase the strength of neural responses to salient stimuli by identifying the stimuli that are novel or that represent a change according to recent past sensory events (Näätänen 1992) (temporal salience detection). On the basis of these mechanisms which translate physical salience into weighted neural representation (*black arrow* "D1"; "D" for distracter), the sensory inputs that receive the strongest neural response are those that are able to capture attention, even if these inputs are not explicitly attended by the individual (bottom-up or stimulus-driven selection). At the second level, processing prioritization is based on ongoing cognitive aims and high-order motivations, and the selection is then voluntarily controlled towards the sensory inputs that allow to achieve these aims and to satisfy motivations (*dark gray arrows* "T"; "T" for target) (top-down or goal-directed selection). The balance between top-down and bottom-up selection depends on several variables. First, top-down selection is under the control of working memory that maintains active the aims and the features of the to-be-attended information during the achievement of the task (Desimone and Duncan 1995). Second, the features of the targets are defined by the attentional set that helps attention to search and identify the relevant information in the environment. A consequence of the activity of attentional setting is that distracter stimuli that share one or more features with the attended targets (*black arrow* "D2") will also enter into the focus of attention (*dotted gray square*) (Folk et al. 1992). Third, attention abilities will be more or less loaded during selection (Lavie 2010). Under high-load selection, attention is narrowed on the processing of relevant information and distracters are rejected. To the contrary, under low selection, information processing is less selective; distracters will also be perceived, and their ability to gain control over cognitive activity will depend on the ability of executive functions to inhibit interference (Adapted from Legrain et al. (2009b))

et al. 2013). Second, searching and maintaining attention on the relevant stimulus should be effortful in order to avoid using attentional resources to process irrelevant distracters (attentional load hypothesis; Legrain et al. 2005; Roa Romero et al. 2013). Third, attention to the relevant stimulus should be controlled by executive functions in order to actively shield the processing of the attended stimulus from distraction (Legrain et al. 2013). The latter aspect emphasizes the role of working memory by allowing active maintenance of the goals of ongoing cognitive activities during the task in order to help attention to target the relevant stimuli (Desimone and Duncan 1995).

1.4 Spatial Perception

The role of the representation of space in the perception of nociceptive stimuli has been recently highlighted. For instance, a study has observed, in patients who showed hemispatial neglect syndrome after a stroke, that the perception of a nociceptive stimulus depends on the ability to localize stimuli in space and on the integrity of cortical structures such a posterior parietal and prefrontal areas (Liu et al. 2011). Some of these patients were able to report correctly the occurrence of a nociceptive stimulus only when this was applied on the hand contralateral to the lesion site. The perception of the same stimulus was extinguished when it was delivered concomitantly with another nociceptive stimulus on the ipsilesional hand (nociceptive extinction). Other patients were also able to identify correctly the occurrence of the nociceptive stimulus applied to the contralesional hand, but they localized it as if it has been applied to the ipsilesional hand (nociceptive allesthesia).

The ability to localize nociceptive stimuli is important because it allows the detection of which part of the body is potentially threatened. It is also of primary importance to identify in external space the position of the object that might be the cause of damage in order to prompt and to guide defensive motor responses towards the location of the threat. These considerations underline the importance of coordinating the representation of the body space and the representation of external space. The brain normally takes into account different frames of reference when coding the spatial position of sensory information (Fig. 1.2; see Vallar and Maravita 2009). One type of reference framework relates to the anatomical reference frames, which are based on the existence of a spatial organization of sensory receptors in receptive fields which project to separate populations of neurons. The primary somatosensory and motor cortices are somatotopically organized and contain a spatially organized representation of the cutaneous surface of the body (Penfield and Boldrey 1937). However, this type of frame of reference alone is unable to integrate the perception of which part of the body is stimulated and the perception of the position of external objects in contact with the body. In other words, defensive motor responses cannot be spatially guided towards the threat efficiently if the position of nociceptive stimuli is not remapped according to both the position of the stimulated body part and the position of the threatening object in external space. The peripersonal frame of reference is of particular interest because it allows integrating the body space and the space surrounding it. Indeed, this frame allows coding the position of
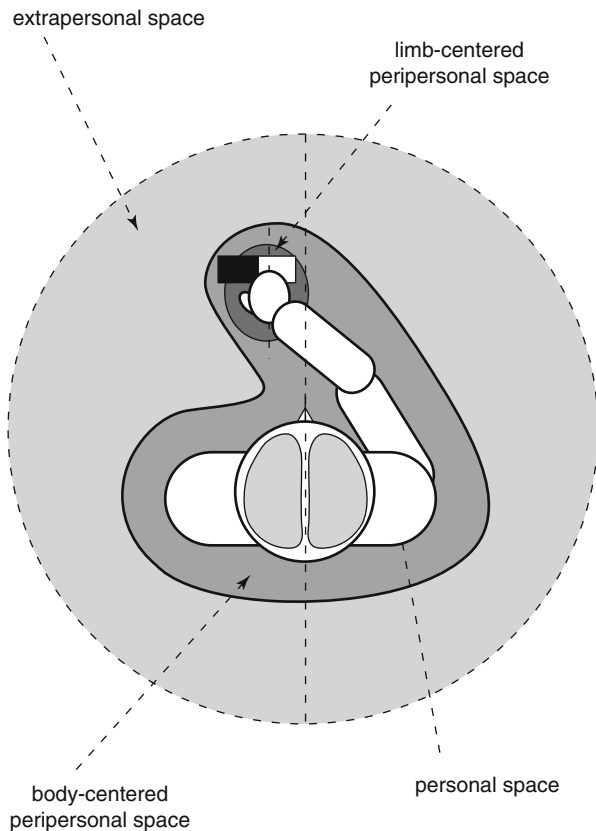
Fig. 1.2 Different frames of reference to perceive body and extra-body spaces. Three main reference frames can be dissociated. The personal reference frame corresponds to the space of the body. This frame can be dissociated into a somatotopic personal frame based on the anatomical projection of somatosensory receptive fields in spatially ordered groups of neurons and a spatiotopic personal frame using external space as a coordinate system. According to this second reference frame, as illustrated in the figure, we are able to recognize, eyes closed, that the right hand, that crosses the midline of the body, is touched by a right-sided object, despite the fact that somatosensory inputs are sent to the left hemisphere. Spatiotopic reference frames integrate therefore somatosensory and proprioceptive information. The peripersonal frame of reference corresponds to a coordinate system integrating body space and external space close to the body. This reference frame allows the integration of somatosensory information with visual and auditory information when visual and auditory stimuli occur close to the body. The peripersonal reference frame can be centered on the body; the sagittal midline of the body is used as a coordinate to separate the left and right parts of space. It can also be centered on each limb; the limb itself is then used as coordinate. Therefore, the peripersonal reference frame is considered as an interplay of body-part-centered coordinates mapping stimuli from the different senses and moving in space with the body part onto which these maps are anchored. The extrapersonal frame of reference corresponds to a reference frame used to perceive the far space, that is, to explore environment by movements of the eyes and the limbs. Finally, these reference frames were defined according to an egocentric perspective, that is, relative to the observer's own body. According to an allocentric object-centered perspective, spatial coordinates are defined relative the object itself (e.g., in the illustration the white part of the rectangle is in the right side relative to the black part, while both parts are in the left space of the observer) (Adapted from Legrain (2011))

somatosensory stimuli on the body space and the position of external stimuli (i.e., visual or auditory) occurring close to the body part on which the somatosensory stimuli are applied (see Holmes and Spence 2004; Maravita et al. 2003). The peripersonal frame of reference is specifically relevant to help guide direct manipulation of objects (Rizzolatti et al. 1997), unlike a more extrapersonal frame of reference which is more useful to explore the space by eye movements and to prepare reaching movements. Moreover, it is believed to be crucial for the organization of defensive motor actions (Graziano and Cooke 2006).

The existence of a peripersonal frame of reference to map the position of nociceptive stimuli supposes firstly the existence of multimodal interactions between nociceptive inputs and sensory inputs from other modalities. For instance, it has been suggested that vision of the limb onto which nociceptive stimuli are applied can modify the cortical processing of these nociceptive stimuli and the elicited pain (Longo et al. 2009; Mancini et al. 2011; Romano and Maravita 2014). In addition, Sambo et al. (2013) showed that the judgment about the occurrence of nociceptive stimuli could depend on the relative position of the limbs. They used a temporal order judgment task during which healthy blindfolded volunteers had to judge which of two nociceptive stimuli applied to either hand was perceived as being delivered first. The task was either performed with the hands in an uncrossed posture or with hands crossed over the sagittal midline of the body. This crossing-hand procedure is often used to induce a competition between somatotopic and spatiotopic frames of reference (when crossed, the left hand is right sided and the right hand left sided) (e.g., Shore et al. 2002; Smania and Agliotti 1995; Spence et al. 2004). The authors showed that judgments were much more complicated when the hands were crossed, suggesting that the perception of nociceptive stimuli was affected by a space-based frame of reference. It was also shown that crossing hands alters the processing of intensity of the stimuli and modifies brain responses to those stimuli (Gallace et al. 2011; Torta et al. 2013). These data support the idea that nociceptive inputs are integrated in multimodal representations of the body (Legrain et al. 2011; Haggard et al. 2013) in a brain network extending far beyond the classic nociceptive cortical network (Moseley et al. 2012b). More striking evidence was recently reported by De Paepe et al. (2014b) who provided data supporting the existence of a peripersonal frame of reference to map nociceptive stimuli. They used a temporal order judgment task with nociceptive stimuli applied to either hand and showed that the judgments were systematically biased by the occurrence of a visual stimulus in one side of space. Indeed, this visual cue facilitated the perception of the nociceptive stimulus applied to the ipsilateral hand, at the expenses of the stimulus applied to the opposite hand. Most important, this bias was significantly greater when the visual cue was presented close to the hand as compared to when it was presented 70 cm from the front of the hand. Using the crossing-hand procedure, additional experiments showed that this visuo-nociceptive spatial congruency effect was also influenced by the position of the limb (De Paepe et al. 2014a). For instance, the perception of a nociceptive stimulus applied to the left hand was facilitated by a proximal left-sided visual stimulus when the hands were uncrossed, but by a proximal right-sided visual stimulus when they were crossed. One important question

that remains to be addressed regards the neuronal mechanisms supporting such multimodal integration of nociceptive inputs. Animal studies have largely supported the notion that the peripersonal processing of tactile stimuli relies on the existence of multimodal neurons in the monkey's premotor and parietal cortices firing to the occurrence of tactile stimuli and visual stimuli when the latter are presented close to the adjacent somatosensory receptive fields (Graziano et al. 2004; see Macaluso and Maravita 2010 for a discussion about similar mechanisms in humans). Regarding nociception, only one study found similar multimodal neurons in the monkey's inferior parietal lobe (Dong et al. 1994).

The importance of the interaction between nociception, pain, and the representation of body space is also illustrated by the neuropsychological investigation of patients with chronic pain and more specifically in patients with complex regional pain syndrome (CRPS) (Moseley et al. 2012b; Legrain et al. 2012a). In addition to their sensory, motor, and vegetative symptoms, CRPS patients also suffer from unilateral cognitive deficits leading to impaired perception and impaired utilization of the affected limb. For this reason, CRPS patients were suspected to present with a "neglect-like" symptomatology (e.g., Förderreuther et al. 2004; Galer and Jensen 1999; Moseley 2004). Although the comparison to the symptomatology observed in poststroke patients with hemispatial neglect syndrome is still a matter of debate (see Legrain et al. 2012a; Punt et al. 2013), cortical changes observed in CRPS do not only affect areas involved in sensory and motor functions (Krause et al. 2006; Maihöfner et al. 2004) but also those involved in more complex and multisensory processing (Maihöfner et al. 2007). Several neglect-like symptoms were described such as asomatognosia (loss of body limbs' ownership) (Galer and Jensen 1999), hypo- and bradykinesia (movements are difficult to initiate and slower) (Frettlöh et al. 2006; Galer and Jensen 1999), impaired mental image (Moseley 2005), and impaired schema (Schwoebel et al. 2001; Moseley 2004) of the CRPS limb (see Legrain et al. 2012a for a review). Classic neuropsychological testing of neglect did not reveal major deficits in extra-body space (Förderreuther et al. 2004; Kolbe et al. 2012). Conversely, body space evaluations revealed phenomena of referred sensations such as allesthesia or synchiria in response to tactile stimuli applied to the CRPS limb (Acerra and Moseley 2005; Maihöfner et al. 2006; McCabe et al. 2003). Moseley et al. (2009) showed that temporal order judgments of tactile stimuli applied to either hand in a normal posture were biased at the expenses of the stimulus applied to the CRPS hand, suggesting a deficit similar to tactile extinction. But, surprisingly, the orientation of the perceptual bias was influenced by the position of the hands: when the hands were crossed, the perception of the stimulus applied to the healthy hand was in this case biased at the advantage of the stimulus applied to the CRPS hand. It was hypothesized that CRPS patients do not specifically neglect the perception of the CRPS limb but rather the part of the body placed in the side of space where the CRPS limb normally resides. The authors also showed significant changes of limb temperature when the limbs were crossed over the body midline (Moseley et al. 2012a). Finally, based on an experimental procedure aimed to misalign vision and proprioception using prismatic goggles, they suggested that the influence of spatial representation on body perception and temperature was mostly

driven by visual features rather than the proprioceptive perception of the position of the CRPS limb (Moseley et al. 2013). For these authors, the neglect-like symptoms observed in CRPS might reveal an altered representation of the body space organized along the sagittal midline of the body (Moseley et al. 2012b). The studies reviewed here above also show that CRPS-related symptoms can alter, not only somatotopic representations, but also spatiotopic representations of the body space (Moseley et al. 2009). These misaligned spatial representations would have been caused by maladaptive changes in cortical plasticity due to the initial musculoskeletal trauma (Moseley et al. 2012b) or implicit behavioral strategies to avoid limb provocation (Marinus et al. 2011). Altered body representations might in turn impair sensory perception and autonomic regulation of the pathological hemibody.

However, these assumptions were challenged by studies that showed that neglect-like symptoms cannot be locked to the side of space corresponding to the CRPS limb. Sumitani et al. (2007b) evaluated body representation in CRPS patients by means of visual estimates of the body midline. A visual stimulus was flashed and moved horizontally on a screen about 2 m in front of the participants. Patients were asked to guide verbally the visual stimulus until they estimated that the stimulus was positioned on the sagittal plane of their body midline. When the task was performed in the dark, their estimations were shifted significantly towards the side of space ipsilateral to their CRPS hand, as if, in the present case, they neglected the side of space corresponding to their healthy limb (for opposing results, see Kolbe et al. 2012; Reinersmann et al. 2012). As a consequence of nerve block following lidocaine injection, those estimates of the body midline tended to shift to the other hemispace, that is, the side of space contralateral to the CRPS hand (Sumitani et al. 2007b). These data suggest that the unbalanced body representation, as evaluated by visual body midline judgment task, is caused by attentional shifts due to excessive information coming from the affected limb, a hypothesis sharply in contrast with the assumption of a disownership of the CRPS limb (Moseley et al. 2012b). These discrepancies between the observed data across different studies emphasize that CRPS symptoms cannot be strictly paralleled to those observed in hemispatial neglect consequent to a stroke. Punt et al. (2013) argued that the CRPS-related motor symptoms such as hypo- and bradykinesia can be interpreted as a consequence to a learned nonuse consecutive to conditioned reduced attempts to move the pathological limb. Punt et al. (2013) added that representational and perceptual deficits were too subtle to be clinically relevant. Legrain et al. (2012a) suggested instead that neuropsychological testing performed until now was not adequate enough to reveal perceptual deficits specific to the CRPS pathophysiology. These authors recommended also a systematic investigation of spatial perception abilities across the different sensory modalities and, then, across the different frames of reference, using similar experimentally controlled procedures (see also Rossetti et al. 2013). In any case, the data reviewed in this paragraph suggest that chronic pain states such as CRPS can be useful to investigate the impact of pain on the abilities to represent and perceive the body and the surrounding space (Legrain et al. 2011; Moseley et al. 2012b) and the integration of nociceptive inputs in such cognitive representations (Haggard et al. 2013).

1.5   Action Selection

Peripersonal space is the privileged space for grasping and manipulating objects, but also for preparing defensive actions towards proximal objects that appear to be threatening. However, motor control and action selection have rarely been investigated in pain research. Yet, it is known that motor and premotor areas are activated by nociceptive stimuli (Gelnar et al. 1999; Frot et al. 2012). Using transcranial magnetic stimuli, Algoet et al. (2013) showed that nociceptive stimuli can modify motor excitability of the muscles of the arm and the hand onto which the stimulus is applied. It was also shown that the decision to move or to not move the hand onto which the noxious stimulus was applied altered the electrophysiological responses to this stimulus (Filevitch and Haggard 2012). But the neurophysiological mechanisms underlying the selection and the preparation of an action in response to nociceptive stimuli are still unknown. Recent studies suggest that reflex motor responses such as the eye blink reflex triggered by hand electrocutaneous stimulation can be controlled by high-order cognitive functions (Sambo et al. 2012a, b; Sambo and Iannetti 2013). These authors showed an increase of the magnitude of the eye blink reflex when the hand onto which the stimuli were applied approached the face. The authors concluded that this increase in the motor response could index the boundary of a defensive peripersonal representation of the face. However, because in these studies no external visual stimulus approaching the face was used as a control, the authors could not confirm the main role of vision nor exclude a causal role of personality traits such as anxiety. In this sense, any conclusion about a link between antinociceptive motor responses and spatial cognition is premature.

1.6   Neuropsychological Rehabilitation

Until now, the usefulness of clinical neuropsychology for the treatment of pain is still underestimated. However, some of the data reviewed above suggest a potential effectiveness for rehabilitation techniques based on cognitive neuropsychology. For instance, due to some similarities between CRPS and hemispatial neglect symptomatologies, Sumitani et al. (2007a) proposed to use in pain patients prismatic adaptation (PA), a noninvasive procedure which combines visual displacement induced by prismatic goggles and sensorimotor coordination to promote a reorganization of spatial cognition (Rossetti et al. 1998). This method allows misdirecting the brain by misaligning the real position and the visually perceived position of a target during a reach-to-point task and forces to compensate pointing movements during adaption by generating a realignment of sensorimotor coordination. PA has been shown to decrease neglect-related symptoms in poststroke patients (Rode et al. 2003). Sumitani et al. (2007a) used PA in five CRPS patients with prisms creating visual

displacement towards the side of space contralateral to the CRPS limb, that is, towards the side of space corresponding to the healthy limb. It is worth noting that Sumitani et al. (2007b) reported that CRPS patients neglected the portion of space corresponding to the healthy limb. Therefore, whereas PA in neglect patients is generally performed with prismatic displacement towards the non-neglected ipsilesional hemispace, Sumitani et al. (2007a) induced prismatic displacement towards the neglected hemispace. While body midline judgments were immediately shifted towards the hemispace ipsilateral to the healthy limb, the authors observed a reduction of pain and other CRPS-related symptoms only two weeks after PA. A follow-up of one single case showed that when PA was performed with a visual displacement towards the CRPS (non-neglected) side, the symptoms worsened. This suggests that the orientation of prismatic shift is a crucial feature for rehabilitation. Bultitude and Rafal (2010) replicated these results, again with PA promoting a visual displacement towards the hemispace ipsilateral to the healthy limb. They also showed that PA was effective in reducing CRPS symptoms only when the pointing task was performed with the CRPS hand, but not when PA was performed with the healthy hand. Despite the low number of cases, two conclusions can be proposed. First, PA seems effective in reducing not only body representation displacements but also CRPS symptoms. This suggests that sensorimotor misalignment during visually guided movements can have a role in CRPS pathophysiology. Second, the fact that the effectiveness of PA in CRPS depends on the specific displacement of vision towards the neglected hemispace and on the specific pointing with the CRPS hand suggests that impaired spatial cognition in hemispatial neglect and CRPS relies on different mechanisms.

1.7   Conclusion

Recent years have seen new interests for theoretical models of cognitive psychology in the field of pain research through analyses of behaviors such as reaction times and temporal order judgments. It is important to note that this approach does not deny the importance of the sensation of pain, nor the existence of neurophysiological mechanisms generating this feeling as specific qualia. Instead, this approach emphasizes the need to take into account the cognitive state of the subject receiving a painful stimulus at a given time and in a particular environment. It also emphasizes the functional role that pain has for adapting sensorimotor functions of the body to a perpetually unstable and potentially threatening environment. The cognitive approach of pain also emphasizes the need to go beyond the purely physiological conceptualization of nociceptive processing and to define a theoretical framework that incorporates pain as an epiphenomenon of a system which represents, perceives, and defends the body and its surrounding space. This approach also proposes a synergy between classical medical intervention and neuropsychological rehabilitation, towards what we would be tempted to call *cognitive physiotherapy*.

References

Acerra NE, Moseley GL (2005) Dysynchiria: watching the mirror image of the unaffected limb elicits pain on the affected side. Neurology 65:751–753

Algoet M, Duqué J, Iannetti GD, Mouraux A (2013) Temporal dynamics and specificity of the motor responses to a transient nociceptive stimulus in humans. Poster presented at the 8th Congress of the European Pain Federation (EFIC), Florence, 9–12 Oct 2013

Allport A (1987) Selection for action: some behavioral and neurophysiological considerations of attention and action. In: Heuer H, Sanders AF (eds) Perspectives on perception and action. Erlbaum, Hillsdale, pp 395–419

Bantick SJ, Wise RG, Ploghaus A, Clare S, Smith SM, Tracey I (2002) Imaging how attention modulates pain in humans using functional MRI. Brain 125:310–319

Boisacq-Schepens N, Crommelinck M (1996) Neuro-psycho-physiologie. 2. Comportement, 3rd edn. Masson, Paris

Broadbent DE (1958) Perception and communication. Pergamon Press, Oxford

Bultitude JH, Rafal RD (2010) Derangement of body representation in complex regional pain syndrome: report of a case treated with mirror and prisms. Exp Brain Res 204:409–418

Crollen V, Collignon O (2012) Embodied space in early blind individuals. Front Psychol 3:272

Crombez G, Baeyens F, Eelen P (1994) Sensory and temporal information about impending pain: the influence of predictability on pain. Behav Res Ther 32:611–622

Crombez G, Eccleston C, Baeyens F, Eelen P (1996) The disruptive nature of pain: an experimental investigation. Behav Res Ther 34:911–918

Crombez G, Eccleston C, Baeyens F, Eelen P (1997) Habituation and interference of pain with task performance. Pain 70:149–154

De Paepe AL, Crombez G, Legrain V (2014a) Beyond the somatotopic organization of pain: evidence for a peripersonal frame of reference during the localization of nociceptive stimuli. Poster presented at the 8th Congress of the European Pain Federation (EFIC), Florence, 9–12 Oct 2013

De Paepe AL, Crombez G, Spence C, Legrain V (2014b) Mapping nociceptive stimuli in a peripersonal frame of reference: evidence from a temporal order judgment task. Neuropsychologia 56:219–228

Desimone R, Duncan J (1995) Neural mechanisms of selective visual attention. Annu Rev Neurosci 18:193–222

Dong WK, Chudler EH, Sugiyama K, Roberts VJ, Hayashi T (1994) Somatosensory, multisensory, and task-related neurons in cortical area 7b (PF) of unanesthetized monkeys. J Neurophysiol 72:543–564

Downar J, Mikulis DJ, Davis KD (2003) Neural correlates of the prolonged salience of painful stimulation. Neuroimage 20:1540–1551

Eccleston C, Crombez G (1999) Pain demands attention: a cognitive-affective model of the interruptive function of pain. Psychol Bull 125:356–366

Egeth HE, Yantis S (1997) Visual attention: control, representation, and time course. Annu Rev Psychol 48:269–297

Filevitch E, Haggard P (2012) Grin and bear it! Neural consequences of a voluntary decision to act or inhibit action. Exp Brain Res 223:341–351

Folk CL, Remington RW, Johnston JC (1992) Involuntary covert orienting is contingent on attentional control settings. J Exp Psychol Hum Percept Perform 18:1030–1044

Förderreuther S, Sailer U, Straube A (2004) Impaired self-perception of the hand in complex regional pain syndrome (CRPS). Pain 110:756–761

Frettlöh J, Hüppe M, Maier C (2006) Severity and specificity of neglect-like symptoms in patients with complex regional pain syndrome (CRPS) compared to chronic limb pain of other origins. Pain 124:184–189

Frot M, Magnin M, Mauguière F, Garcia-Larrea L (2012) Cortical representation of pain in primary sensory-motor areas (SI/MI) – a study using intracortical recordings in humans. Hum Brain Mapp 34:2655–2668

Galer BS, Jensen M (1999) Neglect-like symptoms in complex regional pain syndrome: results of a self-administrated survey. J Pain Symptom Manage 18:213–217

Gallace A, Torta DM, Moseley GL, Iannetti GD (2011) The analgesic effect of crossing the arms. Pain 152:1418–1423

Gelnar PA, Krauss BR, Sheehe PR, Szeverenyi NM, Apkarian AV (1999) A comparative fMRI study of cortical representations for thermal painful, vibrotactile, and motor performance tasks. Neuroimage 10:460–482

Graziano MSA, Cooke DF (2006) Parieto-frontal interactions, personal space, and defensive behavior. Neuropsychologia 44:2621–2635

Graziano MSA, Gross CG, Taylor CSR, Moore T (2004) A system of multimodal areas in the primate brain. In: Spence C, Driver J (eds) Crossmodal space and crossmodal attention. Oxford University Press, Oxford, pp 51–67

Hadjistavropoulos HD, Hadjistavropoulos T, Quine A (2000) Health anxiety moderates the effects of distraction versus attention to pain. Behav Res Ther 38:425–438

Haggard P, Iannetti GD, Longo MR (2013) Spatial sensory organization and body representation in pain perception. Curr Biol 23:R164–R176

Harvey AG, McGuire BE (2000) Suppressing and attending to pain-related thoughts in chronic pain patients. Behav Res Ther 38:1117–1124

Holmes NP, Spence C (2004) The body schema and multisensory representation(s) of peripersonal space. Cogn Process 5:94–105

Hommel B (2010) Grounding attention in action controls: the intentional control of selection. In: Bruya B (ed) Effortless attention. A new perspective in the cognitive science of attention and action. MIT press, Cambridge, pp 121–140

Honoré J, Hénon H, Naveteur J (1995) Influence of eye orientation on pain as a function of anxiety. Pain 63:213–218

Hu L, Zhao C, Li H, Valentini E (2013) Mismatch responses evoked by nociceptive stimuli. Psychophysiology 50:158–173

Iannetti GD, Hughes NP, Lee MC, Mouraux A (2008) Determinants of laser-evoked EEG responses: pain perception or stimulus saliency? J Neurophysiol 100:815–828

Itti L, Koch C (2001) Computational modelling of visual attention. Nat Rev Neurosci 2:194–203

Jacquin-Courtois S, Legrain V, Sumitani M, Miyauchi S, Rossetti Y (2012) Visuo-motor adaptation and bodily representations: from neglect to complex regional pain syndrome. Let Med Phys Readapt 28:93–98

James W (1890) The principles of psychology. H Holt and Co., New York (edition of 1950 by Dover Publications, New York)

Johnson MH, Petrie SM (1997) The effects of distraction on exercise and cold pressor tolerance for chronic low back pain sufferers. Pain 69:43–48

Knudsen EI (2007) Fundamental components of attention. Annu Rev Neurosci 30:57–78

Kolbe L, Lang S, Maihöfner C (2012) Cognitive correlates of "neglect-like syndrome" in patients with complex regional pain syndrome. Pain 153:1063–1073

Krause P, Förderreuther S, Straube A (2006) TMS motor cortical brain mapping in patients with complex regional pain syndrome type I. Clin Neurophysiol 117:169–176

Lavie N (2010) Attention, distraction, and cognitive control under load. Curr Dir Psychol Sci 19:143–148

Legrain V (2011) Where is my pain? Pain 152:467–468

Legrain V, Guérit JM, Bruyer R, Plaghki L (2002) Attentional modulation of the nociceptive processing into the human brain: selective spatial attention, probability of stimulus occurrence, and target detection effects on laser evoked potentials. Pain 99:21–39

Legrain V, Bruyer R, Guérit JM, Plaghki L (2005) Involuntary orientation of attention to unattended deviant nociceptive stimuli is modulated by concomitant visual task difficulty. Evidence from laser evoked potentials. Clin Neurophysiol 116:2165–2174

Legrain V, Perchet C, Garcia-Larrea L (2009a) Involuntary orienting of attention to pain. Neural and behavioral signatures. J Neurophysiol 102:2423–2434

Legrain V, Van Damme S, Eccleston C, Davis KD, Seminowicz DA, Crombez G (2009b) A neuro-cognitive model of attention to pain: behavioral and neuroimaging evidence. Pain 144:230–232

Legrain V, Iannetti GD, Plaghki L, Mouraux A (2011) The pain matrix reloaded. A salience-detection system for the body. Prog Neurobiol 93:111–124

Legrain V, Bultitude JH, De Paepe AL, Rossetti Y (2012a) Pain, body, and space. What do patients with complex regional pain syndrome really neglect? Pain 153:948–951

Legrain V, Mancini F, Sambo CF, Torta DM, Ronga I, Valentini E (2012b) Cognitive aspects of nociception and pain. Bridging neurophysiology with cognitive psychology. Neurophysiol Clin 42:325–336

Legrain V, Crombez G, Plaghki L, Mouraux A (2013) Shielding cognition from nociception with working memory. Cortex 49:1922–1934

Leventhal H, Everhart D (1979) Emotions, pain, and physical illness. In: Izard CE (ed) Emotions in personality and psychopathology. Plenum, New York, pp 263–299

Liu CC, Veldhuijzen DS, Ohara S, Winberry J, Greenspan JD, Lenz FA (2011) Spatial attention to thermal pain stimuli in subjects with visual spatial hemi-neglect: extinction, mislocalization and misidentification of stimulus modality. Pain 152:498–506

Longo MR, Betti V, Aglioti SM, Haggard P (2009) Visually induced analgesia: seeing the body reduces pain. J Neurosci 29:12125–12130

Macaluso E, Maravita A (2010) The representation of space near the body through touch and vision. Neuropsychologia 48:782–795

Maihöfner C, Handwerker HO, Neundörfer B, Birklein F (2004) Cortical reorganization during recovery from complex regional pain syndrome. Neurology 63:693–701

Maihöfner C, Neundörfer B, Birklein F, Handwerker HO (2006) Mislocalization of tactile stimulation in patients with complex regional pain syndrome. J Neurol 253:772–779

Maihöfner C, Baron R, DeCol R, Binder A, Birklein F, Deuschl G, Handwerker HO, Schattschneider J (2007) The motor system shows adaptive changes in complex regional pain syndrome. Brain 130:2671–2687

Mancini F, Longo MR, Kammers MP, Haggard P (2011) Visual distortion of body size modulates pain perception. Psychol Sci 22:325–330

Maravita A, Spence C, Driver J (2003) Multisensory integration and the body schema: close to hand and within reach. Curr Biol 13:R531–R539

Marinus J, Moseley GL, Birklein F, Baron R, Maihöfner C, Kingery WS, van Hilten JJ (2011) Clinical features and pathophysiology of complex regional pain syndrome. Lancet Neurol 10:637–648

McCabe CS, Haigh RC, Ring EFJ, Halligan PW, Wall PD, Blake DR (2003) A controlled pilot study of the utility of mirror visual feedback in the treatment of complex regional pain syndrome (type 1). Rheumatology 42:97–101

McCaul KD, Malott JM (1984) Distraction and coping with pain. Psychol Bull 95:516–533

Melzack R, Casey KL (1968) Sensory, motivational, and central control determinants of pain: a new conceptual model. In: Kenshalo D (ed) The skin senses. Chas C Thomas, Springfield, pp 423–439

Miron D, Duncan GH, Bushnell MC (1989) Effects of attention on the intensity and unpleasantness of thermal pain. Pain 39:345–352

Morley S (2011) Efficacy and effectiveness of cognitive behaviour therapy for chronic pain: progress and some challenges. Pain 152:S99–S106

Moseley GL (2004) Why do people with complex regional pain syndrome take longer to recognize their affected hand? Neurology 64:2182–2186

Moseley GL (2005) Distorted body image in complex regional pain syndrome. Neurology 65:773

Moseley GL, Gallace A, Spence C (2009) Space-based, but not arm-based, shift in tactile processing in complex regional pain syndrome and its relationship to cooling of the affected limb. Brain 132:3142–3151

Moseley GL, Gallace A, Iannetti GD (2012a) Spatially defined modulation of skin temperature and hand ownership of both hands in patients with unilateral complex regional pain syndrome. Brain 135:3676–3686

Moseley GL, Gallace A, Spence C (2012b) Bodily illusions in health and disease: physiological and clinical perspectives and the concept of a cortical 'body matrix'. Neurosci Biobehav Rev 36:34–46

Moseley GL, Gallace A, Di Pietro F, Spence C, Iannetti GD (2013) Limb-specific autonomic dysfunction in complex regional pain syndrome modulated by wearing prism glasses. Pain 11:2463–2468

Näätänen R (1992) Attention and brain function. Erlbaum, Hillsdale

Neisser U (1967) Cognitive psychology. Meredith, New York

Penfield W, Boldrey E (1937) Somatic and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 60:389–443

Peyron R, Garcia-Larrea L, Grégoire MC, Costes N, Convers P, Lavenne F, Mauguière F, Michel D, Laurent B (1999) Haemodynamic brain responses to acute pain in humans. Sensory and attentional networks. Brain 122:1765–1779

Price DD, Harkins SW (1992) The affective-motivational dimension of pain: a two-stage model. Am Pain Soc J 1:229–239

Punt TD, Cooper L, Hey M, Johnson MI (2013) Neglect-like symptoms in complex regional pain syndrome: learned nonuse by another name? Pain 154:200–203

Ramachandran VS, Rogers-Ramachandran D, Stewart M (1992) Perceptual correlates of massive cortical reorganization. Science 258:1159–1160

Reinersmann A, Landwehrt J, Krumova EK, Ocklenburg S, Güntürkün O, Maier C (2012) Impaired spatial body representation in complex regional pain syndrome type 1 (CRPS I). Pain 153:2174–2181

Rizzolatti G, Craighero L (1998) Spatial attention: mechanisms and theories. In: Sabourin M, Craik F, Robert M (eds) Advances in psychological science, vol 2, Biological and cognitive aspects. Psychology Press, East Sussex, pp 171–198

Rizzolatti G, Fadiga L, Fogassi L, Gallese V (1997) The space around us. Science 277:190–191

Roa Romero Y, Straube T, Nitsch A, Miltner WHR, Weiss T (2013) Interaction between stimulus intensity and perceptual load in the attentional control of pain. Pain 154:135–140

Rode S, Salkovskis PM, Jack T (2001) An experimental study of attention, labelling and memory in people suffering from chronic pain. Pain 94:193–203

Rode G, Pisella L, Rossetti Y, Farnès A, Boisson D (2003) Bottom-up transfer of sensory-motor plasticity to recovery of spatial cognition: visuo-motor adaptation and spatial neglect. Prog Brain Res 142:273–287

Romano D, Maravita A (2014) The visual size of one's own hand modulates pain anticipation and perception. Neuropsychologia 57:93–100

Rossetti Y, Rode G, Pisella L, Farnè A, Li L, Boisson D, Perenin MT (1998) Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. Nature 395:166–169

Rossetti Y, Jacquin-Courtois S, Legrain V, Bultitude J, O'Shea J (2013) Le syndrome douloureux régional chronique à la lumière des troubles de la cognition spatiale: des opportunités physio-pathologiques et thérapeutiques? In: Ribnik P, Genty M (eds) Syndrome douloureux chroniques en médecine physique et de réadaptation. Springer, Paris, pp 99–109

Sambo CF, Iannetti GD (2013) Better safe than sorry? The safety margin surrounding the body is increased by anxiety. J Neurosci 33:14225–14230

Sambo CF, Forster B, Williams SC, Iannetti GD (2012a) To blink or not to blink: fine cognitive tuning of the defensive peripersonal space. J Neurosci 32:12921–12927

Sambo CF, Liang M, Cruccu G, Iannetti GD (2012b) Defensive peripersonal space: the blink reflex evoked by hand stimulation is increased when the hand is near the face. J Neurophysiol 107:880–889

Sambo CF, Torta DM, Gallace A, Liang M, Moseley GL, Iannetti GD (2013) The temporal order judgement of tactile and nociceptive stimuli is impaired by crossing the hands over the body midline. Pain 154:242–247

Schwoebel J, Friedman R, Duda N, Coslett HB (2001) Pain and the body schema. Evidence for peripheral effects on mental representations of movement. Brain 124:2098–2104

Seron X (1994) La neuropsychologie cognitive, 2nd edn. Presses Universitaires de France, Paris

Shiffrin RM, Schneider W (1977) Controlled and automatic human information processing. II. Perceptual learning, automatic attending and a general theory. Psychol Rev 84:127–190

Shore DI, Spry E, Spence C (2002) Confusing the mind by crossing the hands. Cogn Brain Res 14:153–163

Smania N, Aglioti S (1995) Sensory and spatial components of somaesthetic deficits following right brain damage. Neurology 45:1725–1730

Spence C, Pavani F, Driver J (2004) Spatial constraints on visual-tactile cross-modal distractor congruency effects. Cogn Affect Behav Neurosci 4:148–169

Sumitani M, Rossetti Y, Shibata M, Matsuda Y, Sakaue G, Inoue T, Mashimo T, Miyauchi S (2007a) Prism adaptation to optical deviation alleviates pathologic pain. Neurology 68:128–133

Sumitani M, Shibata M, Iwakura T, Matsuda Y, Sakaue G, Inoue T, Mashimo T, Miyauchi S (2007b) Pathologic pain distorts visuospatial perception. Neurology 68:152–154

Torta DM, Diano M, Costa T, Gallace A, Duca S, Geminiani GC, Cauda F (2013) Crossing the line of pain: fMRI correlates of crossed-hands analgesia. J Pain 14:957–965

Vallar G, Maravita A (2009) Personal and extrapersonal spatial perception. In: Berntson GG, Cacioppo JT (eds) Handbook of neuroscience for the behavioral sciences. Wiley, New York, pp 322–336

Van Damme S, Legrain V, Vogt J, Crombez G (2010) Keeping pain in mind: a motivational perspective on attentional processing of pain. Neurosci Biobehav Rev 34:204–213

Van Ryckeghem DML, Van Damme S, Crombez G, Eccleston C, Verhoeven K, Legrain V (2011) The role of spatial attention in attentional control over pain: an experimental investigation. Exp Brain Res 208:269–275

Van Ryckeghem DML, Crombez G, Eccleston C, Legrain V, Van Damme S (2013) Keeping pain out of your mind: the role of attentional set in pain. Eur J Pain 17:402–411