

Hypervigilance and pain: The role of bodily threat

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What is that thing called pain?

In everyday life, everybody now and then experiences pain. Although everyone knows how pain feels, it is still hard to formulate a clear description of what pain is. Pain is often regarded as a sensation that is evoked by harmful internal or external stimuli. It usually has a strong negative affective component, and it can hardly be described without referring to the consequences that pain may have on the individual (i.e. tissue damage, emotional implications) (Janssen, 2002). The International Association for the Study of Pain (IASP) defines it as follows: “Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. It is a subjective experience with qualia distinct from other somatosensory sensations. Pain can be classified along a variety of dimensions and one important distinction is according to the mechanisms that are involved in pain. The most common types of pain that can be distinguished are nociceptive, neuropathic and inflammatory pain (Woolf et al., 1998; Woolf, 2004). The first one is triggered by the presence of intense stimuli, most often leading to tissue damage, such as the pain we feel when we burn our hand on a hot oven or when we eat something very cold. This pain fulfills a vital warning function to prevent us from physical harm. It is alarming, sharp, easy to localize and its protective role demands immediate attention and action in order to avoid further tissue damage (Woolf, 2010). Neuropathic and inflammatory pain, on the other hand, are resulting from abnormal functioning and/or lesion of respectively the nervous system or in response to injury of inflammation. Neuropathic pain is often described as a “burning”, “itching”, and/or “electrical” pain. It is not protective, but maladaptive, as the intensity of the pain is no longer in proportion to the nature of the stimulus (Serpell, Makin, & Harvey, 1998). Another classification of pain is according to its duration (King, 2000; Turk & Melzack, 2001). *Acute* pain generally comes on suddenly, accompanied by anxiety or emotional distress. The cause of acute pain can usually be diagnosed and treated, and the pain is self-limiting, that is, it is confined to a given period of time and severity (i.e. pain of a

duration of less than three months). Not every kind of pain can be easily alleviated. *Chronic* pain persists over a longer period of time than acute pain. It is defined as pain that lasted longer than three months or longer than the expected time for recovery after injury or illness. In chronic pain syndromes, it appears that pain symptoms are resistant to almost any medical treatment.

Pain is one of the most common problems in healthcare. In Europe, 19% of the adults experience chronic pain of moderate to severe intensity (Breivik, Collet, Ventafridda, Cohen, & Gallacher 2006). Pain is more prevalent in women than in men and its prevalence is found to increase with age (Bouhassira, Lantéri-Minet, Attal, Laurent, & Touboul, 2008; Català et al., 2002; Chung & Wong, 2007). However, it appears difficult to determine the exact prevalence of chronic pain and the related problems (Carr et al., 2003). Prevalence ratings of chronic pain often vary from 10 to 20% (Gatchel, Peng, Peters, Fuchs, & Turk, 2007). Studies on chronic pain often use different methods to measure pain and they do so with varying sample sizes. The inconsistency can furthermore be explained by the lack of consensus about the definition of chronic pain (Carr et al., 2003; Ospina & Harstall, 2002). Furthermore, chronic pain is not only highly prevalent, it also may have major personal and social impacts, restricting the individual in social and vocational functioning (Breivik et al., 2006; Krismer and Van Tulder, 2007; Vos et al., 2012) and entails enormous financial costs, especially through work absenteeism (Dagenais, Caro, & Haldeman, 2008).

From a biomedical to a biopsychosocial perspective on pain

A long time ago, medical care was largely based upon a “biomedical model”. In this model, it was assumed that there exists a direct relation between tissue damage and pain: the more damage, the more pain one experiences. The Cartesian model formulated by Descartes in 1664 (Descartes as cited in Main & Spanswick, 2000) was one of the precursors of the biomedical model, and stated that body and mind are distinct in the causation and outcomes of diseases. A “golden standard” such as blood pressure, bacterium, and biopsy provided the essential marker for diagnosis, prognosis and treatment. Since the biomedical model of health focused on purely biological factors, additional information about patients (history, environmental, social and psychological influences) often was

regarded as largely irrelevant (Ogden, 2010). This biomedical perspective provided effective solutions for acute pain. Yet, it could not account for a number of observations. Pain can persist long after tissue healing, placebo treatments influence the experience of pain (Wager et al., 2004), and even innocuous stimuli can produce pain (e.g. hyperalgesia).

During the 20th century, it was stated that a more complete understanding of pain must take into account not only biological, but also psychological (mental, emotional and behavioral), and social factors. Beecher (Beecher, as cited in Morley and Vlaeyen, 2010) was one of the first who showed that there is not per se a direct relationship between the experience of pain and the physical damage. He observed that when battle-wounded soldiers were hospitalized after removal from the battlefield, soldiers experienced relatively less pain than would be expected based on observed tissue damage. Built on these observations, Beecher put forward the important role of psychological factors in the explanation of pain experiences. The gate control theory of Melzack and Wall (1965) responded to these shortcomings and paved the way to the biopsychosocial model of pain. This gate control theory proposed that a mechanism in the dorsal horns of the spinal cord acts like a gate that inhibits or facilitates transmission from both afferent nerves (sensory input) and efferent nerves (descending from the brain). When the 'gate' is open, nociceptive messages get through easily and pain can be very intense. When the 'gate' closes, nociceptive messages are prevented from reaching the brain and may not even be experienced. Though, a variety of substances has been identified that have an impact on opening (substantia P.) or closing (endorphins) the 'gate'. Moreover, psychological variables such as past experiences and other cognitive activities have been integrated that might influence the perception of pain, through central mechanisms and descending pathways. In 1980, the biopsychosocial model of pain emerged due to the work of Engel (Engel, 1977) and assumed that pain experiences are influenced by biological, psychological and social factors (Gatchel, et al., 2007). Today, the biopsychosocial model is accepted as the most heuristic approach to chronic pain.

Within this biopsychosocial thinking, a number of psychological variables such as personality, pain-related fear, catastrophizing about pain, have been put forward as important factors of how pain is experienced. One factor that is deemed important in helping to explain the perception of pain in acute and

chronic pain is *attention* (Crombez, Van Damme & Eccleston, 2005). In what follows, we describe what attention is, and we discuss the role of attention in the perception of pain.

Pain and attention: what is their relationship?

Attention is a well-known, but complex psychological construct. One of the first psychologists who described attention was William James, who defined attention as follows: “*Everyone knows what attention is. It is taking possession by the mind in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought... It implies withdrawal from some things in order to deal effectively with other*” (James, 1890).

A functional attentional system serves two apparently contradictory functions (Eccleston & Crombez, 1999; Norman & Shallice, 1986; Van Damme, Legrain, Vogt, & Crombez, 2010). First, it is proposed that much of behavior is automatically triggered in the pursuit of specific goals. Attention ensures that these current goals are fulfilled properly without being distracted by less important demands. The importance of the goals determines how much attention is devoted to these goals. Second, a successful attentional system must also take into account that ongoing behavior might be interrupted when more important demands emerge. At any time, attention may be flexibly switched toward a new superordinate goal to protect an organism from danger (Shallice & Burgess, 1993). An ideal candidate in this respect is pain. Pain is the archetypal warning of danger to an organism: it might interrupt ongoing behavior and urge the individual to escape from the dangerous situation (i.e., more important goal of self-protection) (Chapman, Tuckett, & Song, 2008). Finding a balance between the need for continuity of attentional engagement and the need for attentional interruptibility is necessary for survival (Allport, 1989). In an unpredictable and potentially dangerous situation constantly shifting to new events would result in chaotic behavior, whereas failing to shift to environmental threats is hazardous and potentially dangerous (Van Damme, et al., 2010). Attention to pain might be the result of the interplay between those two potentially contradictory requirements. The distinction between these two forms of attention is similar to

the distinction between bottom-up and top-down influences of attention (Corbetta & Schulman, 2002; Sarter, Givens, & Bruno, 2001).

Bottom-up attention to pain

Suppose you bite your tongue while eating. There is a high chance that this sensation will capture your attention and interrupt your meal for a while. In this example, the capture of attention by pain can be thought of as a *stimulus-driven* or *bottom-up* effect. According to the cognitive-affective model of the interruptive function of pain (Eccleston & Crombez, 1999), this bottom-up mechanism demonstrates the evolutionary benefit of the experience of pain: it informs us about potential bodily damage and urges an adequate (re)action to prevent further injury. In order to investigate the variables underlying the interruptive function of pain, the primary task paradigm was developed (Crombez, Baeyens, & Eelen, 1994; Eccleston, 1994). In this paradigm, participants are asked to execute a primary task, such as detecting and/or discriminating between certain stimuli. While performing this task, painful stimuli are occasionally administered, which participants are instructed to ignore. Several studies using this paradigm showed significant impairment of task performance during the simultaneous presentation of pain (Buhle & Wager, 2010; Crombez, Eccleston, Baeyens, & Eelen, 1997, 1998b; Seminowicz, & Davis, 2007; Richardson, et al., 2010; Van Damme, Crombez, & Eccleston, 2004a) and pain-related information (e.g. pain words, Pincus & Morley, 2001; Roelofs, Peters, Zeegers, & Vlaeyen, 2002; Vancleef & Peters, 2006), thereby demonstrating an attentional interruption by pain. The interference of attention by pain is especially pronounced when pain is salient (Crombez et al., 1994), novel (Crombez, Eccleston, Baeyens, & Eelen, 1996; Legrain, Bruyer, Guérit & Plaghki, 2003) and/or intense (Crombez, Eccleston, Baeyens, & Eelen, 1998a; Eccleston, 1994).

The bottom-up capture of attention by pain has been extensively documented in pain research (e.g. Eccleston & Crombez, 1999; Van Damme et al., 2010). However, also *top-down* or goal-directed attention might play a role. Considerably less research is available that investigated how pain or bodily threat influence the top-down selection of attention.

Top-down attention to pain

Attention can also be directed to painful events by top-down variables, which are regulated according to the relevance of the stimuli relatively to cognitive objectives and motivations. Since pain typically occurs within a context of goal pursuit (Van Damme et al., 2010), the current goals/concerns of an individual might direct attention toward (top-down facilitation) or away (top-down inhibition) from pain or pain-related information. Top-down selection of attention functions as a goal-direct process that prioritizes information relevant for current actions. According to the neurocognitive model of attention to pain (see Figure 1) of Legrain and colleagues (2009), *executive functions in working memory* might play a role in the top-down modulation of attention to pain. Working memory stores and rehearses the information that is important for the current goals and can control involuntary shifts of attention toward irrelevant distracters. Executive functions, such as inhibition, switching ability, and working memory capacity might influence the processing of task-relevant information in order to avoid attentional capture and interference by painful stimuli. Furthermore, the neurocognitive model of attention to pain states that top-down processing is directed by cognitive goals activated in working memory, such as the *attentional load* and *attentional set*. Attentional load refers to the amount of attention one invests in a task. When the overall effort needed to perform the task is high, there is less attention available to invest in task-irrelevant stimuli (Lavie & de Fockert, 2006). When someone is engaged in an activity that is interesting and challenging for our brain, our perception of pain is reduced. Legrain, Bruyer, Guérit, and Plaghki (2005) for example, demonstrated that the interruption of pain was decreased, when attention was strongly engaged in a task. Romero, Straube, Nitsch, Miltner, and Weiss (2013) showed that increasing the perceptual load of attentional resources of a non-pain-related task resulted in reduced intensity ratings of high intensity stimuli. Attentional set refers to a mental set of stimulus features that participants use to identify goal-relevant stimuli (Yantis, 2000). When a stimulus, even when it is not particularly salient, happens to match one of the features in the attentional set, it is more likely to be selected for further processing (see Folk, Remington, & Johnston, 1992; 1993; Yantis, 2000 for attentional set within the context of visual information). Thus, it is proposed that individuals adopt ‘attentional control settings’ including certain stimulus

features or characteristics that are relevant for their goals and that will receive more attention if they are present in the environment (e.g. Van Ryckeghem, Crombez, Eccleston, Legrain & Van Damme, 2013).

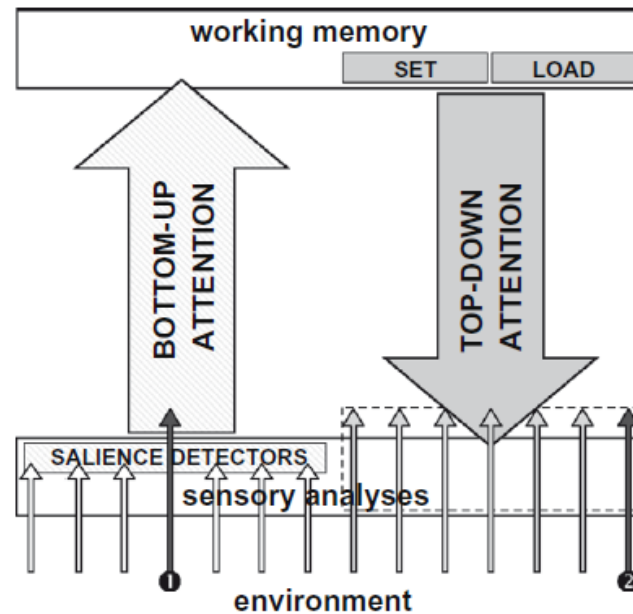


Figure 1. The neurocognitive model of attention to pain of Legrain et al. (2009). Attention can be selected by two different modes. Bottom-up selection corresponds to an unintentional capture of attention by events themselves (arrow 1). Bottom-up attention might be modulated by top-down variables, i.e. intentional and goal-directed processes that prioritizes information relevant for current actions (arrow 2).

Top-down attentional inhibition versus top-down attentional facilitation

Most of the studies investigating top-down cognitive control of pain have mainly focused on top-down *inhibition* mechanisms. The findings of studies on distraction, i.e. the attentional strategy to direct attention away from a painful stimulus, have shown that distraction affects the experience of pain. Most of these studies support the idea that distraction reduces or inhibits pain (e.g. Tracey et al., 2002; Tracey & Mantyh, 2007; Van Damme, Crombez, Van Nieuwenborgh-De Wever, & Goubert, 2008; Van Ryckeghem, Crombez, Van Hulle & Van Damme, 2012; Veldhuijzen, Kenemans, de Bruin, Olivier, & Volkerts, 2006; Verhoeven et al., 2011), but there are also studies in which no distraction effects were found (e.g. Hadjistavropoulos, Hadjistavropoulos, & Quine, 2000; Roelofs, Peters, van der Zijden, & Vlaeyen, 2004), or where opposite results were demonstrated (e.g. Goubert, Crombez, Eccleston, & Devulder, 2004; Keogh, Hatton, & Ellery, 2000).

There is increasing evidence that whether or not a top-down inhibition effect occurs, is dependent upon several other characteristics such as individual variables, working memory capacities, context variables. The influence of working memory capacities in directing attention away from pain-related information has been shown in a study of Legrain, Crombez, and Mouraux (2011a) and Legrain, Crombez, Verhoeven and Mouraux (2011b). When working memory was loaded with pain-unrelated information (e.g. rehearsing the features of the preceding visual targets), there was less interference of novel nociceptive stimuli on task performance. Van Ryckeghem and colleagues (2011) have demonstrated the importance of context variables by showing that the distraction effect is partly the result of the spatial location of the distracting information. It was shown that when participants directed their attention away from the painful stimuli, their responses to these stimuli were slower. Of particular interest, participants perceived the pain stimulus as less painful when a visual cue was presented at a different location compared when the visual cue and electrocutaneous stimulus were presented at the same location. Last, the affective-motivational value of a non-pain-related goal is another essential factor with respect to top-down attentional inhibition (see Van Damme et al., 2010 for theoretical accounts for a motivational basis of attention). It is assumed that distraction will be more effective when the distraction task is related to an important personal goal (Van Damme et al., 2010). Schrooten and colleagues (2012) have demonstrated that attentional bias to pain signals was inhibited when individuals were engaged in the pursuit of another salient, non-pain-related goal (e.g. monetary reward and punishment of the performance on a second task). Likewise, Verhoeven, Crombez, Eccleston & Van Damme (2010) demonstrated that such non-pain-related goals indeed resulted in a higher reduction of pain and showed moreover that these distraction effects were influenced by the level of catastrophic thinking about pain. For low catastrophizers, executing a distraction task while experiencing pain, resulted in less pain as compared to a control group (to which no distraction task was given). Though, for high catastrophizers, executing a distraction task while experiencing pain, resulted in less pain, only when the distraction task was motivationally relevant (e.g. receiving a monetary reward for good task performance). Increasing the motivational relevance of the distraction task increased the effects of distraction, especially for high pain catastrophizers.

Less is however known about the top-down attentional *facilitation* of pain and pain-related information. Recently, an increasing number of studies have shifted their focus toward this topic (e.g. Dowman, 2001; Zampini et al., 2007). Moreover, researchers have especially become interested in the effect of *anticipating* pain on the facilitation of attention. Expecting or anticipating pain might enhance attentional engagement to threat-related information, allowing the initiation of adaptive responses.

Actual pain versus the anticipation of pain

The *anticipatory* response to threatening information has been shown to play an important role in how individuals deal with pain. Being able to anticipate or expect pain might increase access into awareness by assigning priority to stimuli that may signal the occurrence of the object of threat (Öhman, 1979). Accurate prediction of the occurrence of pain has an important protective function, as it allows the individual to avoid bodily harm by the initiation of adaptive responses. The role of learning (conditioning) processes, i.e. the observable changes in behavior due to changes in the internal and external environment (Pierce & Cheney, 2013), have been shown to influence pain perception (e.g. Goubert, Crombez, & Peters, 2004; Vlaeyen, 2015).

Recently, an increasing number of behavioral studies has investigated the effects of conditioned pain signals on the modulation of attention. In an adaptation of a visual search paradigm of Notebaert and colleagues (2011), participants had to search for a target presented in a varying number of colored circles. One stimulus became a signal for pain, as it indicated the possible occurrence of a painful stimulus. On a secondary task, intermixed with the visual search task, half of the participants could attempt to control pain (pressing the spacebar as fast as possible when a certain stimulus was presented). It was shown that individuals who attempted to control pain demonstrated an enhanced prioritization of signals of pain than individuals who did not have this goal. Spence, Bentley, Phillips, McGlone, and Jones (2002) demonstrated that participants were faster to discriminate the spatial location of pain when they were cued to expect a painful stimulus, compared to when they were invalidly cued to expect a visual stimulus. Van Damme, Crombez and Eccleston (2004b) compared the effect of expecting somatosensory stimulation between a pain

group, in which signals predicted painful electrocutaneous stimulation and a control group, in which signals predicted non-painful vibrotactile stimulation. Attentional engagement was equally facilitated by the anticipation of somatosensory information in both groups. Disengagement was more retarded by signals predicting pain than by signals predicting somatosensory information. However, this was only the case for participants high in catastrophic thinking about pain. Furthermore, it was shown that attention is more strongly engaged to a signal of impending pain compared with a cue signaling the absence of pain (Van Damme et al., 2004d). Van Damme, Crombez, Eccleston and Koster (2006) replicated these previous findings by showing enhanced engagement to pain signals compared to control signals. Last, neuroimaging studies have revealed that the anticipation of pain activated similar brain areas that became active during the experience of actual pain (Ploghaus et al., 1999; Porro et al., 2002).

Interestingly, if the scope of the neurocognitive model of attention to pain (Legrain et al., 2009) is broadened, it may allow us to develop a few interesting new hypotheses regarding top-down attentional prioritization. In its current form, the neurocognitive model may only make statements concerning the prioritization of *painful* stimuli. In fact, the model currently states that top-down facilitation of pain occurs when pain stimuli share active pain features defined by the current attentional set. Furthermore, the model does not allow to draw straightforward conclusions under which circumstances the prioritization of attention is displayed and it is limited in the definition of which features are exactly activated in the attentional set when expecting or experiencing pain at a particular region of the body. We can elaborate the current view by assuming that *non-painful* stimuli that share one or more of the pain-related features in working memory, such as modality or location (spatial coordinates) features, will be facilitated by attention.

For instance, in situations where individuals expect pain, an important and highly relevant feature that might become activated in the attentional set, is the location where the painful stimulus is administered. Indirect evidence for this idea can be found in a study of Crombez and colleagues (1998a). Participants were led to believe that on one arm a very intense, painful stimulus could occur. As a result, a mildly painful stimulus at that particular location interfered more with the performance on a cognitive task, than painful stimuli at another location.

This stimulus feature might be especially relevant in patients with chronic pain. Imagine a person who is experiencing low back pain. He/she may be worried about a potential injury. This thought may activate the spatial stimulus representation ‘location’ (i.e. lower back) in working memory. As a result, this person might become more quickly aware of stimuli presented on the back, as these stimuli match location features that are active in the attentional set.

Studies investigating the effect of anticipating pain on the *facilitation* of somatosensory attention are scarce. Several questions regarding the top-down prioritization of attention still remain unsolved. How does our attentional system deal with perceiving somatosensory sensations when pain is expected at a particular region of the body? In what circumstances occurs the possible attentional prioritization effect and what are its boundaries? One of the aims of this PhD thesis is therefore to further explore and gain new insights in the role of *anticipating pain on the top-down prioritization* of attention within the context of the *attentional set* hypothesis of the neurocognitive model of attention to pain.

Hypervigilance for pain

Pain might become the focus of attention because of its immediate relevance for the current goals of the individual. However, in some individuals pain persists, which might result in the enduring fearful appraisal of pain. The current goals and/or thoughts are mainly related to avoidance and escape from pain and remain activated even in situations where protective responses have become redundant (Eccleston & Crombez, 2007; Overmier, 2002). A popular hypothesis states that chronic pain patients might become hypervigilant for or over-attentive to pain and pain-related information. As a result the processing of stimuli related to pain or bodily harm is facilitated. In pain research, hypervigilance to pain-related information has been extensively studied and is often referred to as ‘selective attention’ or ‘attentional bias to pain’ (Asmundson, & Gordon, 2012; Asmundson, Norton, & Norton, 1999; Crombez, Van Ryckeghem, Eccleston & Van Damme, 2013; Lioffi, 2012; Pincus & Morley, 2001; Van Damme et al., 2010). In the following sections, we first elucidate the concept of hypervigilance. Next, we explore the role of hypervigilance in chronic pain within the context of the attentional set hypothesis of the neurocognitive model of attention to pain.

Last, we shed light on the different conceptualizations and operationalizations of hypervigilance and point out some shortcomings and recognize the need for further research.

Hypervigilance: what's in a name?

Etymologically, hypervigilance can be split up into the words 'hyper' and 'vigilance'. Hyper means 'over, above, beyond, exceedingly, to excess'. Vigilance dates from 1560 and means 'wakefulness, watchfulness'. Mackworth (1950) defined vigilance as *'the predisposition to attend to a certain class of events, or the readiness to select and respond to a certain kind of stimulus from the external or internal environment'* (Mackworth, cited in Crombez, Van Damme, & Eccleston, 2005). This vigilance can be achieved through experience or learning by instructions. Therefore, vigilance, or often termed as sustained concentration, is goal-dependent and involves intentional alertness to respond in the right way. Vigilance studies demonstrated that selecting and sustaining attention to pain was prioritized over other possible targets of attention from other modalities by task instructions (Miron, Duncan, & Bushnell, 1989; Van Damme, Crombez, & Eccleston, 2002). Thus, hyper-vigilance refers to a state of excessively sustained alertness.

One of the first authors who described hypervigilance in the context of pain was Richard Chapman (1978). He described a hypervigilant person as someone who is unusually alert to somatic distress signals including, but not limited to pain (Chapman, 1978). In line with Chapman's original usage of the term hypervigilance, hypervigilance should involve *an attentional selection* for certain painful and/or pain-related information at the expense of other information. Therefore, hypervigilance can be seen as the prioritized processing of pain-relevant information in the context of multiple attentional demands (Crombez et al., 2005; Van Damme et al., 2009; Van Damme et al., 2010). Hypervigilance to pain emerges as the working of normal attentional mechanism in abnormal situations (e.g. the chronic presence of high-intensity pain) and when the threat value of pain is high.

Hypervigilance and chronic pain syndromes

Several clinical models of pain have taken into account the role of hypervigilance, by assuming that patients suffering from chronic pain conditions

are characterized by abnormal, excessive attentional processing of pain and pain-related information. The fear-avoidance model of pain (Vlaeyen, Kole-Snijders, Boeren, & van Eek, 1995; Vlaeyen & Linton, 2000; see Figure 2) states that there are two possible reactions when experiencing pain, that is confrontation (i.e. one experiences the pain without worrying about possible negative consequences) or avoidance behavior. The way in which pain is interpreted determines whether it leads to disability or to recovery. More specifically, it is assumed that patients who catastrophize more about their pain (e.g. “I am in so much pain, this will never get better”, “If I bend over, my spine will break”), will become more fearful for movements and or possible injury. As a consequence, individuals may become hypervigilant to bodily signals that may evoke potential harm and may engage in avoidance behavior. This ensures that individuals get into a negative spiral of fear and pain catastrophizing thoughts.



Figure 2. Fear-avoidance model of Vlaeyen and Linton (2000).

Another model that presumes the role of hypervigilance in chronic pain is the model of misdirected problem-solving (Eccleston & Crombez, 2007, see Figure 3). It assumed that patients with enduring pain may start worrying about pain, i.e. doubting about the possible causes of pain and the variety of negative consequences for themselves and others. This results in hypervigilance to pain-related information and the individual might search for solutions to remove the pain. When a suitable solution is found for the pain problem, pain and worry abate. However, when the problem cannot be solved, individuals keep trying to

find solutions. Consequently, a ‘perseverance loop’ is established in which worrying and hypervigilance is increased.

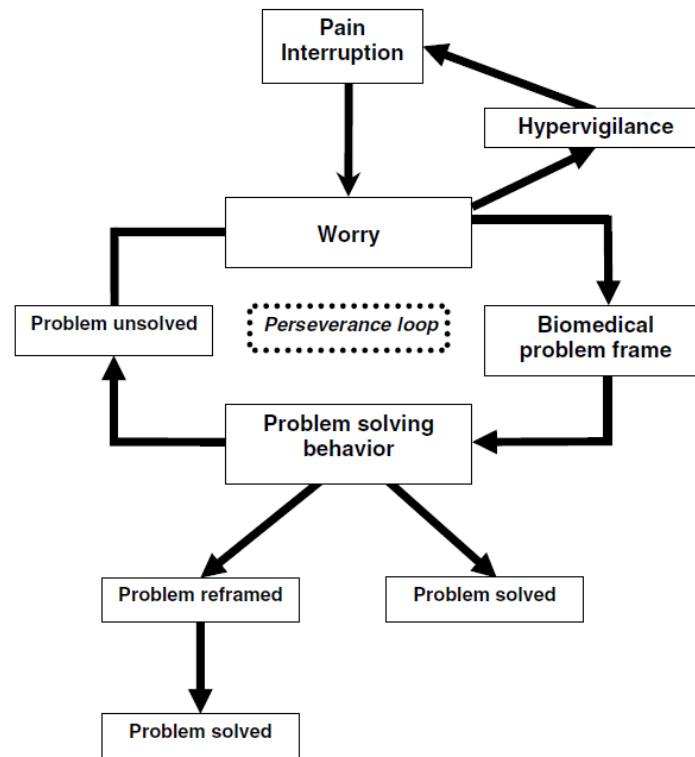


Figure 3. Misdirected problem solving model (Eccleston & Crombez, 2007).

According to the attentional set idea, it can easily be hypothesized that chronic pain patients maintain within their attentional set features of excessive somatosensory expectations for particular locations of the body where they expect to feel pain. Consequently, this might lead to more attention to somatosensory sensations at the painful bodily location. Imagine a person with low back pain, who recently recovered from a serious back injury. Being fearful of re-injury, this person might continuously scan the back in order to detect signals of potential harm. As such, features of excessive somatosensory sensations on the pain-relevant body part (back) might become activated in the attentional set. Stimuli that share one or more features defined by the attentional set, might therefore be prioritized by attention. It is likely that this individual might become more quickly aware of somatosensory sensations at the painful compared to a pain-irrelevant region. Studies investigating this idea are however lacking. Hence, in

this PhD thesis, we aim to investigate hypervigilance in chronic pain patients within the context of the attentional set.

Operationalization of hypervigilance

Hypervigilance has been operationalized in a variety of ways. First, a heightened *sensitivity* for sensory information has sometimes explicitly or implicitly been defined as an indicator for hypervigilance. According to this view, hypersensitivity to pain, increased somatic focus, and health anxiety are all aspects of hypervigilance. Evidence for the presence of 'hypervigilance' in patients with chronic pain has then often been derived from studies showing reduced thresholds and tolerance for pain (Gibson, Littlejohn, Gorman, Helme, & Granges, 1994; Kosek, Ekholm, & Hansson, 1996; McDermid et al., 1996; Mikkelsen, Latikka, Kautiainen, Isomeri, & Isomäki, 1992), and perceptual amplification of painful and even non-painful sensory information (Gracely, Grant, & Giesecke, 2003; Hollins et al., 2009; Maixner, Fillingim, Booker, & Sigurdsson, 1995; Petzke, Gracely, Park, Ambrose, & Clauw, 2003) in patients with chronic pain, such as fibromyalgia and patients with Temporomandibular joint dysfunction (TMD), compared with healthy volunteers. We should, however, be careful in equating hypersensitivity with hypervigilance. Hypervigilance is only one mechanism that may account for research findings demonstrating hypersensitivity in, for example, fibromyalgia patients. Other processes, such as central sensitization (e.g., Arendt-Nielsen & Henriksson, 2007; Staud, Robinson, & Price, 2007), have also been hypothesized to account for lowered pain threshold and tolerance levels in persons with fibromyalgia. It is therefore recommended not to simply equate hypervigilance with hypersensitivity (Crombez et al., 2005; Van Damme et al., 2009).

Second, *self-report instruments* are often used to assess heightened attention toward pain and pain-related information. It has been demonstrated that chronic pain patients tend to show higher scores on those questionnaires, such as the Pain Vigilance and Awareness Questionnaire (PVAQ, McCracken, 1997) and the Body Vigilance Scale (BVS, Schmidt, Lerew, & Trakowski, 1997) than healthy controls (Peters, Vlaeyen, & van Drunen, 2000; Roelofs, Peters, McCracken, & Vlaeyen, 2003; Tiemann et al., 2012). Nevertheless, self-report regarding hypervigilance in chronic pain patients could be criticized. Scores on

these questionnaires depend on the capacity to be able to sufficiently and accurately remember the pain (Roelofs, Peters, Patijn, Schouten, & Vlaeyen, 2004). Moreover, questionnaire querying attention to bodily sensations are often measuring the presence of physical symptoms rather than the excessive attentional focus on these sensations (Crombez, Eccleston, Van den Broeck, Goubert, & Van Houdenhove, 2004). Furthermore, when equating heightened symptom reporting with hypervigilance, we risk that hypervigilance is confused with other central mechanisms that account for hyperalgesia, allodynia, and hyperresponsivity (Crombez et al., 2005, González et al., 2010). Therefore, it is recommended to investigate attentional biases toward pain-related information by means of behavioral paradigms that more directly measure attentional processes and are less susceptible to report bias.

Third, *attentional bias paradigms* investigate the role of hypervigilance processes mainly by using pain-related words or pictures. In the modified Stroop paradigm, i.e. an adaptation of the classical Stroop task (Stroop, 1935), the reaction times are measured needed to name the color of both pain-related and neutral words. It is generally found that words with a negative, threatening meaning interfere more with the naming of the color of these words (for an overview, see MacLeod, 1991). In studies using the modified Stroop paradigm in clinical pain populations, it is hypothesized that chronic pain patients will need more time in naming the color of pain-related words compared with neutral words, as pain words will automatically demand attention. Moreover, chronic pain patients are expected to show more pain-related interference as compared to individuals without a chronic pain condition (Roelofs et al., 2002). Results of studies using this paradigm only partially supported the existence of an attentional bias to pain-related information in chronic pain patients. Roelofs, Crombez, Peters, Verschuere and Vlaeyen (2005), for instance, found no evidence that chronic lower back pain patients displayed selective attention to words related to movement and injury. It is argued that this paradigm rather measures other general information processes, such as preoccupation with the meaning of words or motor responses (e.g. the production of a movement to answer). Overall, the interpretation of the Stroop interference in terms of attention has been criticized (De Ruiter & Brosschot, 1994). Studies using *dot-probe paradigms* have further substantiated the phenomenon of selective attentional bias

(MacLeod, Mathews, & Tata, 1986). In this paradigm, two words (an emotional/pain-related or a neutral word) are presented simultaneously on the left and right side of the screen. Next, one of these two words is replaced by a small dot. Participants are asked to detect the dot as fast as possible and the reaction time is considered to be a measure of the allocation of attention. Evidence for selective attentional bias is seen as a speeding up of detection time in congruent trials (when the dot replaces the emotional word) compared to incongruent trials (when the dot replaces the neutral word) (see Cooper & Langton, 2006; Koster, Verschuere, Crombez, & Van Damme, 2005; Salemink, van den Hout, & Kindt, 2007). Although there is evidence showing that this effect was more pronounced in chronic pain patients as compared to healthy volunteers (Asmundson, Carleton, & Ekong, 2005; Haggman, Sharpe, Nicholas, Refshauge, 2010), other studies have shown a less convincing pattern of results (Lioffi, 2012; Lioffi, Schoth, Bradley, & Mogg, 2009; Sharpe, Dear, Schrieber, 2009). Roelofs and colleagues (2005) demonstrated that chronic pain patients had slower reaction times on trials where the dot replaced a neutral word, which was not the case in healthy volunteers. Sharpe and colleagues (2009) demonstrated that in a group of rheumatoid arthritis patients, attentional biases toward pain are caused by difficulty disengaging rather than hypervigilance. Moreover, a recent meta-analysis by Crombez and colleagues (2013) indicated that there was an attentional bias to pain-related information in chronic pain patients, but that this effect was only small, and, importantly, not significantly different from healthy controls. In sum, studies using the dot-probe paradigm did not allow to draw conclusions regarding attentional prioritization of bodily sensations.

Toward a new approach of hypervigilance

From the previous section, we may conclude that clear evidence for the presence of hypervigilance in individuals with chronic pain is lacking. Overall, the meta-analysis of Crombez and colleagues (2013) of studies measuring attentional prioritization of pain-related information, has shown that the attentional bias effect toward pain was less pronounced in chronic pain patients than expected. Furthermore, no evidence was found for attentional bias toward pain for acute pain, procedural pain and experimental pain. One possible explanation for these findings might be that the paradigms used in these studies may not be suitable to

activate pain schemata/memories, as they only assess the prioritization of pain-related words or pictures, and not of pain or somatosensory stimuli. The use of pain-related words as valid pain stimuli has been questioned, as these are only semantic representations of pain which are barely capable of activating bodily threat (Crombez, Hermans, & Adriaensen, 2000). Several studies have already made use of painful stimuli instead of pain-related words/pictures to investigate differences in attentional bias effects between chronic pain patients and healthy controls by means of the primary task paradigm (de Gier, Peters, & Vlaeyen, 2003; Eccleston, Crombez, Aldrich, & Stannard, 1997; Tiemann et al., 2012; Vangronsveld et al., 2007). Yet, the focus of investigation of these studies was on the interruption of attention by relevant threatening stimuli and did not allow us to draw conclusions about the facilitation of pain and pain-related information in chronic pain samples.

Furthermore, most of the studies investigating hypervigilance are based upon reaction times. For instance, Peters and colleagues (2000, 2002) operationalized hypervigilance as the detection of weak electrical stimuli in combination with a second attention-demanding task, and assumed that hypervigilance for somatosensory sensations should be reflected by the facilitated detection of stimuli that were administered to the painful region of the body, as compared to a non-painful body part. The results revealed no differences in reaction times between fibromyalgia patients (Peters, Vlaeyen, & van Drunen, 2000) as well as patients with chronic low back pain (Peters, Vlaeyen, & Kunnen, 2002) in comparison to control subjects. Although a reaction time approach is useful in homogenous non-clinical samples such as students, it might prove less adequate in clinical samples. It has been shown that attentional bias effects are short-lived (Calvo & Alvero, 2005; Koster, Crombez, Verschuere, Vanvolsem, & De Houwer, 2007). Chronic pain patients are typically characterized by increased reaction time variability and psychomotor slowing, making data noisy (Dick, Eccleston, & Crombez, 2002; Veldhuijzen, Sondaal, & Oosterman, 2012). Consequently, reaction time paradigms may not be well suited for detecting attentional biases to threat in clinical populations. As such, the development of somatosensory hypervigilance paradigms, using innovative attention methods that do not rely on response speed and allow us to measure top-down prioritization of attention, is highly recommended. One of the aims of this PhD

thesis is taking into account these limitations by using an innovative attention paradigm, the Temporal Order Judgment (TOJ) task.

Objectives and aims

In this PhD thesis we aim to (1) systematically investigate the effect of *anticipating* pain on the *top-down prioritization* of attention, (2) investigate whether patients suffering from pain at a specific bodily location are characterized by hypervigilance for sensations at that specific part of the body, and (3) examine whether top-down attentional prioritization is more pronounced in individuals with a tendency to experience bodily sensations as threatening. For the purposes of this PhD, an innovative attention paradigm, the Temporal Order Judgment (TOJ) task was developed that dealt with the limitations of previous paradigms.

Temporal Order Judgment task

A long time ago, Titchener claimed in his ‘law of prior entry’ that ‘*the object of attention comes to consciousness more quickly than the objects which we are not attending to*’ (Titchener, 1908, pp 251). The TOJ task (Piéron, 1952) enables us to investigate this ‘prior entry effect’. In a typical TOJ task (e.g. Shore, Gray, Spry, & Spence, 2005; Spence, Shore, & Klein, 2001; Wada, Yamamoto, & Kitazawa, 2004), two stimuli are presented on two different locations, typically on both hands. The stimulus on one hand is presented before the stimulus on the other hand, with variable stimulus onset asynchronies (SOAs), and participants are asked which hand was stimulated first.

We adapted this typical TOJ task by threatening one of the bodily locations by occasionally administering a painful stimulus. By doing so, we believe that the anticipation of pain might result in the focus of attention on the threatened location of the body. According to Titchener’s law of prior entry, we may expect that one becomes more quickly aware of stimuli in a particular location of the body where pain is expected, relative to stimuli in other regions of the body. Analysis of responses across a range of SOAs allows one to calculate the average time that one stimulus has to lead another in order for the two stimuli to be judged as simultaneous. This has been labeled as the point of subjective simultaneity (PSS). According to the notion of prior entry, the attended stimulus

should have prior entry to awareness. As a consequence, unattended stimuli normally have to be presented prior to attended stimuli in order to be perceived as simultaneous (Spence & Parise, 2010), leading to a shift of the PSS to the unattended side. The claim being that if attending to a threatened location speeds up the perception of stimuli on that particular bodily location, then the PSS should change as a function of the location attended. In sum, the PSS provides information concerning biases in spatial attention resulting from the presentation of bodily threat.

In most of the studies reported in this PhD thesis, two tactile stimuli were presented, one administered on each hand (see Figure 4). These stimuli were separated in time by 1 of 10 randomly assigned SOAs, ranging from -120 ms to 120 ms (-120, -60, -30, -15, -5, +5, +15, +30, +60,+120 ms). Negative values indicate that the left hand is stimulated first, positive values indicate that the right hand is stimulated first. Bodily threat was induced by using two different types of trials, based on the color of a cue. A trial started with the presentation of a colored cue (either blue or yellow). One of the two colors of the cues signaled the possible occurrence of a painful stimulus on one hand (threat trials). The other color of the cue signaled that no pain would follow (control trials) (see Figure 5).



Figure 4. Example of experimental setup. Tactors (large round circles) were placed on both hands. Electrodes for painful stimulation were placed on one hand. In order to induce threat, colored cues were used that signaled whether or not a painful stimulus could be administered.

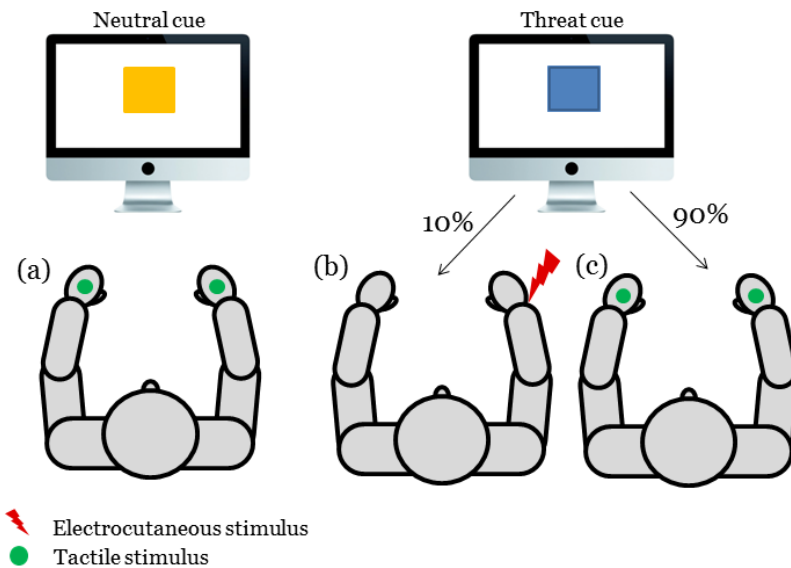


Figure 5. (a) Example of a neutral trial (b) Example of a threat trial in which the electrocutaneous stimulation was presented on the right hand (c) Example of a threat trial without electrocutaneous stimulation.

The primary outcome measure of the studies reported in this PhD thesis is the PSS. The PSS refers to the point at which observers report the two events (right hand first and left hand first) equally often. This is commonly taken to be equivalent to the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time and such equivalent to the SOA value corresponding to a proportion of left/right hand first responses of 0.5. Figure 6 provides a graphical presentation of the PSS. The PSS refers to the point of intersection of 0.5 percentage on the y-axis (right hand first and left hand first reported equally often) with zero on the x-axis (equivalent to the SOA at which participants perceive the two stimuli as occurring at the same time). A positive value indicates that the stimulus contralateral to the side of threat had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS means that stimuli on the threatened hand are perceived more rapidly than stimuli on the neutral hand. In our design, we might expect that in control trials, the PSS might fluctuate around zero (no spatial bias), whereas the PSS in threat trials might be positive (bias toward threat).

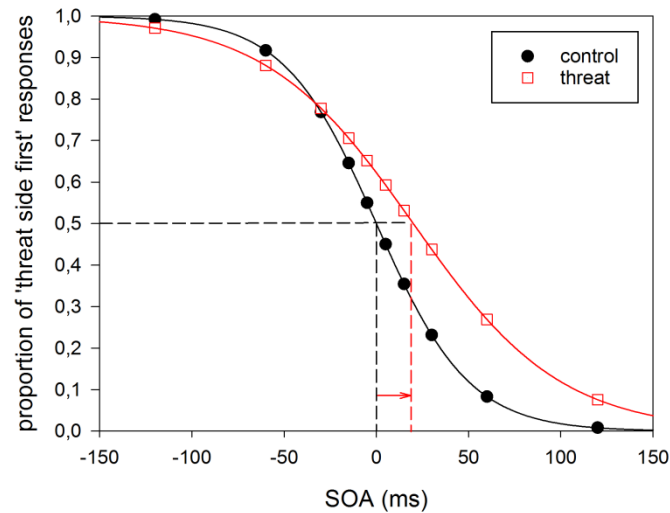


Figure 6. Simulation of an ideal scenario of the PSS. Data are plotted as a proportion of responses that coincided with the side on which the threatening stimuli were presented (y-axis), as a function of stimulus onset asynchrony (SOA, x-axis), for control trials and threat trials. The responses are recoded so that negative values on the left side of the x-axis indicate that the threatened hand was stimulated first, while positive values indicate that the neutral hand was stimulated first. The PSS (the point of intersection of 0.5 percentage on the y-axis with 0 on the x-axis) is 0 for control trials. The curve of the threat trials is shifted toward the neutral side, indicating that the tactile stimulus presented on the neutral hand had to be presented several milliseconds before the tactile stimulus on the threatened hand in order to have equal chance of the stimulus at the threatened hand of being perceived first. As the JND corresponds to $0.675/\text{slope}$, the steeper the slope, the smaller the JND.

Another parameter of the TOJ task that has often been used, is the just noticeable difference (JND). The JND indicates the interval needed to achieve 75% correct performance, and as such provides a standardized measure of the sensitivity of participants' temporal perception. The larger the JND interval, the more difficult the task, the less the performance. Since the JND is less relevant to our hypotheses, the JND is only calculated in studies of this PhD thesis where performance is relevant (e.g. chapter 4).

Outline dissertation

Part I

The first research line of this PhD thesis consists of several studies conducted with healthy volunteers, in which we investigated the effect of expecting pain at a particular region of the body on the top-down prioritization of attention.

In **chapter 1**, it was investigated whether the anticipation of pain at a specific location of the body might result in the prioritization of somatosensory sensations occurring at that particular location. The basic design of the TOJ task was tested in which participants had to indicate which of 2 tactile stimuli that were administered to each hand at a range of stimulus onset asynchronies (SOAs), was presented first. The color of a cue (1 of 2 colors) signaled the possible occurrence of a painful stimulus (threat trials) or no painful stimulus (control trials) on one hand. We tested whether tactile stimuli in threat trials would be perceived earlier in time on the hand where pain is expected compared to the neutral hand.

In **chapter 2**, the spatial boundaries of the prioritization effect were tested. More specifically, it was investigated how specific the spatial features of bodily threat are encoded in participants' attentional set. Two experiments were performed in which the distance between the pain and the tactile stimulus was manipulated. Participants expected pain either proximal to one of the tactile stimuli (near condition; on the hand in both experiments) or more distant on the same body part or on a different body-part at the same body side (far condition; arm and leg in respectively experiment 1 and experiment 2). We hypothesized that if only the exact location of the pain is encoded, prioritization should be limited to those somatosensory inputs that are in close proximity to the bodily location where pain is expected (near condition). However, if the spatial features of bodily threat are encoded in a more general manner, prioritization should be also present in the far conditions.

Chapter 3 investigated whether the prioritization effect is limited to somatosensory information (modality-specific hypothesis) or generalizes to other sensory modalities (multisensory hypothesis). One study is described in which participants performed tactile and visual TOJ tasks while either expecting a

painful stimulus on one of the hands or expecting no painful stimulus. We expected that if the attentional prioritization is modality-specific, the prioritization effect would be larger in the tactile condition compared to the visual conditions. In contrast, no differences between the tactile and visual conditions should be expected if the prioritization effect would be multisensory.

In **chapter 4**, it was investigated whether the threat-related prioritization effect is due to somatosensory input occurring at the same body part as pain (somatotopic reference frame of threat localization) or rather because of corresponding spatial encoding of somatosensory input and pain independent of the body part on which they occur (spatiotopic reference frame of threat localization). In two experiments, participants performed a tactile TOJ task in which their arms were placed symmetrically on the table in half of the blocks (uncrossed condition). In the other half of the blocks, they were asked to cross their arms over the body midline (crossed condition), so that the location of the pain stimulus on the left (right) arm was closer in space to the tactile stimulus on the contralateral hand than to the tactile stimulus on the ipsilateral hand. Again, a painful stimulus was either expected on one of the forearms or no painful stimulus was expected. We hypothesized that if the effect of threat of pain on one arm was due to enhanced processing of somatosensory input on the same body part of pain (somatotopic reference frame), tactile stimuli would be perceived more rapidly on the hand ipsilateral to the threatened arm in both conditions. However, if the threat-related prioritization effect was the result of corresponding spatial encoding of somatosensory input and pain independent of the body part on which they occurred (spatiotopic reference frame), we expected that in the crossed condition, tactile stimuli would be perceived more rapidly on the hand contralateral to the threatened arm than on the hand ipsilateral to the threatened arm.

Part II

The second research line of this PhD thesis consists of two studies in which the idea was investigated that patients suffering from pain at a specific body location, are characterized by heightened attentional processing for bodily sensations at that specific location. Experimental pain was no longer induced, since we assumed that the clinical problem would be sufficient to activate the

affected location in the attentional set. The TOJ paradigm was applied in samples of patients with unilateral temporomandibular joint dysfunction (TMD) and unilateral knee pain patients.

In **chapter 5**, it was investigated whether pain patients with unilateral *acute* knee pain prioritize tactile information on the pain-relevant knee compared with the pain-irrelevant knee. Patients performed a TOJ task in which they had to decide on which knee the first tactile stimulus was presented. In order to maximize threat of pain, patients were led to believe that they would have to perform several stressful knee movements immediately after the task. It was expected that stimuli would be perceived more rapidly on the painful knee than on the non-painful knee.

Chapter 6 investigated whether patients with *chronic* unilateral TMD, i.e. chronic pain on one side of the jaw are becoming more quickly aware of somatosensory sensations at the side of the jaw in comparison with a healthy control sample without pain on the jaw. As a first step, we conducted two pilot experiments in undergraduate students (experiment 1) and healthy volunteers from the general population (experiment 2) to test whether threat of experimental pain on one side of the face resulted in attentional prioritization of tactile stimuli on that side of the face. In a third experiment, patients performed a TOJ in which two tactile stimuli were presented, one administered to each jaw. TMD patients were compared with samples of healthy volunteers, adequately matched on demographic variables. Hypervigilance in TMD patients should be reflected by a bias of attention toward the pain-relevant location, i.e., prioritization of tactile stimuli in the pain-relevant compared to the pain-irrelevant region of the body. As such, we expected that TMD patients might become more quickly aware of tactile sensations presented on the painful jaw compared to the non-painful jaw. Such effect was not expected in the group of healthy volunteers.

Part III

In **chapter 7**, it was investigated whether top-down attentional prioritization is more pronounced in individuals with a tendency to experience bodily sensations as threatening. In previously described experiments with healthy volunteers, participants were asked to complete several self-report

measures concerning trait-related bodily threat appraisal (e.g. PVAQ, PCS) and state-related bodily threat appraisal (fear and expectation of painful stimulation during the experiment). Both data of these self-report measures and the behavioral measure of threat-related prioritization (TOJ task) of studies with healthy volunteers were merged and analyzed across studies. We expected that if individual differences in bodily threat appraisal played a role in the threat-related attentional prioritization of somatosensory sensations in healthy volunteers, there would be positive associations between our behavioral and self-report measures.

Finally, in **the general discussion** the main findings of the different studies are highlighted, interpreted and integrated. Furthermore, clinical and theoretical implications, limitations of the current studies and ideas for future research are discussed.

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Part I

The anticipation of pain at a specific location of the body prioritizes tactile stimuli at that location¹

Abstract

This study investigated whether one becomes more quickly aware of innocuous somatosensory signals at locations of the body where pain is anticipated. Undergraduate students (N=20) indicated which of two stimuli that were administered to each hand using a range of stimulus onset asynchronies (SOAs), was presented first. Participants were instructed that the color of a cue (one of two colors) signaled the possible occurrence of pain on one hand (threat trials). The other color of the cue signaled that no pain would follow (control trials). Results showed that during threat trials tactile stimuli on the hand where pain was expected, were perceived earlier in time than stimuli on the “neutral” hand. These findings demonstrate that the anticipation of pain at a particular location of the body resulted in the prioritization in time of somatosensory sensations at that location, indicating biased attention towards the threatened body part. The value of this study for investigating hypervigilance for somatosensory signals in clinical populations such as patients with chronic lower back pain is discussed.

¹ Vanden Bulcke, C., Van Damme, S., Durnez, W., & Crombez, G. (2013). The anticipation of pain at a specific location of the body prioritizes tactile stimuli at that location. *Pain, 154*, 1464-1468.

Introduction

Attention is a central component in pain theories aiming to explain amplified pain perception, disability, and distress (Chapman, 1978; Eccleston & Crombez, 1999; Legrain et al., 2009; Rollman, 2009; Van Damme, Legrain, Vogt, & Crombez, 2010). Influential is the idea that patients with chronic pain are characterized by hypervigilance, referring to a preoccupation with bodily threat signals as a result of which attention prioritizes pain-related information at the cost of other environmental demands (Crombez, Van Damme, & Eccleston, 2005; Vlaeyen & Linton, 2000). A recent meta-analysis (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013) of studies measuring attentional prioritization of pain-related information indicated that the available evidence supporting this idea is weak. However, the paradigms typically used in these studies may not be suitable to activate pain schemata/memories, as they only assess the prioritization of pain-related words or pictures, and not of pain or somatosensory stimuli. Hence, the use of somatosensory attention paradigms has been recommended (Crombez et al., 2013; Van Damme et al., 2010). The present study is a step into this endeavor.

If fearful anticipation of pain leads to heightened attention to pain-related information (Crombez et al., 2005; Legrain et al., 2009; Van Damme et al., 2010), we hypothesized that this would result in the prioritization of -even innocuous - somatosensory input at body locations where pain is expected to occur. Indeed, according to Titchener's (1908) law of prior entry, stating that attended stimuli come to consciousness more quickly than unattended stimuli (see Spence & Parise, 2010), we may expect that one becomes more quickly aware of somatosensory stimuli in a particular location of the body where pain is expected, relative to somatosensory stimuli in other regions of the body. Evidence for our hypothesis is yet limited. In a study of Crombez and colleagues (1998), healthy volunteers were led to believe that a very intense, almost intolerable painful stimulus could occur at one particular location of the body. As a result, a mildly painful stimulus at that particular location interfered more with the performance of an ongoing, cognitive task, than pain stimuli at another location. However, no studies have investigated whether the anticipation of pain makes one more quickly aware of non-painful somatosensory information in the threatened body part relative to other body parts.

The aim of the present study was to specifically test this idea. We investigated in healthy persons whether the anticipation of (experimentally induced) pain in one hand results in a prioritization of innocuous tactile stimuli at that hand, using a tactile Temporal Order Judgment (TOJ) task (Spence, Shore, & Klein, 2001). Participants were required to report which one of two tactile stimuli, one administered to each hand at a range of different stimulus onset asynchronies (SOAs), was perceived first. Performance on this task provides information about which hand is prioritized by attention (see Spence & Parise, 2010; Van Damme, Gallace, Spence, Crombez, & Moseley, 2009). Participants were instructed that the color of a cue (one of two colors) signaled the possible occurrence of pain on one hand (threat trials). The other color of the cue signaled that no pain would follow (control trials). We hypothesized that in threat trials tactile stimuli would be perceived earlier in time on the hand where pain was expected than on the “neutral” hand.

Method

Participants

Twenty undergraduate psychology students (19 female and 1 male; mean age, 18.3 years; all white Caucasian) participated to fulfill course requirements. All participants had normal or corrected-to-normal vision and normal hearing. All but 2 were right-handed as reported by self-report. Sixteen participants reported to have experienced pain during the last six months (average of 12 days in 6 months). Seven participants reported to feel pain at the moment of testing, but the average rating of the intensity of the pain for these 7 participants was low ($M=2.29$, $SD=1.38$) on a Likert scale where 0 indicated ‘no pain’ and 10 ‘worst pain ever’. Participants rated their general health on average as ‘very good’ and none of all participants reported to have a current medical or mental disorder. All participants gave informed consent and were informed to be free to terminate the experiment at any time. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experiment lasted for approximately 1 hour and 15 minutes.

Apparatus and stimulus material

Tactile stimuli (10 ms duration; 200Hz) were presented by means of two resonant-type tactors (C-2 TACTOR, Engineering Acoustics, Inc., Florida, <http://www.eaiinfo.com/>) consisting of a housing of 3.05 cm diameter and 0.79 cm high, with a skin contactor of 0.76 cm diameter. Prior to the start of the experiment, the perceived stimulus intensities at both tactor locations were individually matched (Weinstein, 1968). This was done by means of a double random staircase procedure, based on the 'simple up-down method' of Levitt (Levitt, 1971). In a first phase, 24 stimuli presented on the left hand were judged relative to a reference stimulus with maximum intensity (power = 0.21 Watt) on a 5-point Likert scale ranging from 1 ('no sensation') to 5 ('maximum intensity'). The intensity that elicited an averaged rating of 3 was used as the stimulus intensity for the left hand, and was the reference stimulus for the second phase. In the second phase 24 stimuli on the right hand were judged relative to the reference stimulus on the left hand on a 5-point Likert scale (1 = 'more than less strong', 2 = 'less strong', 3 = 'equally strong', 4 = 'stronger', 5 = 'much stronger'). The intensity that elicited an averaged rating of 3 was used as the intensity of the stimulus at the right hand.

Painful stimuli were electrocutaneous stimuli delivered by constant current stimulators (Digitimer DS5 2000, Digitimer Ltd, England, <http://www.digitimer.com/index.htm>). Electrocutaneous stimuli consisted of trains of 20 ms sinusoid pulses with a frequency of 50 Hz, and were delivered via two lubricated Fukuda standard Ag/AgCl electrodes (1 cm diameter) for 200 ms. Intensity of the electrocutaneous stimuli was determined for each participant individually by means of a random staircase procedure. For each hand, 20 electrocutaneous stimuli were presented to participants (start intensity between 0 and 1.5 mA) and self-reports were collected on an 11-point Likert scale (0 = 'no sensation'; 10 = 'unbearable pain'). The pain intensity that elicited an average rating of 7 was selected as the pain stimulus for the proper experiment (Arntz, Dreessen, & De Jong, 1994).

Tactile Temporal Order Judgment paradigm

The task was programmed and controlled by the INQUISIT Millisecond software package (Inquisit 3.0, Millisecond Software LLC, Seattle, WA, <http://www.millisecond.com/>) on a laptop (HP Compaq nc 6120). Each trial

began with a fixation cross (1000 ms) in the middle of the screen, followed by a colored cue (1000 ms), indicating whether or not a painful electrocutaneous stimulus could follow on one hand. A yellow rectangle (10 by 10 cm) indicated that no electrocutaneous stimulus would follow (control trials). A blue rectangle (10 by 10 cm) indicated that a painful electrocutaneous stimulus on one hand could follow (threat trials). In 10% of all threat trials, the pain stimulus was actually delivered instead of the two tactile stimuli. Participants were not informed about the proportion of pain stimuli. On trials without pain stimulus (90% of threat trials and all control trials), two tactile stimuli were administered, one on each hand. These stimuli were separated in time by one of 10 randomly assigned stimulus onset asynchronies (SOAs) ranging from -120 to +120 ms (-120, -60, -30, -15, -5, +5, +15, +30, +60, +120 ms; negative values indicate that the left hand was stimulated first) [see also Shore, Gray, Spry, & Spence, 2005; Van Damme et al., 2009]. Participants were asked to report aloud on which hand the tactile stimulus was presented first. When a pain stimulus replaced a tactile TOJ trial, participants were informed that no response had to be given. Responses were coded by the experimenter using a keyboard.

Procedure

Participants were tested individually. First, the TOJ task was explained to the participants. They were also informed that an electrocutaneous stimulus would be used during the experiment and that “most people find this kind of stimulation unpleasant”. After participants gave their informed consent, they were seated in front of the experimental apparatus. The forearms were positioned symmetrically on the table. The tactors were placed on the metacarpal of each hand. Electrodes were attached to both hands between thumb and index finger, in the sensory territory of the superficial radial nerve. The skin at the electrode sites was first abraded with a peeling cream (Nihon Kohden, Tokyo, Japan) to reduce skin resistance. Participants were instructed that the color of a cue (one of two colors) signaled the possible occurrence of pain on one hand. The other color of the cue signaled that no pain would follow. Before the start of each block, participants were informed on which hand (left or right) they could expect painful stimuli. Participants had to report aloud which one of two tactile stimuli, one administered to each hand was presented first. Accuracy of participants’

responses was emphasized, rather than speed. Participants wore headphones (Wesc, Conga) during the experiment. White noise (42.2 dB) was presented continuously through the headphones to mask the noise resulting from the operation of the tactors. The participants were not given any feedback about their performance.

The session began with a practice block of twenty-three trials (1 trial per SOA for control trials; 1 trial per SOA for threat trials; 3 electrocutaneous trials). Following this, four blocks of 105 trials (5 trials per SOA for control trials; 5 trials per SOA for threat trials, 5 pain trials) were randomly presented with the two possible locations of pain (left hand or right hand) alternating between blocks and counterbalanced between participants.

Self-report measures

After each test phase, participants had to rate several questions about concentration (“To what extent have you made an effort to this task?”, “To what extent did you concentrate on this task?”), attention to painful/tactile stimuli (“To what extent did you pay attention to the painful/tactile stimuli?”), pain experience (“How painful did you find the electrocutaneous stimuli?”), anxiety (“How anxious were you during this block?”), fatigue (“To what extent did you find this task tiring?”) on an eleven-point numerical rating scale (anchored 0 = not at all and 10 = very strongly). As a manipulation check, we were especially interested in the ratings of fear (“To what extent were you afraid that the blue/yellow cue would be followed by a painful stimulus?”) and expectations (“To what extent did you expect that the blue/yellow cue would be followed by a painful stimulus?”). Participants were also asked to complete the Pain Vigilance and Awareness Scale (PVAQ) (McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002) and the Pain Catastrophizing Scale (PCS) (Crombez, Hermans, & Adriaensen, 2000; Sullivan, Bishop, & Pivik, 1995). These data were collected for meta-analytical purposes and are not reported in detail here.

Results

Self-report data and manipulation check

Participants rated the electrocutaneous stimuli as moderately painful ($M = 5.38$, $SD = 1.77$). Furthermore, they reported to be more afraid during threat trials ($M = 5.86$, $SD = 1.76$) than during control trials ($M = 0.05$, $SD = 0.17$) ($t(19) = 14.85$, $p < 0.01$; $d = 3.32$ [95% CI: 2.20, 4.44]). Finally, they expected a painful electrocutaneous stimulus more strongly during threat trials ($M = 6.16$, $SD = 1.69$) than during control trials ($M = 0.11$, $SD = 0.25$) ($t(19) = 15.31$, $p < 0.01$; $d = 3.43$ [95% CI: 2.28, 4.58]). Mean questionnaire scores were 10.90 ($SD = 11.16$) for the PCS and 36.30 ($SD = 8.96$) for the PVAQ.

TOJ data handling

In a TOJ task, it is recommended (Shore et al., 2005; Spence et al., 2001) to exclude participants from statistical analysis when any of the PSS values is greater than the highest SOA (± 120 ms) and when participants have less than 80% accuracy on the trials with the largest SOA tested (± 120 ms). No participants had to be excluded for these reasons. Trials following trials with electrocutaneous stimulation were removed from data analysis to avoid that (1) potential effects would be mainly driven by trials directly following painful stimulation or (2) after-effects of pain would interfere with the tactile TOJ (max. 10% of all trials).

The analyses were based on the procedure described by Spence and colleagues (2001) (see also Shore et al., 2005; Van Damme et al., 2009). The proportions of 'right-hand-first' responses for all trials at each SOA, for threat presented on the right hand, and the proportion of 'left-hand-first' responses for all trials at each SOA, for threat presented on the left hand, were converted into the corresponding z-scores using a standardized normal distribution. The best-fitting straight line was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS) and the just noticeable difference (JND) values for the subsequent statistical analyses (see Figure 1). The PSS refers to the point at which observers report the two events (right hand first and left hand first) equally often. This is considered equivalent to the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time. We recoded the PSS data so that a positive value

indicates that the stimulus contralateral to the side of threat had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS means that stimuli on the threatened hand are perceived more rapidly than stimuli on the other hand. The JND is monotonically related to the slope of the psychometric function and indicates the interval needed to achieve 75% correct performance, and as such provides a standardized measure of the sensitivity of participants' temporal perception. A repeated measures analysis of variance (ANOVA) with the factor Trial type (threat versus control) was performed on the PSS and JND data (note that we had no specific hypotheses concerning the JND index). For ease of comparison with the norms of Cohen (1988), we calculated effect sizes for dependent samples using the formula of Dunlap and colleagues (Borenstein, Hedges, Higgins, & Rothstein, 2009). We determined whether Cohen's d was small (0.20), medium (0.50), or large (0.80) (Cohen, 1988). We also report the 95% confidence intervals (95% CI) of the effect sizes.

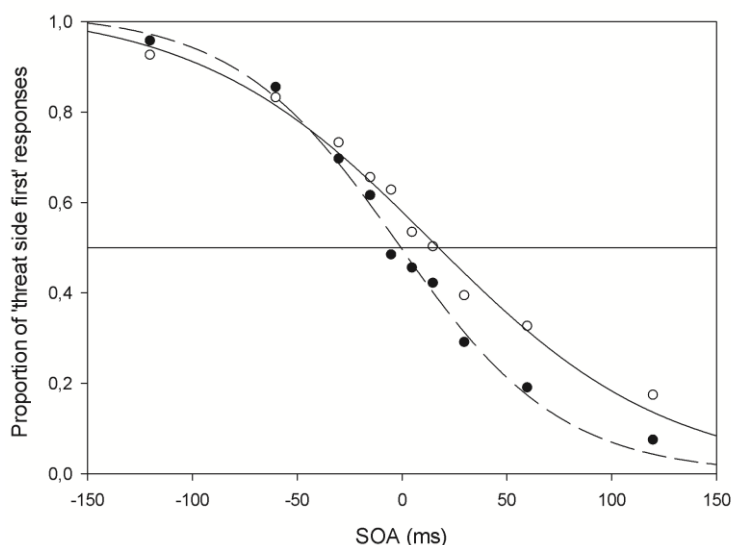


Figure 1. Temporal order judgment data: average of the fitted data for all participants. Data are plotted as a proportion of responses that coincided with the side on which the threatening stimuli were presented (y-axis), as a function of stimulus onset asynchrony (SOA, x-axis), for control trials (broken line) and threat trials (solid line). $R^2 = 0.99$.

PSS

The main effect of Trial Type was significant ($F(1,19) = 9.71, p < 0.01$), with threat trials showing a larger PSS ($M = 25.37$ ms, $SD = 20.48$) than control trials ($M = 8.71$ ms, $SD = 11.15$) ($d = 0.70$ [95% CI: 0.21, 1.19]) (see Figure 2). These results suggest that tactile stimuli on the “pain” hand were prioritized. Table 1 represents the PSS values for threat and control trials for each participant individually. The PSS from both control and threat trials differed significantly from the actual point of simultaneity (0 ms), respectively $t(19) = 3.49, p < 0.01$ and $t(19) = 5.54, p < 0.001$. These results suggest that even when participants were cued that no painful stimulus would follow (control trials), they perceived tactile stimuli on the “pain” hand faster than on the “neutral” hand. When excluding the two left-handed participants or the only male participant, the results remain the same. Also when the data are analyzed without exclusion of trials immediately following a pain stimulus, the results remain the same. Finally, no significant associations were found between the PSS values and the scores on the PVAQ and PCS.

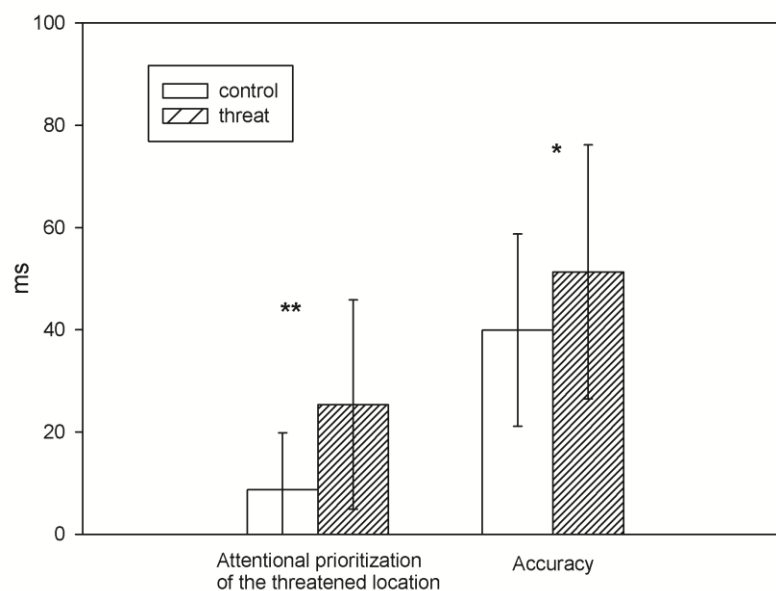


Figure 2. Indexes for attentional prioritization of the threatened location (PSS) and for accuracy (JND) (in ms and with standard errors) in control and threat trials (* $p < 0.05$, ** $p < 0.01$).

Table 1

Single-subject PSS values (in ms) for control and threat trials. Positive values mean that stimuli on the “neutral” hand had to be presented before stimuli on the hand where pain was expected, to be judged as simultaneous. Negative values mean that stimuli on the hand where pain was expected, had to be presented before stimuli on the “neutral” hand to be judged as simultaneous.

Participant	Control	Threat	Participant	Control	Threat
1	2,93	31,50	11	-0,52	67,69
2	25,40	23,30	12	8,79	24,38
3	14,16	26,06	13	5,40	30,24
4	41,47	23,96	14	0,72	4,33
5	-4,50	-2,83	15	5,48	33,21
6	-7,31	7,08	16	1,80	74,97
7	20,11	18,10	17	9,58	39,42
8	11,58	7,94	18	2,94	-2,30
9	1,25	47,14	19	14,05	20,83
10	14,67	12,19	20	6,08	20,14

JND

There was a main effect of Trial type ($F(1,19) = 6.90, p < 0.05$), revealing that the JND was larger in threat trials ($M = 51.35, SD = 24.85$) compared to control trials ($M = 39.93, SD = 18.81$) ($d = 0.59$ [95% CI: 0.11, 1.06]) (see Figure 2). When excluding the two left-handed participants or the only male participant, the results remain the same. Also when the data are analyzed without exclusion of trials immediately following a pain stimulus, the results remain the same. Finally, no significant associations were found between the JND values and the scores on the PVAQ and PCS.

Discussion

The present study investigated whether one becomes more quickly aware of innocuous somatosensory stimuli in a region of the body where pain is anticipated. Our data indicate that when participants made judgments regarding which of two tactile stimuli had been presented first, stimuli on the “neutral” hand had to precede stimuli on the hand on which pain was expected for the two stimuli to be perceived as simultaneous (PSS). This indicates that people perceive stimuli presented on the hand on which pain was expected more rapidly than stimuli presented on the “neutral” hand. Crucially, this effect was significantly larger in threat trials than in control trials. The effect was medium to large

according to conventional norms for effect sizes. Thus, when participants anticipated pain at a particular location of the body, they became more quickly aware of innocuous somatosensory signals at that location of the body. To the best of our knowledge, it is the first study demonstrating that anticipating pain in a particular body part prioritizes somatosensory input at that body part. According to the prior entry hypothesis (Titchener, 1908), attended stimuli are perceived more rapidly than simultaneously presented stimuli that are not attended. Our results thus indicate that tactile attention was prioritized towards the location of the body where pain was expected.

The current findings fit well in a recently developed neurocognitive model of attention to pain (Legrain et al., 2009). The model incorporates two modes on how attention is prioritized by pain-related information. On the one hand, bottom-up capture of attention by pain is an involuntary process that demands attention, interrupts ongoing goals, and prioritizes appropriate behaviors to escape from bodily threat. Top-down attention, on the other hand, is an intentional and goal-directed process that prioritizes information relevant for current goals or actions. It is proposed that top-down selection occurs by means of an attentional set, defined as a mental set of stimulus features that participants use to identify goal-relevant stimuli. All stimuli that meet one or more of these features will capture attention. In the present study, the anticipation of pain at a particular body location may have led to increased somatosensory expectations within participants' attentional set, as a result of which they prioritized somatosensory input at that location.

The paradigm proposed in this study may be useful to assess hypervigilance in chronic pain patients. It is typically assumed that chronic pain patients are characterized by an excessive focus of attention for – even innocuous - bodily sensations, although convincing evidence is currently lacking (Peters, Vlaeyen, & van Drunen, 2000; Peters, Vlaeyen, & Kunnen, 2002). In line with the neurocognitive model of attention to pain (Legrain et al., 2009), it may be that chronic pain patients maintain features of excessive somatosensory expectations within their attentional set for particular locations of the body where they expect to feel pain. For example, patients with chronic lower back pain (CLBP) or temporomandibular joint dysfunction (TMD) may tend to focus their attention to bodily sensations specifically in the back or face, respectively. When applying the

TOJ paradigm in these samples, pairs of tactile stimuli could consist of a stimulus at a pain-relevant location (e.g., back in CLBP, jaw in TMD) and a stimulus at a pain-irrelevant location. Hypervigilance should then be reflected by a bias of attention towards the pain-relevant location, i.e., prioritization of tactile stimuli in the pain-relevant compared to the pain-irrelevant region of the body.

Our study marks a shift in research methods to investigate attentional mechanisms related to pain in two ways. First, most of the previous work in this area has focused on *visual* attention, i.e. the measurement of biases in attention to pain-related visual stimuli such as words, pictures, or conditioned cues. A meta-analysis of Crombez and colleagues (2013) about attentional bias to pain-related information indicated that chronic pain patients display an attentional bias towards pain-related words or pictures, but this bias was of a small effect size, and did not significantly differ from that of control groups. Visual stimuli may, however, not be suitable to activate pain schemata/memories, and therefore, research using somatosensory attention paradigms is recommended (Crombez et al., 2000; Crombez et al., 2013; Van Damme et al., 2010). Our study is one of the first doing so. Second, behavioral studies investigating hypervigilance typically rely on reaction times. Such an approach may be less suitable for clinical populations. It is well-known that chronic pain patients are often characterized by cognitive impairment and psychomotor slowing, which increases reaction time variability and reduces sensitivity to detect effects (Van Damme, Crombez, & Notebaert, 2008). Here, a tactile TOJ task was used, which provides a sensitive measure for detecting biases in spatial attention irrespective of response speed (Spence & Parise, 2010; Spence et al., 2001; Van Damme et al., 2009). Such approach may prove more useful for further research in clinical samples.

A number of issues deserve further discussion. First, this study was conducted with healthy volunteers, using experimental pain. Therefore, one must be cautious in generalizing the results to chronic pain patients. Our findings need extension in clinical pain populations. Second, in this study we specifically examined the effects of *anticipated* pain on tactile attention. As it has been shown that tactile perception may be reduced by *actual* pain, either experimental (Bolanowski, Gescheider, Fontana, Niemic, & Tromblay, 2001; Harper & Hollins, 2012) or chronic (Moseley, 2008), an intriguing question is how the presence of

pain during tactile TOJ's would affect attentional prioritization effects. Third, analysis of the JND data revealed that participants were less accurate in making tactile TOJs on trials in which bodily threat was induced compared to control trials. Although we had no specific hypotheses regarding the JND, this reduced accuracy in tactile TOJs following the anticipation of pain is in line with studies showing that painful somatosensory stimuli interfere with task performance (e.g., Crombez, Eccleston, Baeyens, & Eelen, 1998; Vancleef & Peters, 2006; Van Damme, Crombez, & Eccleston, 2004; Van Ryckeghem, Crombez, Eccleston, Liefoghe, & Van Damme, 2012). Forth, it should be noted that also in control trials the PSS differed significantly from the actual point of simultaneity (oms). In other words, even when participants were cued that no painful stimulus would follow, they perceived tactile stimuli on the "pain" hand faster than on the "neutral" hand, suggesting that also in these trials attention was prioritized – to some extent - to the "pain" hand. A possible explanation could be that participants in a so-called 'safe situation' still fear that a painful stimulus would follow. Although the self-report measures do not seem to confirm this (participants almost never expected a painful electrocutaneous stimulus during control trials), the retrospective nature of these ratings may have prevented the detection of subtle expectations during the control trials. Fifth, we did not use a control condition in which a non-painful somatosensory stimulus at a specific location of the body was anticipated. Although it has already been demonstrated that visual cues signaling a painful stimulus attract more attention than visual cues signaling a non-painful tactile stimulus (Van Damme et al., 2004; Van Damme & Legrain, 2012), it is possible that part of the prioritization effect in our study is not unique to the anticipation of pain. It is recommended that future studies should include an adequate control condition. Sixth, despite the fact that the statistical analysis confirmed our hypothesis, with a moderate to large effect size, we noticed substantial individual variability. It would be interesting to examine which variables may explain this variability. We recommend follow-up studies in which potential theoretically relevant moderators, such as the affective-motivational relevance of pain (Crombez et al., 2005; Van Damme et al., 2010), are experimentally manipulated. Finally, our study does not allow conclusions about how close somatosensory stimuli should be to the pain location in order to be prioritized by attention. Therefore, it would be interesting to investigate in

future studies if the prioritization of somatosensory attention is limited to the exact location of nociception, or if it is generalized to the whole body part or even the whole side of the body.

In conclusion, the current findings indicate that the anticipation of pain at a particular location of the body results in prioritization in time of innocuous somatosensory sensations at that particular location of the body. This suggests that our brain prioritizes tactile information at threatened body parts. The paradigm used here may be a promising tool to investigate somatosensory hypervigilance in clinical populations.

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Are the spatial features of bodily threat limited to the exact location where pain is expected?¹**Abstract**

Previous research has revealed that anticipating pain at a particular location of the body prioritizes somatosensory input presented there. The present study tested whether the spatial features of bodily threat are limited to the exact location of nociception. Participants judged which one of two tactile stimuli, presented to either hand, had been presented first, while occasionally experiencing a painful stimulus. The distance between the pain and tactile locations was manipulated. In Experiment 1, participants expected pain either proximal to one of the tactile stimuli (on the hand; near condition) or more distant on the same body part (arm; far condition). In Experiment 2, the painful stimulus was expected either proximal to one of the tactile stimuli (hand; near) or on a different body-part at the same body side (leg; far). The results revealed that in the near condition of both experiments, participants became aware of tactile stimuli presented to the “threatened” hand more quickly as compared to the “neutral” hand. Of particular interest, the data in the far conditions showed a similar prioritization effect when pain was expected at a different location of the same body part, as well as when pain was expected at a different body part at the same body side. In this study the encoding of spatial features of bodily threat was not limited to the exact location where pain was anticipated, but rather generalized to the entire body part and even to different body parts at the same side of the body.

¹ Vanden Bulcke, C., Crombez, G., Spence, C., & Van Damme, S. (2014). Are the spatial features of bodily threat limited to the exact location of where pain is expected? *Acta Psychologica*, 153, 113-119.

Introduction

Imagine a man playing football who suddenly experiences an intense, shooting pain in his leg after a vigorous tackle. There is a high chance that this pain will capture his attention and interrupt his game. In this example, the capture of attention by pain can be thought of as a stimulus-driven or bottom-up effect (Gallace & Spence, 2014; Legrain et al., 2009; McGlone, Lloyd, & Tipper, 1999). Many studies have already demonstrated that attention is unintentionally captured by pain when it is intense, unpredictable, and/or novel (Crombez, Baeyens, & Eelen, 1994; Eccleston & Crombez, 1999; Legrain et al., 2012). However, the bottom-up capture of attention by pain can be modulated by goal-directed or top-down variables, as when pain is the subject of a person's current goals, thoughts, and/or intentions (Crombez, Van Damme, & Eccleston, 2005; Van Damme, Legrain, Vogt, & Crombez, 2010). Imagine another football player who has recently recovered from a serious ankle injury. When starting to play football again, being fearful of re-injury, he may focus his attention on the injured body part and, hence, quickly become aware of any – even innocuous – bodily sensation that may occur there. As such, attention to pain may be the result of the interplay between bottom-up and top-down factors in a similar way to what has also been extensively reported in the context of visual attention (Desimone & Duncan, 1995; Yantis, 2000).

According to the neurocognitive model of attention to pain (Legrain, et al., 2009), the top-down modulation of attention to somatosensory information occurs by means of the activation of an attentional set. This is defined as the set of stimulus features that participants keep in working memory to identify goal-relevant information. When a stimulus, even when it is not particularly salient, happens to match one of the features in the attentional set, it is more likely to be selected for further processing (Downman, 2001; Folk, Remington, & Johnston, 1992; Van Ryckeghem, Crombez, Eccleston, Legrain, & Van Damme, 2013; Yantis, 2000; Zampini et al., 2007). Thus, when one expects pain to occur, a stimulus that shares features with pain, such as its sensory modality or its stimulus location, may also be preferentially attended to (Legrain, et al., 2009).

To date, few studies have attempted to investigate this idea. Crombez and his colleagues (Crombez, Eccleston, Baeyens, & Eelen, 1998) investigated the interruptive effect of mild experimental pain stimuli on the performance of a

cognitive task. Pain stimuli could be administered to either arm, and participants were led to believe that on one arm a very intense, painful stimulus could sometimes occur. Interestingly, the interruptive effect was significantly larger when a pain stimulus arrived at the “threatened” arm in comparison to the other arm, although on both arms only mild stimuli were actually presented. Recently Vanden Bulcke, Van Damme, Durnez, and Crombez (2013) specifically examined whether experimentally induced threat of pain would speed up the processing of innocuous tactile stimuli presented at the bodily location where the painful stimulus was expected, using a Temporal Order Judgment (TOJ) paradigm. Participants indicated which one of two tactile stimuli administered to each hand, had been presented first. Crucially, the participants expected that a painful stimulus would occasionally be administered on one of their hands. The results revealed that the participants became aware of tactile stimuli on the “threatened” hand more quickly than on the “neutral” hand.

While the results of these previous studies (Crombez et al., 1998; Vanden Bulcke et al., 2013) are consistent with the idea of top-down prioritization of the pain-related bodily location, it is as yet unclear how specific the spatial features of bodily threat are encoded in the attentional set. If only the *exact* location of the pain is encoded, top-down prioritization should be limited to those somatosensory inputs that are in close proximity to the specific bodily location where the painful stimulus is expected. However, it is also possible that the spatial features of bodily threat are encoded in a more general manner, for instance, in terms of the body part where the painful stimulus is anticipated, or in terms of the side of the body where the pain is expected. The aim of the present study was to investigate the specificity of the spatial features of pain in the attentional set. We report two experiments in which a tactile TOJ task was used for stimuli presented to the hands. In the first experiment, a painful stimulus was occasionally administered, either proximal to one of the tactile stimuli, i.e., the hand (near condition), or more distant on the same body part, i.e., the arm (far condition). In the second experiment, a painful stimulus was occasionally administered either proximal to one of the tactile stimuli, i.e., the hand (near condition) or on a different body part at the same body side, i.e., the leg (far condition). With regard to the “near” condition, we hypothesized that in both experiments, tactile stimuli would be perceived more rapidly on the “threatened”

hand than on the “neutral” hand (see also Van Damme, Gallace, Spence, Crombez, & Moseley, 2009; Vanden Bulcke et al., 2013). With regard to the “far” condition, we examined whether tactile stimuli would be perceived more rapidly on the hand of the “threatened” arm (Experiment 1) or the hand ipsilateral to the threatened leg (Experiment 2), than on the other hand.

Experiment 1

Method

Participants

Thirty-four undergraduate students (25 females, 9 males; mean age = 20.4 years; all white Caucasian) participated to fulfill course requirements. All of the participants had normal or corrected-to-normal vision and normal hearing. All but three of the participants reported being right-handed. The participants rated their general health on average as ‘good’ and none of the participants reported having a current medical condition or mental disorder. Although a student group is often described as healthy, pain can be a prevalent symptom amongst this group, and is therefore best documented. Twenty-eight of the participants reported having experienced pain during the last six months (average of 24.3 days in 6 months). Thirteen of these participants reported feeling pain at the time of testing, but the average rating of the intensity of this pain was low ($M = 2.91$; ranging from 1 to 6, $SD = 1.44$) on a Likert scale where 0 indicated ‘no pain’ and 10 the ‘worst pain ever’. All of the participants gave their informed consent and were free to terminate the experiment at any time should they so desire. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experimental session lasted for approximately 1 hour.

Apparatus and materials

Tactile stimuli (10 ms duration; 200Hz) were presented by means of two resonant-type tactors (C-2 TACTOR, Engineering Acoustics, Inc., Florida, <http://www.eaiinfo.com/>) consisting of a housing of 3.05 cm diameter and 0.79 cm high, with a skin contactor of 0.76 cm diameter. Prior to the start of the experiment, the perceived stimulus intensities at both tactor locations were

individually matched (Weinstein, 1968). This was done by means of a double random staircase procedure, based on the ‘simple up-down method’ of Levitt (1971). In a first phase, 24 stimuli presented on the left hand were judged relative to a reference stimulus, which was defined as the maximum intensity (power = 0.21 Watt) on a 5-point Likert scale ranging from 1 (‘no sensation’) to 5 (‘maximum intensity’). The intensity that elicited an averaged rating of 3 was used as the stimulus intensity for the left hand, and was the reference stimulus for the second phase. In the second phase, 24 stimuli on the right hand were judged relative to the reference stimulus on the left hand, once again using a 5-point Likert scale (1 = ‘much weaker’, 2= ‘weaker’, 3= ‘equally strong’, 4= ‘stronger’, 5= ‘much stronger’). The stimulus intensity that elicited an averaged rating of 3 was used as the intensity of the stimulus at the right hand.

Painful stimuli were delivered by means of two constant current stimulators (Digitimer DS5 2000, Digitimer Ltd, England, <http://www.digitimer.com/index.htm>). Each stimulator consisted of trains of 20 ms sinusoid pulses with a frequency of 50 Hz and a duration of 200 ms. Painful stimuli were delivered via two pairs of lubricated Fukuda standard Ag/AgCl electrodes, each pair consisting of an anode and cathode (1 cm diameter). One pair of electrodes was attached on the forearm, the other pair of electrodes on the hand. The intensity of the electrocutaneous stimuli was determined for each participant individually by means of a random staircase procedure. For each hand, 20 electrocutaneous stimuli were presented to participants (starting intensity between 0 and 1.5 mA) and self-reports were collected on an 11-point Likert scale (0 = ‘no sensation’; 10 = ‘unbearable pain’). The pain intensity that elicited an average rating of 7 was selected as the pain stimulus for the main experiment (Arntz, Dreessen, & De Jong, 1994; Vanden Bulcke et al., 2013).

The task was programmed and controlled by the INQUISIT Millisecond software package (Inquisit 3.0, Millisecond Software LLC, Seattle, WA, <http://www.millisecond.com/>) on a laptop (HP Compaq nc 6120).

TOJ paradigm

In the TOJ task (Piéron, 1952), two tactile stimuli were administered, one on either hand, separated by one of 10 randomly assigned stimulus onset asynchronies (SOAs) ranging from -120 to +120 ms (-120, -60, -30, -15, -5, +5,

+15, +30, +60, +120 ms; negative values indicate that the left hand was stimulated first) (see also Vanden Bulcke et al., 2013). The participants were instructed to report aloud the hand on which the first tactile stimulus was presented, and the experimenter registered the answers using a keyboard. A trial started with the presentation of a fixation cross (1000 ms) in the middle of the screen, followed by a colored cue (either blue or yellow, of 1000 ms duration), indicating whether or not a painful stimulus could follow on one specific location (threat and control trial, respectively). Which color of cue was associated with threat was counterbalanced across the participants. Before the start of each block of trials, the participants were told on which location (hand or forearm) they should expect the painful stimulation to be delivered. In 10% of the threat trials, the pain stimulus was actually delivered instead of the two tactile stimuli (pain trials), but the participants were not informed about this contingency. The participants were informed that no response had to be given in such trials.

Procedure

Upon arrival at the laboratory, the participants received the task instructions and were told that an electrocutaneous stimulus would be used during the experiment and that “most people find this kind of stimulation unpleasant” (Crombez, et al., 1998; Van Damme, Crombez, & Eccleston, 2004a). After the participants had given their written informed consent, they were seated in front of the experimental apparatus. Their forearms were positioned symmetrically on the table. The tactors were placed on the dorsal side of their hand, with the center on the middle of the third metacarpal. One pair of electrodes was attached on the hand dorsum between thumb and index finger, in the sensory territory of the superficial radial nerve. The other pair of electrodes was placed on the proximal third of the muscle belly of the brachioradialis of the same limb (approximately 3 cm below the lateral epicondyle). To visualize the brachioradialis, the participants were asked to flex the elbow with the forearm in pronation, while the experimenter provided resistance against the distal end of the radius. As such, the muscle belly of the brachioradialis is well visible and enables the experimenter to attach the electrode exactly on the muscle belly. The skin at the electrode sites was first abraded with a peeling cream (Nihon Kohden, Tokyo, Japan) to reduce the resistance of the skin. The participants were

informed that they would have to decide on each trial which stimulus had been presented first. The accuracy of participants' responses was emphasized, rather than the speed. The participants wore headphones (Wesc, Conga) during the experiment. White noise (42.2 dB) was presented continuously through headphones to mask the noise resulting from the operation of the tactors. The participants were not given any feedback concerning their performance.

The session began with a practice block of twenty-three trials (1 trial per SOA for control trials, 1 trial per SOA for threat trials, 3 pain trials). Following this, four blocks of 105 trials (5 trials per SOA for control trials, 5 trials per SOA for threat trials, 5 pain trials) were presented. The two possible pain locations (hand or arm) were alternated between blocks and the order was counterbalanced between participants. The side on which pain was expected (left vs. right limb) was counterbalanced between participants.

Self-report measures

After each test phase, the participants had to rate several questions concerning their concentration ('To what extent have you made an effort to perform this task?', 'To what extent did you concentrate on this task?'), attention to painful/tactile stimuli ('To what extent did you pay attention to the painful/tactile stimuli?'), pain experience ('How painful did you find the electrocutaneous stimuli?'), anxiety ('How anxious were you during this block?'), fatigue ('To what extent did you find this task tiring?') on eleven-point numerical rating scales (anchored 0 = not at all and 10 = very strongly). As a manipulation check, we were especially interested in the participant's ratings of fear ('To what extent were you afraid that a painful stimulus would be administered by the blue/yellow cue?') and expectations ('To what extent did you expect that a painful stimulus would be administered by the blue/yellow cue?'). Before the experiment, the participants were asked to complete the Pain Vigilance and Awareness Scale (PVAQ; McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002) and the Pain Catastrophizing Scale (PCS; Sullivan, Bishop, & Pivik, 1995; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove, 2002). These data were collected for meta-analytical purposes and are not reported in detail here.

Data-analysis

In TOJ studies, it is common practice (Shore, Gray, Spry, & Spence, 2005; Spence, Shore, & Klein, 2001) to exclude those participants from statistical analysis when (1) any of the PSS values is greater than the highest SOA (± 120 ms) tested, (2) participants have less than 80% accuracy on the trials with the largest SOA tested (± 120 ms). Four participants (women, all right-handed) had to be excluded for the first reason, one participant (female, right-handed) for the second reason. Trials following trials with electrocutaneous stimulation were removed from subsequent data analysis in order to avoid the possibility that: (1) potential effects would be mainly driven by trials directly following painful stimulation; or (2) after-effects of pain would interfere with the tactile TOJ (max. 10% of all trials).

The analyses were based on a procedure that has been commonly described in the literature (Shore et al., 2005; Spence et al., 2001; Van Damme et al., 2009). The proportions of 'left-hand-first' and 'right-hand-first' responses for threat presented on the left and right side, respectively, for all trials at each SOA, were converted into the corresponding z-scores using a standardized cumulative normal distribution (probits). The best-fitting straight line was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS) values for the subsequent statistical analyses (see Figure 1). The PSS refers to the point at which observers report the two events (right hand first and left hand first) equally often. This is commonly taken to be equivalent to the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time and such equivalent to the SOA value corresponding to a proportion of *left/right hand first responses* of 0.5. The PSS is computed as the opposite of the intercept divided by the slope from the best-fitting straight line. The sign of the PSS in which threat was presented on the right hand was reversed. Subsequently, for each participant, the final PSS values was calculated by taking the average of the PSS values for threat presented on the left side and the reversed PSS values for threat presented on the right side. Hence, a positive value indicates that the stimulus contralateral to the side of threat had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS indicates that stimuli on the threatened hand are perceived more rapidly than those presented to the other hand. In sum, the PSS provides

information concerning biases in spatial attention resulting from the presentation of bodily threat. A repeated measures analysis of variance (ANOVA) with the factors Cue (within; threat versus control), Location (within; near versus far) and Pain Side (between; left versus right) was performed on the PSS data. For ease of comparison with the norms of Cohen (1988), we calculated effect sizes for independent samples using the formula of Dunlap and colleagues (Dunlap, Cortina, Vaslow, & Burke, 1996). For interaction effects, difference scores were used to obtain Cohen's d . A difference score was calculated for threat versus control trials, which was then compared between the near and far condition. We determined whether Cohen's d was small (0.20), medium (0.50), or large (0.80) (Cohen, 1988). We also report the 95% confidence intervals (95% CI) of the effect sizes.

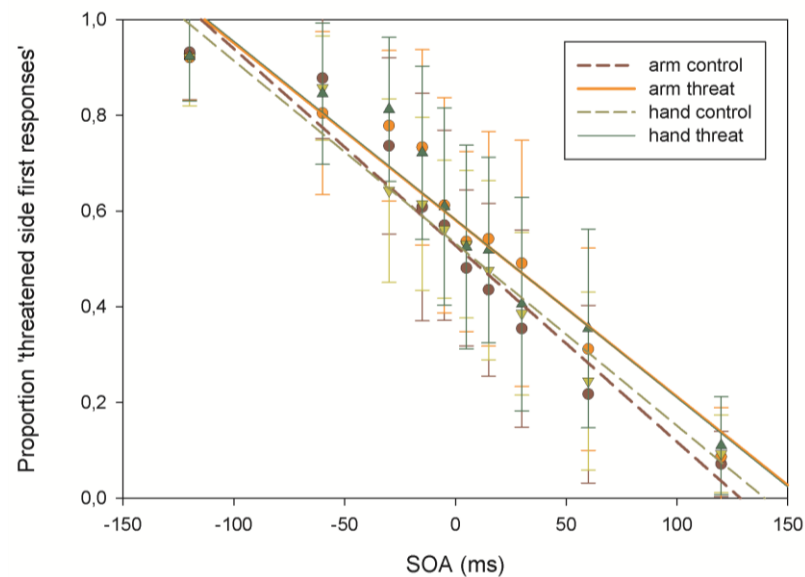


Figure 1. Temporal order judgment (TOJ) data for Experiment 1. Average of the fitted data for all participants. Data are plotted as a proportion of responses that coincided with the side on which the threatening stimuli were presented (y-axis), as a function of stimulus onset asynchrony (SOA, x-axis). The different conditions are represented by different symbols and line styles (see legend).

Results

Manipulation check

Participants reported being more afraid during the threat trials ($M = 5.70$, $SD = 2.51$) than during the control trials ($M = 0.19$, $SD = 0.40$) ($t(28) = 12.45$, $p < 0.001$; $d = 2.56$ [95% CI: 1.73, 3.39]). Furthermore, the participants reported a

higher expectation of a painful electrocutaneous stimulus during threat trials ($M = 5.78$, $SD = 2.26$) than during control trials ($M = 0.32$, $SD = 0.68$) ($t(28) = 12.93$, $p < 0.001$; $d = 3.10$ [95% CI: 1.99, 4.21]). Finally, the participants rated the electrocutaneous stimuli as moderately painful ($M = 5.81$, $SD = 2.11$).

PSS

The main effect of Cue was significant ($F(1,27) = 6.04$, $p = 0.02$), with threat trials ($M = 20$ ms, $SD = 34$) showing a larger PSS than control trials ($M = 9$ ms, $SD = 24$) ($d = 0.36$ [95% CI: 0.03, 0.70]). The main effect of Location was not significant ($F(1,27) = 0.91$, $p = 0.35$) ($d = 0.10$ [95% CI: -0.15, 0.35]), meaning that, on average, the PSS was similar in the near and far conditions ($M = 16$ ms; $SD = 28$ and $M = 13$ ms; $SD = 31$, respectively) (see Figure 2). Of particular interest, there wasn't a significant interaction between Cue and Location ($F(1,27) = 0.65$, $p = 0.43$) ($d = 0.16$ [95% CI: -0.21, 0.52]), indicating that the difference in PSS between the threat trials and control trials was similar in both the near and the far conditions. Note that there was a significant effect of the Side of the Pain ($F(1,27) = 6.41$, $p = 0.02$), larger PSS values were observed in subjects who attended the pain on the left side ($M = 25$ ms; $SD = 29$) as compared to PSS values in subjects who attended pain on the right side ($M = 5$ ms; $SD = 27$) ($d = 0.74$ [95% CI: 0.16, 1.33])². However, the Side on which the Pain was delivered did not interact with the hypothesized effects. Thus it can be concluded that the threat effects were independent of the side of the body that was threatened. None of the other interactions were significant.

² To check whether differences in perceived and physical pain intensities between the two groups could account for the main effect of side of pain, we conducted a series of independent t-tests. We found no significant differences in perceived intensity (per) of the painful stimuli between participants who received painful stimulation on the left ($M_{hand} = 5.85 \pm 2.36$; $M_{arm} = 6.96 \pm 2.37$) of right side ($M_{hand} = 5.69 \pm 2.20$; $M_{arm} = 6.09 \pm 2.09$) of the limb ($t_{perhandleft, perhandright}(27) = 0.19$, $p = 0.85$, $t_{perarmleft, perarmright}(30) = 1.03$, $p = 0.31$) nor in physical intensity (phy) of the painful stimuli between participants who received painful stimulation on the left ($M_{hand} = 2.16$ mA \pm 0.68; $M_{arm} = 2.26$ mA \pm 0.63) of right side ($M_{hand} = 2.35$ mA \pm 0.38; $M_{arm} = 2.51$ mA \pm 0.60) of the limb ($t_{phyhandleft, phyhandright}(27) = -0.89$, $p = 0.39$, $t_{phyarmleft, phyarmright}(30) = -1.12$, $p = 0.28$). Furthermore, paired-sampled t-tests indicated no significant differences in perceived intensity (per) and physical intensity (phy) of the tactile stimuli between the left and right hand ($t_{per}(28) = -1.38$, $p = 0.18$; $t_{phy}(28) = 0.48$, $p = 0.63$). Moreover, no significant differences were found in physical as well as perceived intensity of the tactile stimuli between the left and right hand for participants who received painful stimulation on the left neither for participants who received painful stimulation on the right side of the limb ($t_{perpainleft}(13) = -1.27$, $p = 0.23$; $t_{perpainright}(14) = -0.62$, $p = 0.55$; $t_{hyppainleft}(13) = 1.38$, $p = 0.19$; $t_{hyppainright}(14) = -0.94$, $p = 0.36$).

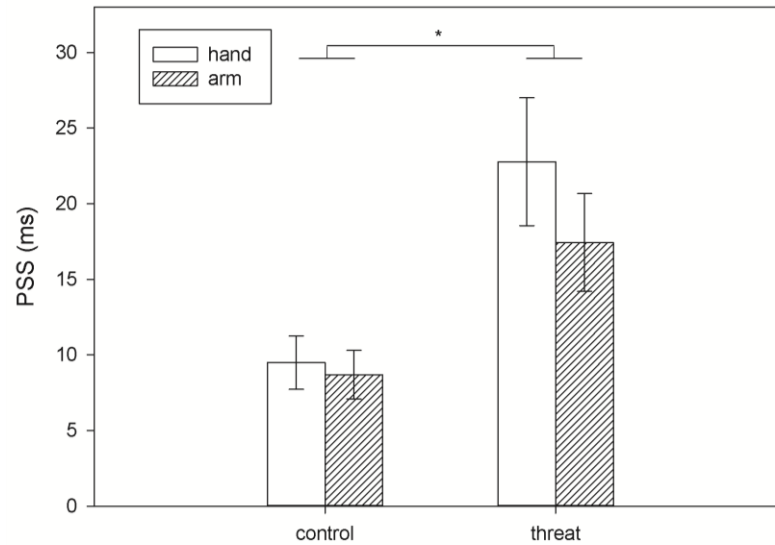


Figure 2. Index for attentional prioritization (PSS) of the threatened hand and arm (in ms and with standard errors) in control and threat trials. Positive values indicate that stimuli on the threatened hand were perceived more rapidly than those presented to the other hand, whereas negative values indicate that stimuli on the neutral hand were perceived more rapidly than those presented to the threatened hand (* $p < 0.05$).

Interim discussion

The results of Experiment 1 demonstrate that when participants made judgments regarding which of two tactile stimuli had been presented first, stimuli presented on the hand on which pain was expected were perceived more rapidly than stimuli presented on the “neutral” hand. Thus, in line with our previous research (Vanden Bulcke et al., 2013), it was shown that when participants anticipated pain at a particular location of the body, they became more quickly aware of somatosensory signals at that bodily location. Of specific interest, even when pain was anticipated at the arm, tactile stimuli on the hand of the “threatened” arm were perceived more rapidly than tactile stimuli on the other hand. In this experiment, the findings suggest that the encoding of spatial features of bodily threat may not be limited to the exact location where pain is anticipated. In our second experiment, we investigated whether the prioritization of tactile stimuli on the hand is still present even when bodily threat is induced on more extreme distant body parts on the same side of the body, for example on the leg. Therefore, in Experiment 2, a painful stimulus was occasionally administered either proximal to one of the tactile stimuli, i.e., the hand (near condition) or on a different body part at the same body side, i.e., the leg (far condition). As in the

first experiment, the participants had to decide which one of two tactile stimuli had been presented first.

Experiment 2

Method

Participants

Thirty-four undergraduate students (29 female and 5 male; mean age, 21.94 years; all white Caucasian) took part in this study. The participants were given 8 Euros in return for taking part. All of the participants had normal or corrected-to-normal vision and normal hearing. All but 5 were right-handed by self-report. Twenty-six participants reported having experienced pain during the last six months (average of 19.08 days in 6 months). Fifteen of these participants reported feeling pain at the time of testing, but the average rating of the intensity of this pain was low ($M = 2.69$; ranging from 1 to 8, $SD = 2.27$) on a Likert scale where 0 indicated 'no pain' and 10 indicated the 'worst pain ever'. The participants rated their general health on average as 'very good' and none of them reported having a current medical or mental disorder. All of the participants gave their informed consent and they were free to terminate the experiment at any time. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experimental session lasted for approximately 1 hour.

Apparatus and materials

The same apparatus and stimulus characteristics were used as in Experiment 1.

TOJ paradigm

The task was identical to Experiment 1, with the exception that the participants received the electrocutaneous stimuli on the hand in half of the blocks, whereas in the other half of the blocks, they were presented to the musculus tibialis anterior (ankle) instead.

Procedure

The procedure was almost identical to that used in Experiment 1. One pair of electrodes was attached on the dorsum of the hand, between the thumb and index finger, in the region of the superficial radial nerve. The other pair of electrodes was placed on the distal part of the musculus tibialis anterior, which was standardized at 1/3 on the line between the tip of the fibula and the tip of the medial malleolus. To control of the exact location, the musculus tibialis anterior was visualized by asking an active dorsal flexion in the ankle while sitting on an examination table.

Self-report measures

The questionnaires and self-report measures were the same as in Experiment 1.

Data-analysis

The measures and the analyses of the data were identical to Experiment 1. Again, the best-fitting straight line on the z-scores was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS) values for the subsequent statistical analyses (see Figure 3).

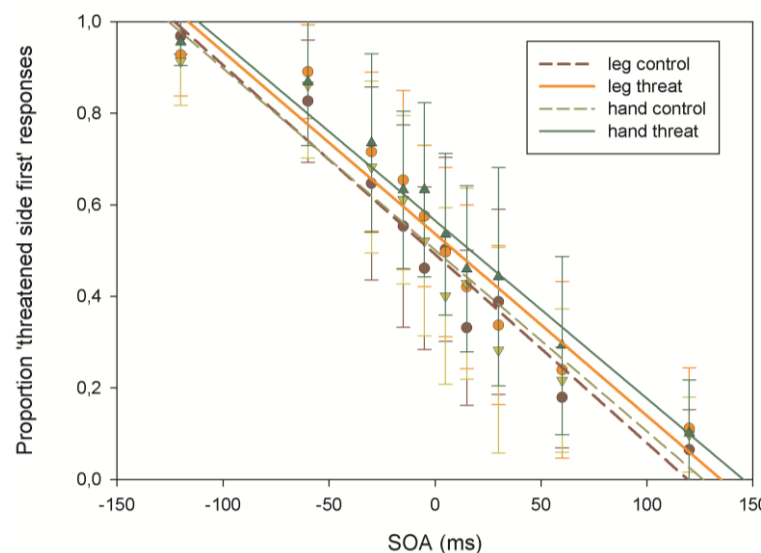


Figure 3. Temporal order judgment (TOJ) data for Experiment 2. Average of the fitted data for all participants. Data are plotted as a proportion of responses that coincided with the side on which the threatening stimuli were presented (y-axis), as a function of stimulus onset asynchrony (SOA, x-axis). The different conditions are represented by different symbols and line styles (see legend).

Exclusion criteria were the same as for Experiment 1. Three of the participants (all women, two right-handed and one left-handed) had an accuracy of less than 80% on those trials with the largest SOA tested (± 120 ms) and were therefore removed from data analysis.

Results

Manipulation check

Participants reported being more afraid during threat trials ($M = 4.86$, $SD = 2.57$) than during the control trials ($M = 0.06$, $SD = 0.28$) ($t(30) = 10.28$, $p < 0.001$; $d = 2.69$ [95% CI: 1.59, 3.79]). Furthermore, the participants reported a higher expectation of a painful electrocutaneous stimulus during the threat trials ($M = 4.91$, $SD = 2.12$) than during the control trials ($M = 0.07$, $SD = 0.40$) ($t(30) = 12.63$, $p < 0.001$; $d = 3.10$ [95% CI: 1.94, 4.25]). Finally, the participants rated the electrocutaneous stimuli as being moderately painful ($M = 5.01$, $SD = 1.97$).

PSS

The main effect of Cue was significant ($F(1,29) = 17.44$, $p < 0.01$), with threat trials ($M = 13$ ms, $SD = 27$) showing a larger PSS than the control trials ($M = -1$ ms, $SD = 23$) ($d = 0.55$ [95% CI: 0.27, 0.83]). There was no main effect of Location ($F(1,29) = 1.25$, $p = 0.27$) ($d = 0.12$ [95% CI: -0.08, 0.32]), meaning that, on average, the PSS was not different between the near and far conditions ($M = 4$ ms, $SD = 22$, and $M = 7$ ms, $SD = 27$, respectively). Of particular interest, there was no significant interaction between Cue and Location ($F(1,29) = 0.005$, $p = 0.94$) ($d = 0.01$ [95% CI: -0.34, 0.37]), indicating that the difference between the threat and control trials was similar in both the near and the far conditions (see Figure 4). All other main and interaction effects were non-significant (all $F < 1$)³.

³ Independent *t*-tests indicated no significant differences in perceived intensity (per) of the painful stimuli between participants who received painful stimulation on the left ($M_{hand} = 4.25 \pm 2$; $M_{leg} = 4.56 \pm 2.11$) of right side ($M_{hand} = 5.57 \pm 1.95$; $M_{leg} = 5.60 \pm 2.21$) of the limb ($t_{perhandleft, perhandright}(30) = -0.43$, $p = 0.67$, $t_{perlegleft, perlegright}(28) = -0.04$, $p = 0.97$) nor in physical intensity (phy) of the painful stimuli between participants who received painful stimulation on the left ($M_{hand} = 2.01 \text{ mA} \pm 0.53$; $M_{leg} = 2.23 \text{ mA} \pm 0.72$) of right side ($M_{hand} = 1.74 \text{ mA} \pm 0.75$; $M_{leg} = 1.88 \text{ mA} \pm 0.98$) of the limb ($t_{phyhandleft, phyhandright}(30) = -0.98$, $p = 0.38$, $t_{phylegleft, phylegright}(28) = -0.46$, $p = 0.65$). Furthermore, paired-sampled *t*-tests indicated no significant differences in perceived intensity (per) and physical intensity (phy) of the tactile stimuli between the left and right hand ($t_{per}(30) = -0.19$, $p = 0.85$; $t_{phy}(30) = 1.02$, $p = 0.31$). Moreover, no significant differences were found in physical as well as perceived intensity of the tactile stimuli between the left and right hand for participants who received painful stimulation on the left neither for participants who received painful stimulation on the right side of the limb ($t_{perpainleft}(16) = 0.18$, $p = 0.86$; $t_{perpainright}(13) = -0.54$, $p = 0.60$; $t_{hypainleft}(16) = 1.26$, $p = 0.23$; $t_{hypainright}(13) = -0.10$, $p = 0.92$).

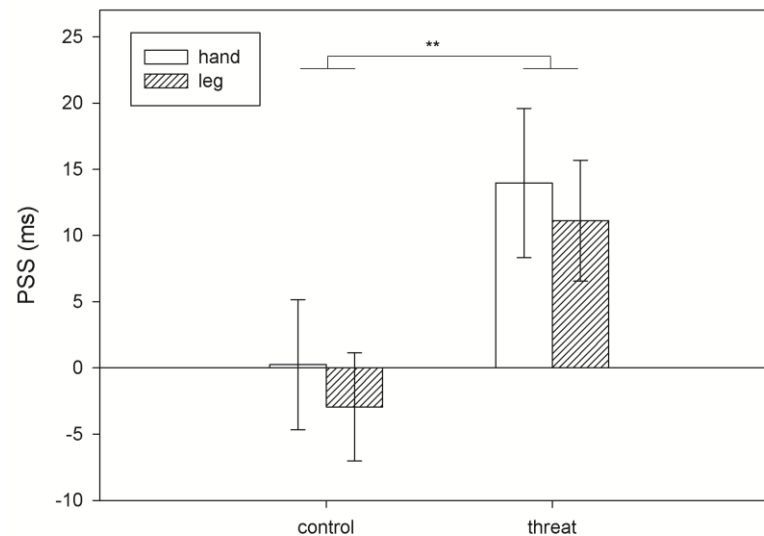


Figure 4. Index for attentional prioritization (PSS) of the threatened hand and leg (in ms and with standard errors) in control and threat trials. Positive values indicate that stimuli on the threatened hand are perceived more rapidly than those presented to the other hand, whereas negative values indicate that stimuli on the neutral hand are perceived more rapidly than those presented to the threatened hand (** $p < 0.01$).

Discussion

We investigated how specific the spatial features of bodily threat are encoded in the attentional set. In the two experiments reported here, the participants made tactile TOJs for stimuli presented to the hands, while occasionally experiencing a painful stimulus. We manipulated the distance between the pain and the tactile stimulus locations (near versus far). In the first experiment, pain was expected either proximal to one of the tactile stimuli (on the hand) or more distant on the same body part (arm). In our second experiment, the painful stimulus was expected either proximal to one of the tactile stimuli (on the hand) or on a different body-part at the same body side (leg). The results revealed that, in the near condition of both experiments, the participants became aware of tactile stimuli presented to the “threatened” hand more quickly as compared to the “neutral” hand. Of particular interest, the data in the far condition in both experiments showed a similar prioritization effect when pain was expected at a different location of the same body part, as well as when pain was expected at a different body part at the same body side.

Our study replicates the findings of a previous experiment (Vanden Bulcke, et al., 2013) demonstrating that the anticipation of pain at one hand results in the

prioritization of somatosensory sensations at that hand. Particularly intriguing in the case of the present study, and an important extension of the previous study, is our finding that the prioritization of tactile stimuli as a result of pain anticipation was not limited to the exact bodily location where pain was expected. More specifically, we found that prioritization also occurred when pain was expected at a different location on the same body part (arm) or at a different part of the body on the same body side (leg). The results of our studies suggest that the spatial features of bodily threat in our studies were not encoded in terms of the exact location where pain was anticipated, but in a more general manner, i.e., body part or even body side.

The paradigm proposed in this study may be useful to assess hypervigilance, i.e. a heightened attentional processing of painful and/or somatosensory information, in chronic pain patients. More precisely, hypervigilance is defined as a goal-dependent, attentional process that emerges when the threat value of pain is high, the fear system is activated, and the individual's current concern is to escape and avoid pain (Crombez et al., 2005). It is typically assumed to play an important role in pain perception and disability in chronic pain problems (Crombez, et al., 2005; Vlaeyen & Linton, 2000). Individuals who appraise bodily sensations as dangerous and who fear (re)injury, were thought to be more likely to scan the body for threatening sensations (Vlaeyen & Linton, 2000). Hence, we might generate interesting new hypotheses in this regard. For instance, it could be hypothesized that the fear of pain and re-injury often experienced by patients with musculoskeletal disorders will emerge as the attentional prioritization of the region of the body where they expect to feel pain. We may further speculate that such prioritization may possibly exceed the exact pain relevant location and may extend to related bodily locations.

One can question whether anticipating pain not only involves a heightened attention to somatosensory sensations at those locations that are pain-relevant, but also leads to a perceptual amplification of bodily sensations. Several studies (Geisser et al., 2003; Hollins et al., 2009) have demonstrated that chronic pain patients show an increase in the perceived intensity of somatosensory stimulation although such perceptual amplification is not limited to the somatosensory modality. Note, however, that in those studies somatosensory perception was not specifically measured in pain-relevant bodily locations. Therefore, it could be

questioned what role spatial location plays with regard to perceptual amplification. Interesting in this regard is the study by Van Ryckeghem et al. (2013). They instructed their participants to rate the intensity and the unpleasantness of somatosensory stimuli, after they had localized either a somatosensory or an auditory target at one particular location. Their results showed that the painful stimulus was experienced as less painful and less unpleasant when attending to an auditory target, particularly when pain was not at the attended spatial location.

Some issues should be considered when interpreting the results of the current study. First, as we made use of experimental pain to induce bodily threat in pain-free undergraduate students, one might ask to what extent the same process occurs in real life pain situations. It would certainly be interesting for future research to investigate this phenomenon in patients with unilateral pain problems, e.g., those suffering from unilateral knee pain. Based on the findings reported here, it might be expected that these patients would prioritize tactile sensations on the location where they expect to feel pain (e.g., knee) and on those bodily locations that are further away of the pain-relevant body location (e.g., tactile sensations presented on the ankles). Second, the more general encoding of the spatial features of bodily threat in the attentional set may also be the result of the response characteristics of the TOJ task. Participants must encode targets on a left-right dimension ('left-side first' or 'right-side first'), which may have led to encoding of bodily threat in the attentional set in the same manner (on the left or right side of the body). One possible solution to address this issue would be conducting a similar TOJ task in which the response dimensions of the stimulus are orthogonal to the coding dimensions of bodily threat. A TOJ with four possible tactile locations (two on the left and two on the right hand, placed one above the other) is recommended in which participants have to indicate which one of two tactile stimuli administered to each hand, was presented first (the upper or the lower one) (Gallace, Soto-Faraco, Dalton, Kreukniet, & Spence, 2008). Another option would be to make use of a simultaneity judgment (SJ) task (Axelrod, Thompson, & Cohen, 1968; Zampini, Shore, & Spence, 2005), in which participants have to judge whether or not two tactile stimuli delivered to the left and right hand were presented simultaneous. In contrast to the TOJ task, participants do not need to compute the location of the tactile stimuli in order to

judge whether or not they occur simultaneously. Third, it is important to note that our study paradigm does not allow for conclusions to be drawn about the effects of actual pain on tactile perception, and is only informative for the assessment of effects of anticipated pain on tactile processing. While the latter typically refers to cognitive mechanisms, the former rather refers to sensory interactions between pain and tactile stimuli, such as touch gating, the phenomenon that tactile thresholds are elevated by the concomitant presence of pain, especially when they are presented in close proximity (Bolanowski, Gescheider, Fontana, Niemiec, & Tromblay, 2001; Harper & Hollins, 2012). Fourth, we did not use a control condition in which a non-painful somatosensory stimulus at a specific location of the body was anticipated. Stimuli might become relevant in many other ways, which might also result in prioritized processing. As we only used painful stimuli, we cannot draw any conclusions about the specificity of our prioritization effect. However, it has previously been demonstrated that visual cues signaling a painful stimulus attract more attention than visual cues signaling a non-painful tactile stimulus (e.g., Van Damme, Eccleston, & Crombez, 2004b; Van Damme, Eccleston, Crombez, & Goubert, 2004c; Van Damme & Legrain, 2012). Although we assume that our effect is mainly due to the affective-motivational relevance of the pain stimulus, it is possible that part of the prioritization effect in our study is not unique to the anticipation of pain. It might have been mediated by other mechanisms (e.g. arousal) to some extent (Vogt, De Houwer, Koster, Van Damme, & Crombez, 2008). Future studies should include an adequate control condition and may wish to investigate the role of potential mediating mechanisms. Fifth, one can argue that our studies are variant of the classic cueing effect (Posner, 1980). That is, when people expect a painful stimulus in one hemi-space, attention is oriented to that side of the body and facilitates the processing of somatosensory input occurring on the same half of the body. Here, cues might have triggered the painful location, which in turn might have resulted in the orientation of attention towards that threatened bodily location. As such, stimuli that are presented at that location will be facilitated. Finally, in the two experiments reported here, only two spatial locations were used to test the generalization of the prioritization effect. To draw conclusions about the specific boundaries of this effect, it would

be interesting for further research to systematically vary several different graduations on a spatially-defined dimension.

In conclusion, we found that the anticipation of a painful stimulus results in the prioritization of somatosensory sensations in the region where individuals expect to feel pain. Furthermore, the results of our study also extend previous findings and suggest that the encoding of spatial features of bodily threat is not limited to the exact location where pain is anticipated. In our studies, the top-down prioritization of somatosensory sensations is generalized to the entire body part and even to different body parts at the same side of the body.

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Is the attentional prioritization on a location where pain is expected modality-specific or multisensory?¹

Abstract

Previous research suggests that anticipating pain at a particular location of the body prioritizes somatosensory input at that location. The present study tested whether this prioritization effect is limited to somatosensory information (modality-specific hypothesis) or generalizes to other sensory modalities (multisensory hypothesis). Thirty-four undergraduate students performed tactile and visual Temporal Order Judgment (TOJ) tasks while either expecting a painful stimulus on one of the hands (threat), or expecting no pain stimulus (control). Participants judged in half of the blocks which one of two tactile stimuli, administered to either hand within a range of different stimulus onset asynchronies (SOA), had been presented first (tactile condition). In the other half of the blocks, pairs of visual stimuli, presented on either hand, had to be judged (visual condition). Analyses revealed that only in threat trials, the participants became aware of stimuli on the threatened hand more quickly as compared to the neutral hand, replicating the prioritization effect. Of particular interest, this effect was not different between the tactile and the visual conditions. This suggests that the anticipation of pain results in multisensory prioritization of information at the threatened body location.

¹ Vanden Bulcke, C., Crombez, G., Durnez, W., & Van Damme, S. (under review). Is the attentional prioritization on a location where pain is expected modality-specific or multisensory?

Introduction

Pain fulfills an important protective function, as it is an archetypal warning of danger to an organism. Rapidly detecting and responding to bodily threats is undoubtedly necessary to prevent us from physical injury (Crombez, Van Damme, Eccleston, 2005; Dowman, 2011). Attention has been put forward as a central component in the adequate detection of bodily threats. Pain may be captured by attention in an involuntary, bottom-up way. As a result, ongoing behavior is interrupted, which allows dealing efficiently with a potentially dangerous situation (Eccleston & Crombez, 1999; Legrain, Van Damme, Eccleston, Davis, Seminowicz, & Crombez, 2009). Many studies have already demonstrated that pain is indeed prioritized over competing information (Crombez, Baeyens, & Eelen, 1994; Eccleston, 1995; Legrain, Perchet, & García-Larrea, 2009; Tiemann et al., 2012; Vangronsveld et al., 2007).

Successful adaptation is, however, also supported by the ability to anticipate pain, by gathering knowledge about the association between cues and the occurrence of pain, as such preparing the organism for adequate action (Bolles & Fanselow, 1980; Ohman, 1979; Vlaeyen & Linton, 2012). When pain is expected or anticipated, attention may be directed in a top-down manner, resulting in prioritization of pain-relevant information (Van Damme, Crombez, & Eccleston, 2004a). It has been proposed that individuals adopt ‘attentional control settings’, consisting of certain stimulus features or characteristics that are relevant for their actions. These stimulus features will receive more attention if they are present in the environment (Corbetta & Shulman, 2002; Folk et al., 1992; Yantis, 2000). Accordingly, if pain is expected, attention may be preferentially allocated to stimuli that match active pain-related features in the attentional set (Legrain et al., 2009; Van Damme, Legrain, Vogt, & Crombez, 2010). The location where one expects pain to occur may be an important feature. Imagine a person who is experiencing low back pain. He or she may be worried about a potential injury and anticipate changes in pain in certain situations. This may activate the spatial stimulus representation ‘location’ (i.e. lower back) in working memory. As a result, this person might become more quickly aware of bodily sensations in the back, as these sensations match location features that are present in the attentional set.

There is some empirical evidence for this idea. Crombez, Eccleston, Baeyens, and Eelen (1998) investigated the interruptive effect of mild experimental pain stimuli on the performance of a tone discrimination task. Pain stimuli could be administered to either arm, and participants were told that on one arm a very intense, painful stimulus could sometimes occur, although in reality, on both arms the same mild stimuli were presented. Interestingly, the interruptive effect of the pain stimuli was larger when they were administered at the “threatened” arm in comparison to the “neutral” arm. More recently Vanden Bulcke, Van Damme, Durnez, and Crombez (2013) examined whether experimentally induced threat of pain would speed up the processing of innocuous tactile stimuli in a region of the body where pain is expected. Participants made judgments regarding two tactile stimuli, one administered to each hand, had been presented first. Crucially, expectation of a painful stimulus on one of the hands was experimentally induced. It was demonstrated that the expectation of pain resulted in faster awareness of tactile stimuli at the threatened hand compared to the neutral hand.

However, there are some unresolved issues from the studies described above. Specifically, in these studies only somatosensory stimuli were used. As a result, it is not clear yet if prioritization of the threatened location *only* applies to stimuli in the somatosensory modality, or whether it also affects the processing of stimuli in other sensory modalities. Recent neurophysiological studies indicate that the detection of bodily threat concerns a *multimodal* network. An extensive cortical network of the brain, including somatosensory, insular, cingulate, frontal as well as parietal areas, functions as a multisensory salience detection system through which significant events for the body’s integrity are detected (Legrain, Iannetti, Plaghki, & Mouraux, 2011; Van Damme & Legrain, 2012). More specific, it has been shown that there exist cross-modal interactions between pain stimuli and visual stimuli occurring close to the pain location (e.g., De Paepe, Crombez, Spence, & Legrain, 2014; Favril, Mouraux, Sambo, & Legrain, 2014; Van Damme, Crombez, & Lorenz, 2007). Accordingly, these findings raise the question whether the expectation of pain at a particular location of the body also leads to the prioritized processing of *non-somatic* information at the threatened location. Interesting in this regard are the findings of a study of Van Damme and colleagues (2009). Participants made judgments regarding which of two tactile

stimuli administered to each hand, or two auditory stimuli close to each hand, had been presented first. It was found that the presentation of a physical threat picture (e.g., a knife) in front of one or the other hand shortly before the pair of stimuli, resulted in quicker awareness of stimuli at the side of the picture, and that this effect was larger for tactile than for auditory trials. These findings suggest a modality-specific effect, i.e. physical threat shifts attention to somatosensory rather than auditory information at its location. However, in the study of Van Damme et al. (2009) only visual representations of physical threat were used, so it has to be investigated if a similar effect can be found when there is actual threat of pain. Furthermore, only auditory stimuli were used for the non-somatosensory modality, and it would be interesting to involve other sensory modalities such as vision.

The aim of the present study was to test two conflicting hypotheses, i.e., whether the attentional prioritization to a location where pain is expected is modality-specific or multisensory. We investigated in healthy volunteers, using a TOJ task, whether the anticipation of (experimentally induced) pain at one hand, makes one more quickly aware of stimuli at the threatened hand relative to the other hand. In half of the blocks, participants were asked to indicate which of two tactile stimuli, one administered to each side of the hand at a range of different stimulus onset asynchronies (SOAs), was perceived first (tactile condition). In the other half of the blocks, pairs of visual stimuli had to be judged (visual condition). Each trial was preceded by a tone (high or low frequency) that signaled the possible occurrence of pain on one hand (threat trials). The other frequency of the tone signaled that no pain would follow (control trials). In line with the study of Vanden Bulcke et al. (2013), we expected that stimuli would be perceived more rapidly on the threatened hand than on the neutral hand (see also Vanden Bulcke, Crombez, Spence, & Van Damme, 2014). In addition, if the attentional prioritization would be modality-specific (see Van Damme et al., 2009), we expected this prioritization effect to be larger in the tactile condition than in the visual condition. In contrast, if the prioritization effect would be multisensory (Legrain et al., 2011), no differences between the tactile and the visual conditions should be expected.

Method

Participants

Thirty-four undergraduate students (25 females, 9 males; mean age = 20.4 years; all white Caucasian) participated to fulfill course requirements. All of the participants had normal or corrected-to-normal vision and normal hearing. All but two of the participants reported being right-handed. The participants rated their general health on average as 'very good'. Although a student group is often described as healthy, pain is a prevalent symptom (Crombie, Croft, Linton, LeResche, & Von Korff, 1991) and is therefore best documented. Twenty-six of the participants reported having experienced some form of pain in the last six months (average of 38.1 days in 6 months). Twelve of the participants reported feeling pain at the moment of testing, but the average rating of the intensity of the pain for these thirteen participants was low ($M = 2.75$, ranging from 1 to 5, $SD = 1.29$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'. All of the participants gave their informed consent and were free to terminate the experiment at any time should they so desire. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experimental session lasted for approximately 1 hour.

Apparatus and materials

Tactile stimuli (10 ms duration; 200Hz) were presented by means of two resonant-type tactors (C-2 TACTOR, Engineering Acoustics, Inc., Florida, <http://www.eaiinfo.com/>) consisting of a housing of 3.05 cm diameter and 0.79 cm high, with a skin contactor of 0.76 cm diameter. Prior to the start of the experiment, the perceived stimulus intensities at both tactor locations were individually matched (Weinstein, 1968). This was done by means of a double random staircase procedure, based on the 'simple up-down method' of Levitt (Levitt, 1971). In a first phase, 24 stimuli presented on the left hand were judged relative to a reference stimulus, which was defined as the maximum intensity (power = 0.21 Watt) on a 5-point Likert scale ranging from 1 ('no sensation') to 5 ('maximum intensity'). The intensity that elicited an averaged rating of 3 was used as the stimulus intensity for the left hand, and was the reference stimulus for the second phase. In the second phase, 24 stimuli on the right hand were judged relative to the reference stimulus on the left hand again on a 5-point Likert scale

(1 = 'much weaker', 2 = 'weaker', 3 = 'equally strong', 4 = 'stronger', 5 = 'much stronger'). The stimulus intensity that elicited an averaged rating of 3 was used as the intensity of the stimulus at the right hand. Visual stimuli were presented by means of two green-light emitting diodes (LEDs) and were illuminated for 10 ms.

Painful stimuli were electrocutaneously delivered by means of two constant current stimulators (Digitimer DS5 2000, Digitimer Ltd, England, <http://www.digitimer.com/index.htm>). Each stimulator consisted of trains of 20 ms sinusoid pulses with a frequency of 50 Hz and a duration of 200 ms. Painful stimuli were delivered via two pairs of lubricated Fukuda standard Ag/AgCl electrodes, each pair consisting of an anode and cathode (1 cm diameter). The intensity of the electrocutaneous stimuli was determined for each participant individually by means of a random staircase procedure. For each hand, 20 electrocutaneous stimuli were presented to participants (starting intensity between 0 and 1.5 mA) and self-reports were collected on an 11-point Likert scale (0 = 'no sensation'; 10 = 'unbearable pain'). The pain intensity that elicited an average rating of 7 was selected as the pain stimulus for the main experiment (Arntz, Dreessen, & De Jong, 1994; Vanden Bulcke, et al., 2013).

The task was programmed and controlled by the INQUISIT Millisecond software package (Inquisit 3.0, Millisecond Software LLC, Seattle, WA, <http://www.millisecond.com/>) on a laptop (HP Compaq nc 6120).

TOJ paradigm

In the tactile TOJ task (Piéron, 1952), two stimuli were administered, one on either hand, separated by one of 10 randomly assigned stimulus onset asynchronies (SOAs) ranging from -120 to +120 ms (-120, -60, -30, -15, -5, +5, +15, +30, +60, +120 ms; negative values indicate that the left hand was stimulated first) (see also Vanden Bulcke et al., 2013, 2014). The participants were instructed to report aloud the hand on which the first stimulus was presented and the experimenter registered the answers using a keyboard. We adapted the classical tactile TOJ task by using two different types of target stimuli, pairs of visual and pairs of tactile stimuli, which were alternated between blocks. A trial started with the presentation of a red fixation LED (1000 ms) in between both hands, followed by a high (1000 Hz) or low (250 Hz) tone of 1000 ms duration, indicating whether or not a painful electrocutaneous stimulus could

follow on one specific location (control vs. threat trials). Which tone was associated with threat was counterbalanced across the participants. Before the start of each block of trials, the participants were told on which location (left or right hand) they could expect the painful stimulation to be delivered. In only 9.09% of the threat trials, the pain stimulus was actually delivered instead of the two stimuli (pain trials), but the participants were not informed about this contingency. The participants were informed that no response had to be given in pain trials.

Procedure

Upon arrival at the laboratory, the participants received the task instructions. They were told that an electrocutaneous stimulus would be used during the experiment and that “most people find this kind of stimulation unpleasant” (Crombez, et al., 1998; Van Damme, Crombez, & Eccleston, 2004). After the participants gave their written informed consent, they were seated in front of the experimental apparatus. Their forearms were positioned symmetrically on the table. The tactors were placed in the middle of the third metacarpal of each hand. On top of these tactors, the visual LEDs were attached. Electrodes were placed on both hands between thumb and index finger, in the sensory territory of the superficial radial nerve. The skin at the electrode sites was first abraded with a peeling cream (Nihon Kohden, Tokyo, Japan) to reduce the resistance of the skin. The participants were informed that they would have to decide on each trial which stimulus had been presented first. The accuracy of participants’ responses was emphasized rather than the speed. The participants wore headphones (Wesc, Conga) during the experiment. Pink noise (42.2 dB) was presented continuously during headphones to mask the noise resulting from the operation of the tactors. The participants were not given any feedback concerning their performance.

The session began with two practice blocks (one with pairs of visual stimuli, one with pairs of tactile stimuli) of eleven trials each (1 trial per SOA for control trials, 1 trial per SOA for threat trials, 1 pain trial). Following this, 4 blocks of 105 trials (50 threat trials; 50 control trials; 5 pain trials) were presented. In two blocks, visual stimuli had to be judged (visual condition). In the other two blocks, tactile stimuli were presented (tactile condition). The order of presentation was

randomized between blocks. The two possible pain locations (left or right hand) were alternated between blocks and the order was counterbalanced between participants. Before the start of each block, participants were informed about the type of stimuli (visual vs. tactile) and on which hand (left or right) they could expect painful stimuli.

Self-report measures

After each test phase, the participants had to rate several questions concerning their concentration ('To what extent have you made an effort to perform this task?', 'To what extent did you concentrate on this task?'), attention to painful/tactile/visual stimuli ('To what extent did you pay attention to the painful/tactile/visual stimuli?'), pain experience ('How painful did you find the electrocutaneous stimuli?'), anxiety ('How anxious were you during this block?'), fatigue ('To what extent did you find this task tiring?') on eleven-point numerical rating scales (anchored 0 = not at all and 10 = very strongly). As a manipulation check, we were especially interested in the participant's ratings of fear ('To what extent were you afraid that a painful stimulus would be administered by the high/low tone?') and expectations ('To what extent did you expect that a painful stimulus would be administered by the high/low tone?'). The participants were also asked to complete the Pain Vigilance and Awareness Scale (PVAQ) (McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002) and the Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove, 2002). These data were collected for meta-analytical purposes and are not reported in detail here.

Results

Data-analysis

In TOJ studies, it is common practice (Shore, Gray, Spry, & Spence, 2005; Spence, Shore, & Klein, 2001) to exclude those participants from statistical analysis when (1) any of the PSS values is greater than the highest SOA (± 120 ms) tested, or when (2) participants have less than 80% accuracy on the trials with the largest SOA tested (± 120 ms). One participant (female, right-handed) had to be excluded for the first reason, two participants (women, both right-

handed) for the second reason. Trials in which the painful stimulus was actually delivered were excluded for analysis. Trials following trials with electrocutaneous stimulation were removed from subsequent data analysis in order to avoid the possibility that (1) potential effects would be mainly driven by trials directly following painful stimulation or (2) after-effects of pain would interfere with the tactile TOJ (max. 9.52% of all trials).

The analyses were based on a procedure that has been commonly described in the literature (Shore et al., 2005; Spence et al., 2001; Van Damme et al., 2009; Vanden Bulcke et al., 2013). The proportions of 'left-hand-first' and 'right-hand-first' responses for threat presented on the left and right side, respectively, for all trials at each SOA, were converted into the corresponding z-scores using a standardized cumulative normal distribution (probits). The best-fitting straight line was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS) values for the subsequent statistical analyses. The PSS refers to the point at which observers report the two events (right hand first and left hand first) equally often. This is commonly taken to be equivalent to the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time and such equivalent to the SOA value corresponding to a proportion of left/right hand first responses of 0.5. The PSS is computed as the opposite of the intercept divided by the slope from the best-fitting straight line. The sign of the PSS in which threat was presented on the right hand was reversed. Subsequently, for each participant, the final PSS values was calculated by taking the average of the PSS values for threat presented on the left side and the reversed PSS values for threat presented on the right side. Hence, a positive value indicates that the stimulus contralateral to the side of threat had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS indicates that stimuli on the threatened hand are perceived more rapidly than those presented to the other hand. In sum, the PSS provides information concerning biases in spatial attention resulting from the presentation of bodily threat. A repeated measures analysis of variance (ANOVA) with the factors Cue (within; threat versus control), Modality (within; tactile versus visual) and Pain Side (within; left versus right) was performed on the PSS data. For ease of comparison with the norms of Cohen (1988), we calculated effect sizes for independent samples using the formula of Dunlap and

colleagues (1996). For interaction effects, difference scores were used to obtain Cohen's d . A difference score was calculated for threat versus control trials, which was then compared between the tactile and visual stimuli. We determined whether Cohen's d was small (0.20), medium (0.50), or large (0.80) (Cohen, 1988). We also report the 95% confidence intervals (95% CI) of the effect sizes.

Manipulation check

Participants reported being more afraid during the threat trials ($M = 4.96$, $SD = 2.19$) than during the control trials ($M = 0.63$, $SD = 1.09$) ($t_{30} = -9.97$, $p < 0.001$; $d = 1.79$ [95% CI: 1.22, 2.36]). Furthermore, they expected a painful electrocutaneous stimulus more during the threat trials ($M = 5.65$, $SD = 1.94$) than during control trials ($M = 0.60$, $SD = 0.97$) ($t_{30} = -12.78$, $p < 0.001$; $d = 2.30$ [95% CI: 1.63, 2.98]). Finally, the participants rated the electrocutaneous stimuli as moderately painful ($M = 5.59$; ranging from 2.5 to 8.75, $SD = 1.79$). Mean questionnaire scores were 8.40 ($SD = 5.77$) for the PCS and 40.97 ($SD = 7.71$) for the PVAQ.

PSS

A graphical presentation of the effects is provided in Figure 1. The main effect of Cue was significant ($F(1,30) = 6.10$, $p = 0.02$), with threat trials ($M = 8.92$ ms, $SD = 22.73$) showing a larger PSS than control trials ($M = -1.50$ ms, $SD = 11.47$) ($d = 0.57$ [95% CI: 0.08, 1.05]). The main effect of Modality was not significant ($F(1,30) = 1.07$, $p = 0.31$; $d = 0.16$ [95% CI: -0.25, 0.58]), meaning that, on average, the PSS in the visual TOJ ($M = 1.81$; $SD = 17.50$) was not different from the PSS in the tactile TOJ ($M = 5.61$; $SD = 27.37$). T -tests revealed that, in both the visual and tactile condition, none of the PSS values in control trials were significantly different from 0, respectively, $t(30) = -1.12$, $p = 0.27$; $d = 0.28$ [95% CI: -0.22, 0.78] and $t(30) = -0.13$, $p = 0.89$; $d = 0.03$ [95% CI: -0.46, 0.51]. In threat trials, the PSS values were significantly different from 0 for the tactile TOJ ($t(30) = 2.04$, $p = 0.05$; $d = 0.52$ [95% CI: 0.01, 1.03]), but not for the visual TOJ ($t(30) = 1.65$, $p = 0.11$; $d = 0.41$ [95% CI: -0.08, 0.41]). However, the crucial Cue x Modality interaction failed to reach statistical significance ($F(1,30) = 0.32$, $p = 0.58$; $d = 0.12$ [95% CI: -0.30, 0.54]), indicating that the effect of anticipated pain was not different between the tactile TOJ ($M_{\text{tactile}(\text{threat-control})} = 12.20$, $SD = 35.10$) and the visual TOJ ($M_{\text{visual}(\text{threat-control})} = 8.63$, $SD = 22.40$).

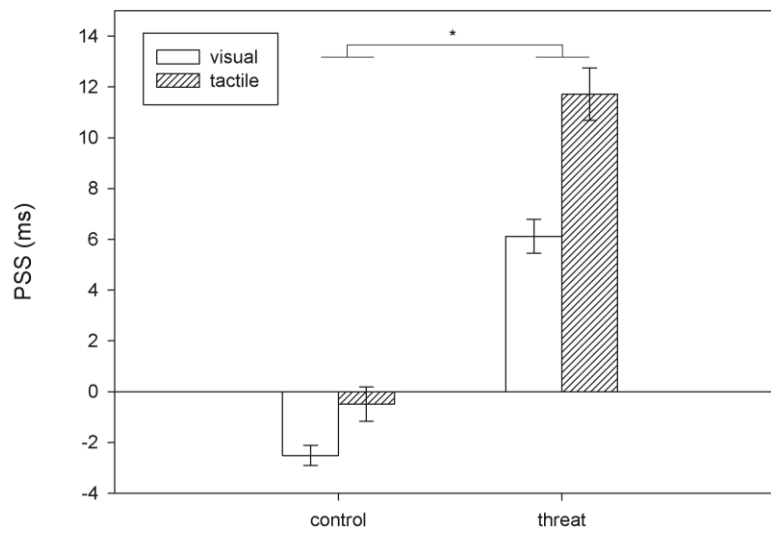


Figure 1. Index for attentional prioritization (PSS) for the visual and tactile condition (in ms and with standard errors) in control and threat trials. Positive values indicate that stimuli on the threatened hand were perceived more rapidly than those presented on the other hand, whereas negative values indicate that stimuli on the neutral hand were perceived more rapidly than those presented on the threatened hand (* $p < 0.05$).

Discussion

This study investigated whether the expectation of pain results in attentional prioritization of the location where pain is expected, and if such prioritization specifically affects the processing of somatosensory information (modality-specific hypothesis) or if it also influences the processing of visual information (multisensory hypothesis). A TOJ experiment was conducted in which pairs of tactile or pairs of visual stimuli were presented, one applied to either hand, while expecting pain on one hand or expecting no pain. The results revealed that, while expecting pain, both tactile and visual stimuli were perceived more rapidly on the threatened hand than on the neutral hand. Overall, our findings suggest that attentional prioritization of the threatened location is not limited to the somatosensory modality, but rather is a multisensory phenomenon.

Most research on attention has considered only one sensory modality at a time (vision, audition,...) (see e.g. Treisman & Gelade, 1980; Spence & Driver; 1994). However, in daily life, people often have to coordinate their attention across modalities. Numerous studies have demonstrated that an efficient attention system promotes the integration of spatially congruent information from different senses (Driver & Spence, 1998; Poliakoff, Miles, Li, & Blanchette,

2007; Spence, et al., 2001; Van Damme et al. 2007). The findings of our study provide further support this idea, and are in line with recent studies demonstrating that adequately responding to bodily threats is supported by a *multimodal* network detecting relevant sensory events (Legrain et al., 2011; Van Damme & Legrain, 2012). The integration of sensations of different modalities at the location of pain may have behavioral advantages, such as allowing a swift response to potential sources of bodily threat.

Our findings are also in line with the idea that a multisensory system monitors the space immediately surrounding our body and detects relevant sensory information. This peripersonal space, i.e. the space immediately surrounding our bodies, wherein objects can be grasped and manipulated without moving toward them (Rizzolatti, Fadiga, Fogassi, & Gallese, 1997), is supposed to rely on the existence of multisensory neurons that respond to stimulation of a specific body-part and to stimuli that occur close to that body part (Graziano & Gross, 1994; Spence & Driver, 2004). It has also been shown that there exist crossmodal links between painful stimuli and proximal visual stimuli (Favril et al., 2014; Van Ryckeghem et al., 2011). The current findings provided further evidence for this idea and fit well with recent work of De Paepe and colleagues (2013). In their study, it was shown that the perception of nociceptive stimuli was biased in favor of the stimulus on the hand adjacent to a unilateral visual cue, especially when the cue was presented in peripersonal space (i.e. near the participant's hand).

However, the current findings seem to contradict the results obtained in the study of Van Damme and colleagues (2009), who found that physical threat shifts attention to somatosensory rather than auditory information at its location. As such, a modality-specific effect was suggested. However, that study only used visual representations of bodily threat, whereas our study used actual threat of pain. Furthermore, it is difficult to equate auditory and visual stimulus pairs in complexity and difficulty. The fact that no prioritization of auditory information towards the threatened location was found in that study could be due to the fact that subjects found it more difficult to localize auditory stimuli compared to more salient visual stimuli. Their study was one of the first that used a TOJ where auditory stimuli were presented in free space (loudspeakers) instead of through headphones. Previous studies showed that visual stimulus localization is more

accurate and less variable than auditory stimulus localization (Battaglia, Jacobs, & Aslin, 2003; Hairston et al., 2003). As a result, it is possible that crossmodal integration between visual and tactile information is more efficient than between auditory and tactile information (Spence, Nicholls, Gillespie, & Driver, 1998).

The present study may be relevant for the study of clinical pain. Theoretical models on *chronic* pain state that as a result of enduring fearful appraisal of pain, chronic pain patients might become hypervigilant for or over-attentive to somatosensory signals, thus facilitating the processing of cues signaling potential pain of bodily harm (Crombez et al., 2005; Eccleston & Crombez, 2007; Rollman, 2009; Vlaeyen & Linton, 2000). Up to now, it has been proven difficult to establish pain-related attentional biases in patients experiencing chronic pain. Most studies investigating the effects of threat upon pain-related biases in attentional processes, have been limited to paradigms measuring attention to semantic pain stimuli (e.g., pain-related words) or pictorial pain stimuli (e.g., images of pain-related activities) (for a review, see Van Damme et al., 2010). It may well be that pain words and/or pictures are not the best stimulus material to investigate attentional biases towards pain-related information (Crombez, Hermans, & Adriaensen, 2000; Dear, Sharpe, Nicholas, Refshuage, 2011). A meta-analysis of Crombez and colleagues (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013) showed that the results of studies using pain words/pictures as stimulus material to investigate pain-related attentional biases are inconsistent and effect-sizes are small. Somatosensory attention paradigms, such as the one used in our study, may be more suitable for measuring pain-related biases in chronic pain patients. It might be interesting to investigate whether chronic pain patients might become more quickly aware of somatic and even non-somatic information in the regions of the body that are most relevant for their pain problem.

A number of issues concerning this study require further consideration. First, participants of our study were pain-free undergraduate students with whom experimental pain stimuli were used. One should be cautious in generalizing its results to other settings and other samples. Further research is needed to establish whether our results can be replicated with a non-student sample experiencing clinically relevant pain. Second, it should be noted that the confidence interval (CI) of the Cue x Modality interaction is relative large. Based

on the results of only one experiment, we cannot definitively draw the conclusion that there is no interaction between Cue and Modality. Though, the upper limit of the CI suggests that possible interaction effects should be expected to be small. Third, it has been proposed that attentional prioritization is dependent upon events that are relevant to the goals of an individual, by the activation of attentional control settings (Van Damme et al., 2010). In threatening situations, it is plausible to assume that pain avoidance goals might be activated. However, in the set-up of our study, participants did not have the option to escape or avoid the painful stimulus. Therefore, it would be interesting to investigate if providing the opportunity to escape or avoid painful stimulation would increase attentional prioritization of the threatened body location (see Notebaert et al., 2011; Durnez & Van Damme, in press).

In conclusion, we have shown that, when expecting pain on one hand, one becomes more quickly aware of both tactile and visual stimuli at the threatened hand than at the neutral hand. The findings support the idea the anticipation of pain results in multisensory prioritization of information at the threatened body location.

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Exploring the limits of attentional prioritization of a threatened bodily location: the confusing effect of crossing the arms¹**Abstract**

Previous research has shown that the threat of pain on one limb results in heightened somatosensory processing on the ipsilateral compared to the contralateral hand. It is yet unclear, however, if such prioritization effect is due to somatosensory input occurring at the same body part as pain (somatotopic reference frame of threat localization) or rather because of corresponding spatial encoding of somatosensory input and pain independent of the body part on which they occur (spatiotopic reference frame of threat localization). To investigate this we compared the effect of threat of pain to one arm on somatosensory processing at the ipsilateral and contralateral hand between two body posture conditions: uncrossed versus crossed arms. In two experiments, participants judged which one of two tactile stimuli administered to either hand within a range of different stimulus onset asynchronies (SOA) had been presented first, while occasionally expecting a painful stimulus at one arm. Participants either positioned their arms symmetrically (uncrossed condition), or crossed their arms over the midline (crossed condition) so that the contralateral hand was closer in space to the pain location than the ipsilateral hand. While in the uncrossed condition results were largely in line with previous findings, no threat-related prioritization effect was observed in the crossed hands condition. Results are discussed in terms of potential conflict between a somatotopic and a spatiotopic frame of reference of bodily threat due to crossing the arms.

¹ Vanden Bulcke, C., & Van Damme, S. (unpublished manuscript). Exploring the limits of attentional prioritization of a threatened bodily location: the confusing effect of crossing the arms.

Introduction

The deployment of attention is typically guided by current goals or concerns. When facing bodily threats such as pain, this might activate goals and/or actions that allow protecting the individual from physical injury (Eccleston & Crombez, 1999; Van Damme, Legrain, Vogt, & Crombez, 2010). Goal-directed attention has been argued to occur by means of a set of stimulus features (i.e. attentional set) that individuals keep in mind to efficiently identify stimuli that are relevant for their current actions. This is believed to facilitate the selection of stimuli that share one or more of these features (Corbetta & Shulman, 2002; Folk, Remington, & Johnston, 1992). According to the neurocognitive model of attention to pain (Legrain et al., 2009), expectation of pain may activate pain-related features in the attentional set, resulting in the prioritization of stimuli that share features with pain. One important feature is the location of pain, because the ability to precisely localize the source of bodily threat is clearly adaptive for survival (Van Damme & Legrain, 2012).

Indirect evidence for this idea can be found in a study of Crombez, Eccleston, Baeyens, and Eelen (1998a). Participants performed an auditory task while occasionally receiving mild pain stimuli on both arms. They were led to expect that on one of the arms, a very intense painful stimulus could occur. Interestingly, task performance was more interrupted when pain stimuli were administered at the “threatened” arm in comparison to the “neutral” arm. A more direct demonstration of top-down prioritization of somatosensory input at a pain-related bodily location was provided by Vanden Bulcke, Van Damme, Durnez and Crombez (2013). In their study, participants made judgments regarding which of two tactile stimuli administered to each hand, had been presented first. Crucially, they expected that a painful stimulus could possibly follow on one of their hands. It was found that the anticipation of pain resulted in faster processing of tactile stimuli at the threatened hand compared to the other hand.

So far, it is still unclear whether such threat-related prioritization effect is due to the enhanced processing of somatosensory input occurring at the same body part as pain (i.e. somatotopic reference frame of threat localization) or rather because of corresponding spatial encoding of somatosensory input and pain independent of the body part on which they occur (i.e. spatiotopic frame of reference of threat localization). In consequence, it is necessary to investigate this

threat-related prioritization effect in situations creating conflict between both reference frames. An ideal way to create such conflict is adapting body posture so that the arms are crossed over the midline. Although in daily life the majority of our actions are executed with the left hand operating at the left side of space and the right hand operating at the right side of space, situations where arms are crossed over the midline occur quite frequently in a number of domains. For instance, in many racquet sports, the left hand is sometimes operating on the right side of space and vice versa for the right hand. When arms are crossed over the midline, it might be possible that somatosensory sensations presented on a neutral body part are located closer in space to the bodily location where threat is expected. Figure 1 represents an uncrossed and crossed arms scenario in which bodily threat is expected on the left arm. In the uncrossed situation, somatosensory input on the ipsilateral hand (left hand) of the threatened body part is closer in space to the pain location than somatosensory input on the contralateral hand (right arm). However, in the crossed arms scenario, the contralateral hand (right hand) is now closer in space to the pain location than the ipsilateral hand (left hand).

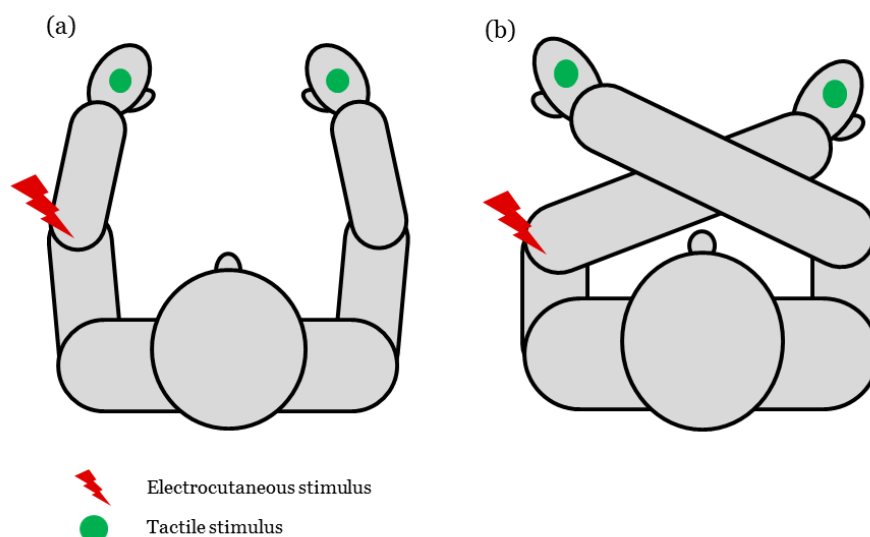


Figure 1. (a) Uncrossed arms situation in which bodily threat is expected on the left arm. The location of the pain stimulus on the left arm is closer in space to the tactile stimulus on the ipsilateral hand (left hand) than to the tactile stimulus on the contralateral hand (right hand). (b) Crossed arms situation in which bodily threat is expected on the left arm. The location of the pain stimulus on the left arm is closer in space to the tactile stimulus on the contralateral hand (right hand) than to the tactile stimulus on the ipsilateral hand (left hand).

The aim of the two studies reported here was to test whether threat-related prioritization is due to somatosensory input being presented on the same body part as pain (i.e. somatotopic reference frame of threat localization) or rather because somatosensory input and pain sharing spatial coordinates in external space independent of the body part on which they occur (i.e. spatiotopic reference frame of threat localization). Participants made judgments regarding which of two tactile stimuli administered to each hand had been presented first (Temporal Order Judgment; TOJ). They were instructed that the color of a cue (1 of 2 colors) signaled the possible occurrence of pain on one arm (threat trials). The other color of the cue signaled that no pain would follow (control trials). The arms of participants were positioned symmetrically on the table in half of the blocks (uncrossed condition). In the other half of the blocks, they were instructed to cross their arms over the body midline (crossed condition), so that the location of the pain stimulus on the left (right) arm was closer in space to the tactile stimulus on the contralateral hand than to the tactile stimulus on the ipsilateral hand. We hypothesized that if the effect of threat of pain on one arm was due to enhanced processing of somatosensory input on the same body part of pain (somatotopic reference frame of threat localization), tactile stimuli would be perceived more rapidly on the hand ipsilateral to the threatened arm in both conditions. However, if the threat-related prioritization effect was the result of corresponding spatial encoding of somatosensory input and pain independent of the body part on which they occurred (spatiotopic reference frame of threat localization), we expected that in the crossed condition, tactile stimuli would be perceived more rapidly on the hand contralateral to the threatened arm than on the hand ipsilateral to the threatened arm.

Experiment 1

Method

Participants

Thirty-eight undergraduate students (33 females, 5 males; mean age = 20.9 years; all white Caucasian) were paid to take part in the experiment. All but six of the participants reported being right-handed. All of the participants had normal

or corrected-to-normal vision and normal hearing. The participants rated their general health on average as 'very good' and none of all participants reported having a current medical or mental disorder. Although a student group is often described as healthy, pain can be a prevalent symptom among this group and is therefore best documented. Twenty-seven of the participants reported having experienced pain during the last six months (average of 24 days in 6 months). Twelve of the participants reported feeling pain at the moment of testing, but the average rating of the intensity of the pain for these thirteen participants was low ($M = 2.42$; ranging from 1 to 5, $SD = 1.31$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'. All of the participants gave their informed consent and were free to terminate the experiment at any time should they so desire. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experimental session lasted for approximately 1 hour and 15 minutes.

Apparatus and materials

Tactile stimuli (10 ms duration; 200Hz) were presented by means of two resonant-type tactors (C-2 TACTOR, Engineering Acoustics, Inc., Florida, <http://www.eaiinfo.com/>) consisting of a housing of 3.05 cm diameter and 0.79 cm high, with a skin contactor of 0.76 cm diameter. Prior to the start of the experiment, the perceived stimulus intensities at both tactor locations were individually matched (Weinstein, 1968). This was done by means of a double random staircase procedure, based on the 'simple up-down method' of Levitt (Levitt, 1971). In a first phase, 24 stimuli presented on the left hand were judged relative to a reference stimulus, which was defined as the maximum intensity (power = 0.21 Watt) on a 5-point Likert scale ranging from 1 ('no sensation') to 5 ('maximum intensity'). The intensity that elicited an averaged rating of 3 was used as the stimulus intensity for the left hand, and was the reference stimulus for the second phase. In the second phase, 24 stimuli on the right hand were judged relative to the reference stimulus on the left hand again on a 5-point Likert scale (1 = 'much weaker', 2 = 'weaker', 3 = 'equally strong', 4 = 'stronger', 5 = 'much stronger'). The stimulus intensity that elicited an averaged rating of 3 was used as the intensity of the stimulus at the right hand.

Painful stimuli were delivered by means of two constant current stimulators (Digitimer DS5 2000, Digitimer Ltd, England, <http://www.digitimer.com/index.htm>). Each stimulator consisted of trains of 20 ms sinusoid pulses with a frequency of 50 Hz and a duration of 200 ms. Painful stimuli were delivered via two pairs of lubricated Fukuda standard Ag/AgCl electrodes, each pair consisting of an anode and a cathode (1 cm diameter). The intensity of the electrocutaneous stimuli was determined for each participant individually by means of a random staircase procedure. For each arm, 20 electrocutaneous stimuli were presented to participants (starting intensity between 0 and 1.5 mA) and self-reports were collected on an 11-point Likert scale (0= 'no sensation'; 10= 'unbearable pain'). The pain intensity that elicited an average rating of 7 was selected as the pain stimulus for the main experiment (Arntz, Dreessen, & De Jong, 1994; Vanden Bulcke, et al., 2013; Vanden Bulcke, Crombez, Spence, & Van Damme, 2014).

The task was programmed and controlled by the INQUISIT Millisecond software package (Inquisit 3.0, Millisecond Software LLC, Seattle, WA, <http://www.millisecond.com/>) on a laptop (HP Compaq nc 6120).

TOJ paradigm

In the TOJ task (Piéron, 1952), two stimuli were administered, one on either hand, separated by one of 10 randomly assigned stimulus onset asynchronies (SOAs). The participants were instructed to report aloud the hand on which the first tactile stimulus was presented, and the experimenter registered the answers using a keyboard. A trial started with the presentation of a fixation cross (1000 ms) in the middle of the screen, followed by a colored cue (either blue or yellow, of 1000 ms duration), indicating whether or not a painful stimulus could follow on one specific location (threat and control trial, respectively). Which color of cue was associated with threat was counterbalanced across the participants.

Before the start of each block of trials, the participants were told on which location (left or right arm) they should expect the painful stimulation to be delivered. In 10% of the threat trials, the painful stimulus was actually delivered instead of the two tactile stimuli (pain trials), but the participants were not informed about the contingency (see Figure 2). The participants were informed that no response had to be given in such trials.

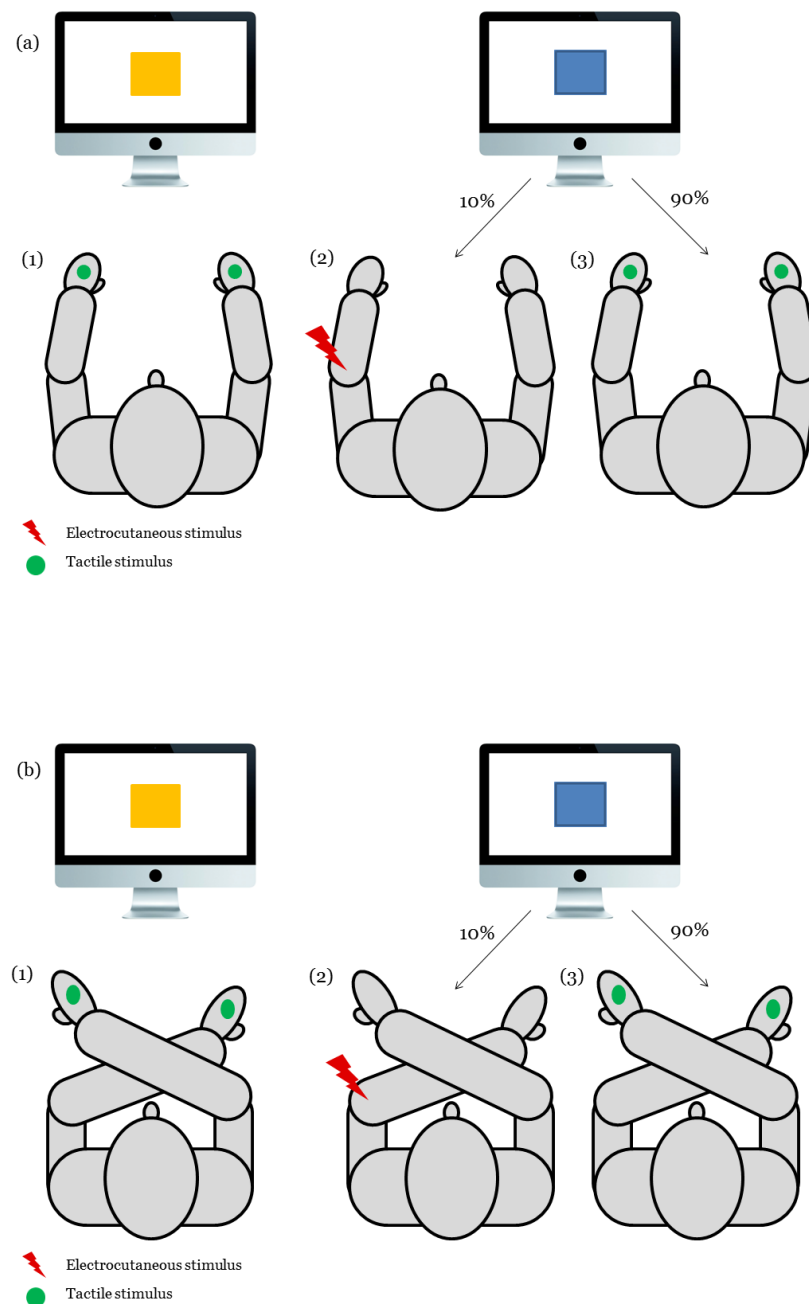


Figure 2. (a) Experimental setup of the uncrossed condition with (1) example of an uncrossed arms control trial (2) example of an uncrossed arm threat trial in which the electrocutaneous stimulation was presented on the left arm and (3) example of a uncrossed arms threat trial without electrocutaneous stimulation. (b) Experimental setup of the crossed condition with similar examples. Which color of cue was associated with threat was counterbalanced across the participants.

Procedure

Upon arrival at the laboratory, the participants received the task instructions and were told that an electrocutaneous stimulus would be used during the experiment and that “most people find this kind of stimulation unpleasant” (Crombez, et al., 1998a; Van Damme, Crombez, & Eccleston, 2004). After the participants had given their written informed consent, they were seated in front of the experimental apparatus. Their forearms were positioned symmetrically on the table. The tactors were placed on the dorsal side of their hand, with the center on the middle of the third metacarpal. The two electrodes were attached on the proximal third of the muscle belly of the brachioradialis of the forearm. To visualize the brachioradialis, the participants were asked to flex the elbow, while the experimenter provided resistance against the distal end of the radius. As such, the muscle belly of the brachioradialis is well visible and enables the experimenter to attach the electrode exactly on the muscle belly. Before the start of the experiment, the participants were told on which location (left or right arm) they should expect the painful stimulation to be delivered. However, the electrodes were attached on both forearms, to ensure visual similarity. Participants were told that only one electrode was working and that they only could expect painful stimuli at that particular location. The skin at the electrode sites was first abraded with a peeling cream (Nihon Kohden, Tokyo, Japan) to reduce the resistance of the skin. The participants were informed that they would have to decide on each trial which stimulus had been presented first. The accuracy of participants’ responses was emphasized, rather than the speed. The participants wore headphones (Wesc, Conga) during the experiment. Pink noise (42.2 dB) was presented continuously through headphones to mask the noise resulting from the operation of the tactors. The participants were not given any feedback concerning their performance.

The session began with two practice blocks, one in which participants had to cross their arms over the midline, one in which participants had their arms uncrossed. Each practice block consisted of twenty-three trials (1 trial per SOA for control trials; 1 trials per SOA for threat trials; 3 pain trials). Following this, four blocks of 105 trials (5 trials per SOA for control trials; 5 trials per SOA for threat trials; 5 pain trials) were presented. The two types of tasks (crossed versus uncrossed condition) were alternated between blocks and the order was

counterbalanced between participants. The side on which pain was expected was (left vs. right forearm) was counterbalanced between participants. In the uncrossed condition, pairs of stimuli were delivered at 10 SOAs ranging from -120 to +120 ms (-120, -60, -30, -15, -5, +5, +15, +30, +60, +120 ms; negative values indicate that the left hand was stimulated first, see Moseley, Gallace & Spence, 2009; Vanden Bulcke et al., 2013; 2014 for similar SOAs). In the crossed condition, the 10 SOA's were three times the SOA's of the uncrossed blocks (-360, -180, -90, -45, -15, +15, +45, +90, +180, +360 ms)².

Self-report measures

After each test phase, the participants had to rate several questions concerning their concentration ('To what extent have you made an effort to perform this task?', 'To what extent did you concentrate on this task?'), attention to painful/tactile stimuli ('To what extent did you pay attention to the painful/tactile stimuli?'), pain experience ('How painful did you find the electrocutaneous stimuli?'), anxiety ('How anxious were you during this block?'), fatigue ('To what extent did you find this task tiring?') on eleven-point numerical rating scales (anchored 0 = not at all and 10 = very strongly). As a manipulation check, we were especially interested in the participant's ratings of fear ('To what extent were you afraid that a painful stimulus would be administered by the blue/yellow cue?') and expectations ('To what extent did you expect that a painful stimulus would be administered by the blue/yellow cue?'). The participants were also asked to complete the Pain Vigilance and Awareness Scale (PVAQ) (McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002) and the Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove, 2002). These data were collected for meta-analytical purposes and are not reported in detail here.

² We have enlarged the range of SOAs in the crossed condition compared to previous used SOAs (e.g. Moseley et al., 2009; Shore, Spry, & Spence, 2002) because an extra manipulation with painful stimuli was added and we believed that those previous used SOAs would be too difficult.

Results

Data-analysis

In TOJ studies, it is common practice (Shore, Gray, Spry, & Spence, 2005; Spence, Shore, & Klein, 2001) to exclude those participants from statistical analysis when (1) any of the PSS values is greater than the highest SOA (± 120 ms for uncrossed hands blocks; ± 360 ms for crossed hands blocks) tested, (2) participants have less than 80% accuracy on the trials with the largest SOA tested (± 120 ms; ± 360 ms). Ten participants (9 females, 1 male; 7 right-handed) had less than 80% accuracy on the trials with the largest SOA tested in the crossed condition, two participants (1 female, 1 male; right-handed) had less than 80% accuracy on the trials with the largest SOA tested in the uncrossed condition. Three participants (all female; 2 right-handed) had to be excluded for the second reason. Trials following trials with electrocutaneous stimulation were removed from subsequent data analysis in order to avoid the possibility that (1) potential effects would be mainly driven by trials directly following painful stimulation or (2) after-effects of pain would interfere with the tactile TOJ (max. 10% of all trials).

The analyses were based on a procedure that has been commonly described in the literature (Shore et al., 2005; Spence et al., 2001; Van Damme, Gallace, Spence, Crombez, & Moseley, 2009). The proportions of 'left-hand-first' and 'right-hand-first' responses for threat presented on the left and right limb, respectively, for all trials at each SOA, were converted into the corresponding z-scores using a standardized cumulative normal distribution (probits). The best-fitting straight line was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS) values for the subsequent statistical analyses (see Figure 3 and Figure 4). The PSS refers to the point at which observers report the two events (right hand first and left hand first) equally often. This is commonly taken to be equivalent to the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time and such equivalent to the SOA value corresponding to a proportion of left/right hand first responses of 0.5. The PSS is computed as the opposite of the intercept divided by the slope from the best-fitting straight line. The sign of the PSS in which threat was presented on the right limb was reversed. Hence, a

positive value indicated that the stimulus contralateral to the threatened limb had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS indicated that stimuli on the threatened limb are perceived more rapidly than those presented to the other limb. In sum, the PSS provides information concerning biases in spatial attention resulting from the presentation of bodily threat. A repeated measures analysis of variance (ANOVA) with the factors Cue (within; threat versus control), Condition (within; crossed versus uncrossed condition) and Pain Side (between; left versus right limb) was performed on the PSS data. For ease of comparison with the norms of Cohen (1988), we calculated effect sizes for independent samples using the formula of Dunlap and colleagues (Dunlap, Cortina, Vaslow, & Burke, 1996). For interaction effects, difference scores were used to obtain Cohen's *d*. A difference score was calculated for threat versus control trials, which was then compared between crossed and uncrossed trials. We determined whether Cohen's *d* was small (0.20), medium (0.50), or large (0.80) (Cohen, 1988). We also report the 95% confidence intervals (95% CI) of the effect sizes.

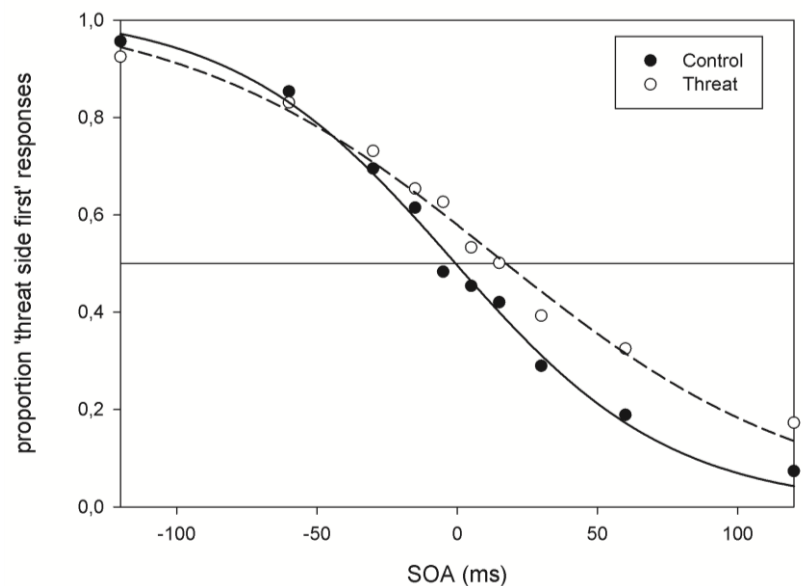


Figure 3. Temporal order judgment (TOJ) data for the uncrossed condition. The figure illustrates the fitted curves from the cumulative data averaged over participants. The x-axis represents the different SOAs between the two tactile stimuli presented in a trial. The responses were recoded so that negative values on the left side of the x-axis indicate that the threatened hand was stimulated first, while positive values indicate that the neutral hand was stimulated first. The y-axis represents the mean proportion of responses according to which the threatened hand was perceived as having been stimulated first. Solid lines illustrate the fitted curves for control trials, broken lines for threat trials.

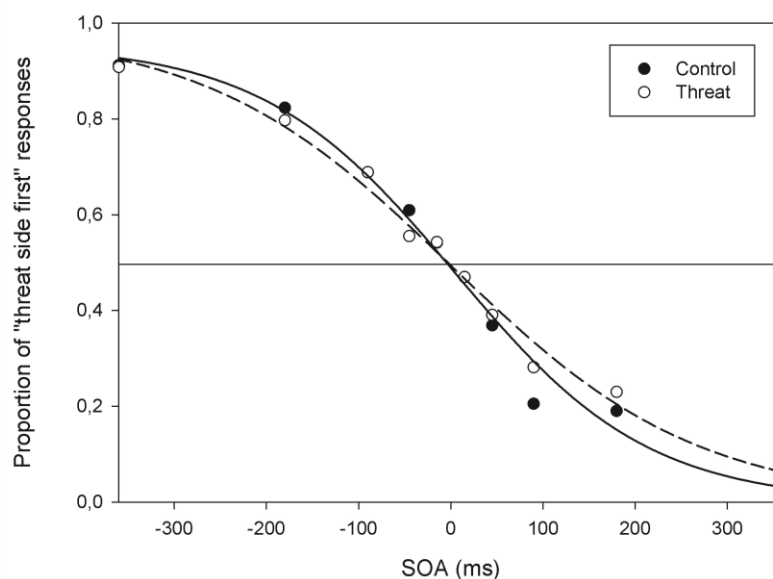


Figure 4. Temporal order judgment (TOJ) data for the crossed condition. The figure illustrates the fitted curves from the cumulative data averaged over participants. The x-axis represents the different SOAs between the two tactile stimuli presented in a trial. The responses were recoded so that negative values on the left side of the x-axis indicate that the threatened hand was stimulated first, while positive values indicate that the neutral hand was stimulated first. The y-axis represents the mean proportion of responses according to which the threatened hand was perceived as having been stimulated first. Solid lines illustrate the fitted curves for control trials, broken lines for threat trials.

Manipulation check

Participants reported being more afraid during the threat trials ($M = 4.47$, $SD = 2.25$) than during the control trials ($M = 0.40$, $SD = 1.00$) ($t_{22} = 7.29$, $p < 0.01$; $d = 2.32$ [95% CI: 1.24, 3.39]). Furthermore, the participants expected a painful electrocutaneous stimulus more often during the threat trials ($M = 5.06$, $SD = 2.30$) than during control trials ($M = 0.73$, $SD = 1.56$) ($t_{22} = 7.52$, $p < 0.01$; $d = 2.20$ [95% CI: 1.14, 3.26]). Finally, the participants rated the electrocutaneous stimuli as moderately painful ($M = 5.34$, $SD = 1.91$). Mean questionnaire scores were 7.96 ($SD = 6.68$) for the PCS and 39.48 ($SD = 8.37$) for the PVAQ.

PSS

The main effect of Cue was not significant ($F(1,21) = 0.05$, $p = 0.82$), with no significant differences between threat trials ($M = 7.76$ ms, $SD = 82.02$) and control trials ($M = 1.85$ ms, $SD = 57.49$) ($d = 0.08$ [95% CI: -0.48, 0.65]). The main effect of Condition was also not significant ($F(1,21) = 3.11$, $p = 0.09$; $d =$

0.38 [95% CI: -0.31, 1.07), meaning that, on average, the PSS was similar in the crossed and uncrossed conditions ($M = -7.85$; $SD = 93.81$ and $M = 17.46$; $SD = 30.37$, respectively) (see Figure 5). *T*-tests revealed that, in the crossed condition, none of the PSS values in control and threat trials were significantly different from 0, respectively, $t(22) = -0.57$, $p = 0.58$ and $t(22) = -0.29$, $p = 0.77$. In the uncrossed condition, the PSS values in both control and threat trials were significantly different from 0, respectively, $t(30) = 2.08$, $p = 0.05$ and $t(30) = 3.40$, $p < 0.01$. Of particular interest, the Cue x Condition interaction failed to reach statistical significance ($F(1,21) = 0.22$, $p = 0.64$; $d = 0.07$ [95% CI: -0.41, 0.56]), indicating that threat effects were not different between the crossed and uncrossed conditions. The Condition x Pain Side interaction was marginally significant ($F(1,21) = 4.03$, $p = 0.058$). Follow-up analyses showed a significant main effect of Condition only when pain was presented at the right arm ($F(1,9) = 4.95$, $p = 0.05$, $d = 0.70$ [95% CI: 0.01, 1.40]), meaning that, on average, the PSS was larger in the uncrossed conditions ($M = 28.36$; $SD = 22.28$) than in the crossed conditions ($M = -35.15$; $SD = 111.76$).

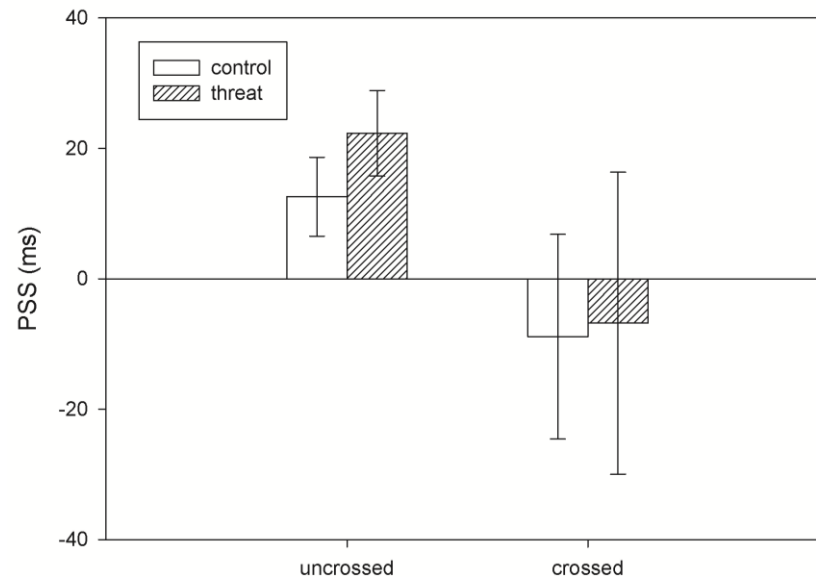


Figure 5. Index for attentional prioritization (PSS) for the uncrossed and crossed condition (in ms and with standard errors) in control and threat trials. Positive values indicate that stimuli on the threatened hand were perceived more rapidly than those presented to the other hand, whereas negative values indicate that stimuli on the neutral hand were perceived more rapidly than those presented to the threatened hand.

Because of the high number of excluded participants as a result of not attaining performance criteria in the crossed condition, we decided in a next step to analyze only the uncrossed condition. This allowed us to include more participants, thereby increasing statistical power to replicate the attentional prioritization effect of previous studies (Vanden Bulcke et al., 2013, 2014). This time only three subjects were eliminated for further analyses: (1) two subjects had less than 80% accuracy on the trials with the largest SOA tested (± 120 ms), (2) one subject had a PSS higher than the highest SOA tested. A repeated measures ANOVA with Cue (threat vs. control; within) and Pain Side (left vs. right; between) showed a significant main effect of Cue ($F(1,33) = 5.14, p = 0.03$) with threat trials ($M = 18.18$ ms, $SD = 28.67$) showing a larger PSS than control trials ($M = 11.05$ ms, $SD = 26.63$) ($d = 0.26$ [95% CI: 0.02, 0.50]). The interaction Cue x Pain Side was marginally significant ($F(1,33) = 3.43, p = 0.07$).

JND

The main effect of Cue was not significant ($F(1,21) = 0.001, p = 0.98$), with no significant differences between threat trials ($M = 106.84$ ms, $SD = 54.45$) and control trials ($M = 106.34$ ms, $SD = 44.97$) ($d = 0.01$ [95% CI: -0.46, 0.46]). The main effect of Condition was significant ($F(1,21) = 84.04, p < 0.01; d = 1.70$ [95% CI: 1.08, 2.33]), meaning that, on average, the JND was larger in the crossed condition ($M = 166.15$; $SD = 74.80$) than in the uncrossed conditions ($M = 47.03$; $SD = 13.77$) (see Figure 6). All interaction effects were not significant (all $F < 1$).

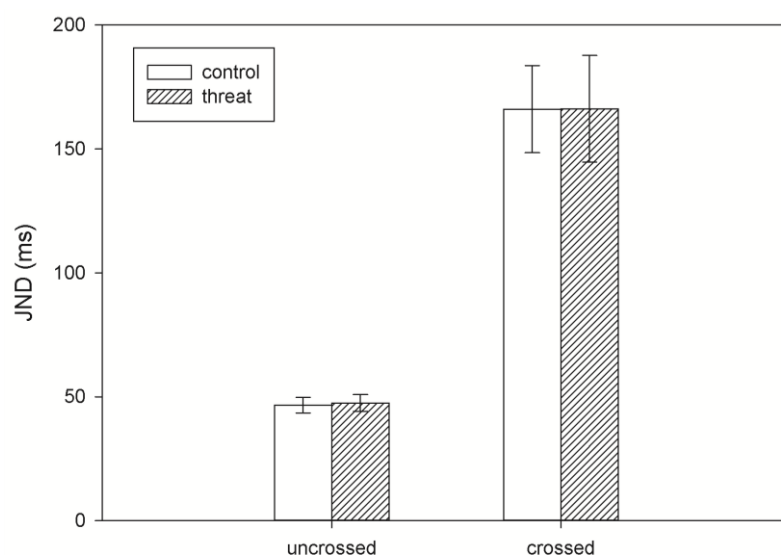


Figure 6. Index for accuracy (JND) in Experiment 1 for the uncrossed and crossed condition (in ms and with standard errors) in control and threat trials.

Interim discussion

The results of the first experiment indicated that overall there was no threat-related attentional prioritization effect, neither in the uncrossed nor in the crossed condition. However, it should be noted that almost half of the participants had to be excluded from analysis due to insufficient accuracy scores on the trials with the largest SOA tested (± 360 ms) in blocks where participants had to cross their hands over the midline. When analyses were only executed on the uncrossed condition, more participants could be included in the analysis and as such more power was obtained. These analyses revealed that tactile stimuli presented on the threatened body part were perceived earlier in time than tactile stimuli presented on the neutral body part, which is in line with the findings of previous studies in which arms were positioned in an uncrossed posture (Vanden Bulcke et al., 2013; 2014).

With regard to the high number of excluded participants as a result of having to cross the arms, it might be suggested that participants found it too confusing to judge which stimulus came first in this unusual body posture. The accuracy level of participants in the crossed condition was indeed very low and this might be one possible reason why we did not find any effects in the crossed condition. Therefore, we conducted a second experiment with some methodological adjustments: (1) the range of SOAs was enlarged to a minimum of 15 ms and a maximum of 600 ms ($\pm 600, \pm 400, \pm 250, \pm 100, \pm 70, \pm 50, \pm 30, \pm 15$ ms; see Sambo et al., 2013 for similar SOAs), (2) the same range of SOAs was used in the crossed and uncrossed conditions to increase the comparability between those conditions, and (3) crossed and uncrossed blocks were not alternated anymore as continuously switching between both types of blocks might be confusing and might have influenced the performance of participants. Two uncrossed blocks were now followed by two crossed blocks or vice versa. Additionally, a short practice block was included before each experiment block to eliminate possible switching effects between a crossed and uncrossed block.

Experiment 2

Method

Participants

Thirty-two undergraduate students (27 females, 5 males; mean age = 21.9 years; all white Caucasian) were paid to take part in the experiment. All of the participants had normal or corrected-to-normal vision and normal hearing. All but two of the participants reported being right-handed. The participants rated their general health on average as 'very good' and none of them reported having a current medical or mental disorder. Nineteen of the participants reported having experienced pain during the last six months (average of 28 days in 6 months). Nine of these participants reported feeling pain at the moment of testing, but the average rating of the intensity of the pain for these thirteen participants was low ($M = 1.22$; ranging from 1 to 2, $SD = 0.44$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'. All of the participants gave their informed consent and were free to terminate the experiment at any time should they so desire. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experimental session lasted for approximately 1 hour and 15 minutes.

Apparatus and materials

The same apparatus and stimulus characteristics were used as in Experiment 1.

TOJ paradigm

The task was identical to Experiment 1, except the following parameters: (1) a larger range of SOAs ($\pm 600, \pm 400, \pm 250, \pm 100, \pm 70, \pm 50, \pm 30, \pm 15\text{ms}$) was used in the crossed and uncrossed conditions; (2) the same range of SOAs was used in both the crossed and uncrossed condition to increase the comparability between both types of blocks; (3) blocks were not alternated anymore; (4) a practice block was now included before each type of block

Procedure

The procedure was identical to that used in Experiment 1. Practice blocks consisted of eighteen trials (1 trial per SOA, 2 pain trials), experimental blocks consisted of 103 trials (6 trials per SOA, 7 pain trials).

Self-report measures

The questionnaires and self-report measures were the same as in Experiment 1.

Results: section 1

Data-analysis

Exclusion criteria were the same as for Experiment 1. Again, the best-fitting straight line on the z-scores was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS) values for the subsequent statistical analyses (see Figure 7). Two participants (all women; right-handed) had an accuracy of less than 80% on those trials with the largest SOA tested (± 600 ms), and were excluded from further analysis.

Manipulation check

Participants reported being more afraid during the threat trials ($M = 4.14$, $SD = 2.64$) than during the control trials ($M = 0.13$, $SD = 0.50$) ($t_{29} = 9.70$, $p < 0.01$; $d = 1.91$ [95% CI: 1.18, 2.66]). Furthermore, the participants expected a painful electrocutaneous stimulus more during the threat trials ($M = 5.05$, $SD = 2.11$) than during control trials ($M = 0.28$, $SD = 0.51$) ($t_{29} = 13.32$, $p < 0.01$; $d = 2.66$ [95% CI: 1.83, 3.49]). Finally, the participants rated the electrocutaneous stimuli as little painful ($M = 3.88$, $SD = 1.78$). Mean questionnaire scores were 18.63 ($SD = 8.15$) for the PCS and 31.83 ($SD = 12.03$) for the PVAQ.

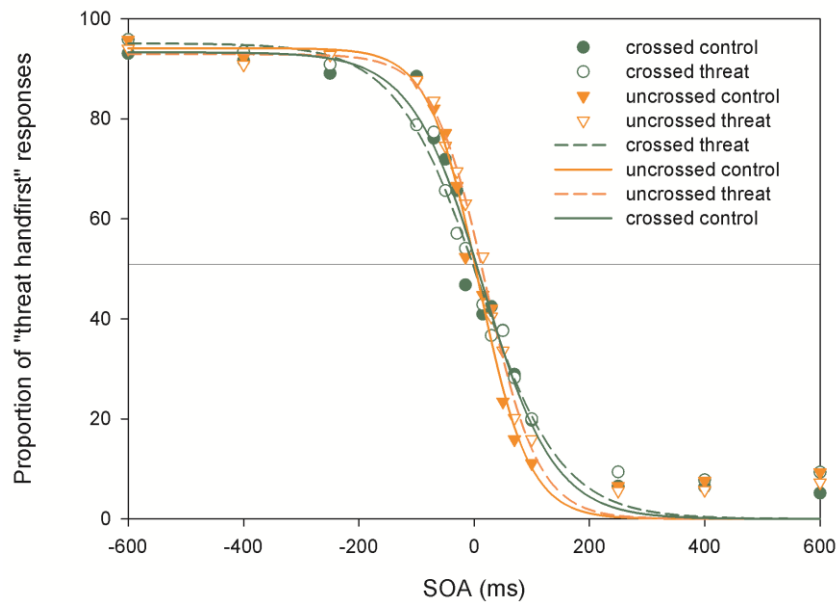


Figure 7. Temporal order judgment (TOJ) data for Experiment 2. The figure illustrates the fitted curves from the cumulative data averaged over participants. The x-axis represents the different SOAs between the two tactile stimuli presented in a trial. The responses were recoded so that negative values on the left side of the x-axis indicate that the threatened hand was stimulated first, while positive values indicate that the neutral hand was stimulated first. The y-axis represents the mean proportion of responses according to which the threatened hand was perceived as having been stimulated first. The different conditions are represented by different symbols and line styles (see legend).

PSS

The main effect of Cue was not significant ($F(1,28) = 0.935$, $p = 0.34$), with no significant differences between threat trials ($M = 12.47$ ms, $SD = 50.09$) and control trials ($M = 2.46$ ms, $SD = 57.60$) ($d = 0.18$ [95% CI: -0.17, 0.54]). The main effect of Condition was not significant ($F(1,28) = 0.49$, $p = 0.49$; $d = 0.14$ [95% CI: -0.22, 0.50]), meaning that, on average, the PSS was not different between the crossed and uncrossed conditions ($M = 3.61$; $SD = 58.57$ and $M = 11.31$; $SD = 50.09$, respectively) (see Figure 8). *T*-tests revealed that, in both the crossed and uncrossed condition, none of the PSS values in control and threat trials were significantly different from 0, respectively, $t_{crossedcontrol}(29) = -0.13$, $p = 0.90$, $t_{crossedthreat}(29) = 0.76$, $p = 0.45$, $t_{uncrossedcontrol}(29) = 0.65$, $p = 0.52$, and $t_{uncrossedthreat}(29) = 1.22$, $p = 0.23$. Of particular interest, there was no significant interaction between Cue and Condition ($F(1,28) = 0.003$, $p = 0.96$; $d = 0.03$ [95% CI: -0.54, 0.59]), indicating that threat-related effects were not different between the crossed and the uncrossed conditions ($F < 1$). Note that there was a significant main effect of Pain Side ($F(1,28) = 25.68$, $p < 0.01$). Larger PSS values were

observed in subjects who expected the pain on the left side ($M = 41.60$ ms, $SD = 63.65$) as compared to subjects who expected pain on the right side ($M = -22.41$ ms, $SD = 58.66$) ($d = 1.02$ [95% CI: 0.28, 1.76])³.

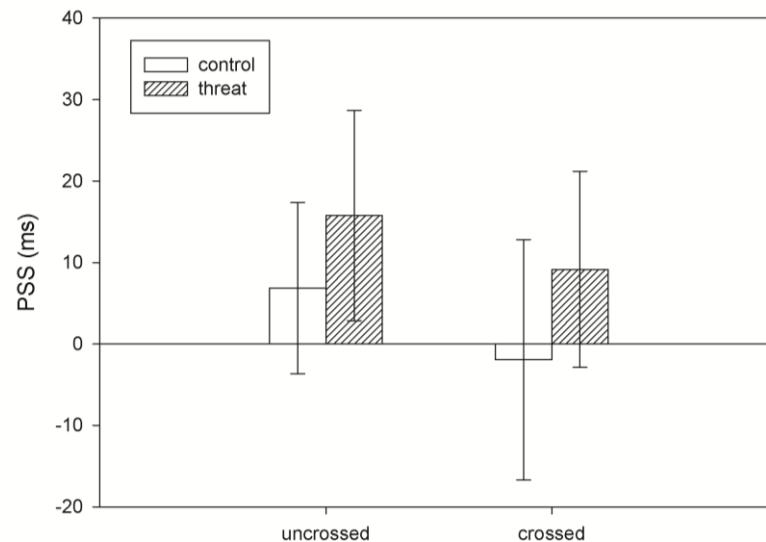


Figure 8. Index for attentional prioritization (PSS) for the uncrossed and crossed condition (in ms and with standard errors) in control and threat trials. Positive values indicate that stimuli on the threatened hand were perceived more rapidly than those presented to the other hand, whereas negative values indicate that stimuli on the neutral hand were perceived more rapidly than those presented to the threatened hand.

In a next step, only the uncrossed condition was analyzed again, to check whether the attentional prioritization effect of previous studies (Vanden Bulcke et al., 2013, 2014) was replicated. One subject had a PSS higher than the highest SOA tested and was therefore excluded for further analysis. A repeated measures ANOVA with Cue (threat vs. control; within) and Pain Side (left vs. right; between) showed no significant main effect of Cue ($F(1,29) = 0.27$, $p = 0.61$), indicating no significant differences between PSS values in threat trials ($M = 10.38$ ms, $SD = 75.83$) compared to control trials ($M = 2.63$ ms, $SD = 61.39$) ($d =$

³ To check whether differences in perceived and physical pain intensities between the two groups could account for the main effect of side of pain, we conducted a series of independent t-tests. We found no significant differences in perceived intensity (per) of the painful stimuli between participants who received painful stimulation on the left ($M = 4.29 \pm 1.68$) or right forearm ($M = 4.13 \pm 1.63$) ($t_{per}(28) = 0.27$, $p = 0.79$) nor in physical intensity (phy) of the painful stimuli between participants who received painful stimulation on the left ($M = 1.33$ mA \pm 0.42) or right forearm ($M = 1.24$ mA \pm 0.41) ($t_{phy}(28) = 0.60$, $p = 0.55$). Furthermore, a paired-sampled t-test showed significant differences in physical intensity of the tactile stimuli between the left and right hand ($t_{per}(29) = 3.34$, $p < 0.01$), indicating larger physical intensities on the left ($M = 0.097$ Watt \pm 0.002) compared to the right hand ($M = 0.075$ Watt \pm 0.004). Moreover, physical tactor intensities differed significantly between the left and right hand for participants who received painful stimulation on the left forearm ($t_{phy}(13) = 2.42$, $p = 0.03$; $M_{painleft} = 0.089$ Watt \pm 0.003; $M_{painright} = 0.075$ Watt \pm 0.004) and for participants who received painful stimulation on the right forearm ($t_{phy}(15) = 2.24$, $p = 0.04$; $M_{painleft} = 0.10$ Watt \pm 0.003; $M_{painright} = 0.08$ Watt \pm 0.006).

0.11 [95% CI: -0.30, 0.52]). The main effect of Pain Side was significant ($F(1,29) = 5.05, p = 0.03$), larger PSS values were observed in subjects who attended the pain on the left side ($M = 28.44$ ms, $SD = 79.12$) as compared to PSS values in subjects who attended pain on the right side ($M = -14.06$ ms, $SD = 49.84$) ($d = 0.64$ [95% CI: 0.11, 1.17]).

JND

The main effect of Cue was not significant ($F(1,28) = 0.39, p = 0.54$), with no significant differences between threat trials ($M = 160.17$ ms, $SD = 25.46$) and control trials ($M = 157.56$ ms, $SD = 23.85$) ($d = 0.11$ [95% CI: -0.23, 0.44]). The main effect of Condition was not significant ($F(1,28) = 0.85, p = 0.36; d = 0.13$ [95% CI: -0.18, 0.45]), meaning that, on average, the JND was not different between the crossed and uncrossed conditions ($M = 160.47, SD = 24.64$ and $M = 157.26, SD = 23.91$, respectively) (see Figure 9). All interaction effects were not significant.

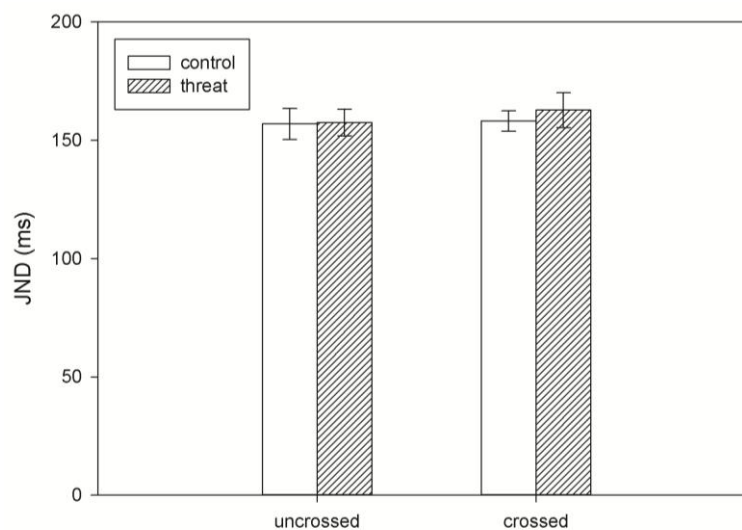


Figure 9. Index for accuracy (JND) in Experiment 2 for the uncrossed and crossed condition (in ms and with standard errors) in control and threat trials.

Results: section 2

A closer look to the longest intervals used in Experiment 2 (± 600 ms and ± 400 ms) showed evidence of a ceiling effect for both the crossed and uncrossed condition. Indeed, almost all participants performed nearly perfectly at these intervals, and only 4 participants had an accuracy less than 80%. Inclusion of these data points did not result in any additional variance. On the contrary, this

could be rather problematic. PSS values were calculated based on the best-fitting *straight* line on the cumulative z-scores. Therefore, inclusion of these data points could have resulted in an artificial reduction in slope, whereas exclusion of these points should lead to a better fitted straight line (for a similar approach, see Shore, et al., 2002; Spence, et al., 2001). Note that in previous figures (see Figure 3, Figure 4 and Figure 7) untransformed data are represented. Fitted curves are those on the cumulative data (proportions) to have a more precise visualization. Figure 10 and Figure 11 represents the same data of Experiment 2, plotted after the proportion of ‘threatened hand first’ responses were converted into z-scores. Figure 10 includes all SOAs, whereas in Figure 11, the longest intervals (± 600 ms and ± 400 ms) were excluded. The corresponding best fitting *straight* lines were added for each condition. It is clear that when the data points of the longest SOAs were excluded, a better fit for the straight line was observed. The average R^2 was 0.78 when all data points were included, whereas the average R^2 was 0.87 when data points of the longest intervals were excluded. Therefore, the following analyses that we report are analyses after exclusion of the largest SOAs (± 600 ms and ± 400 ms).

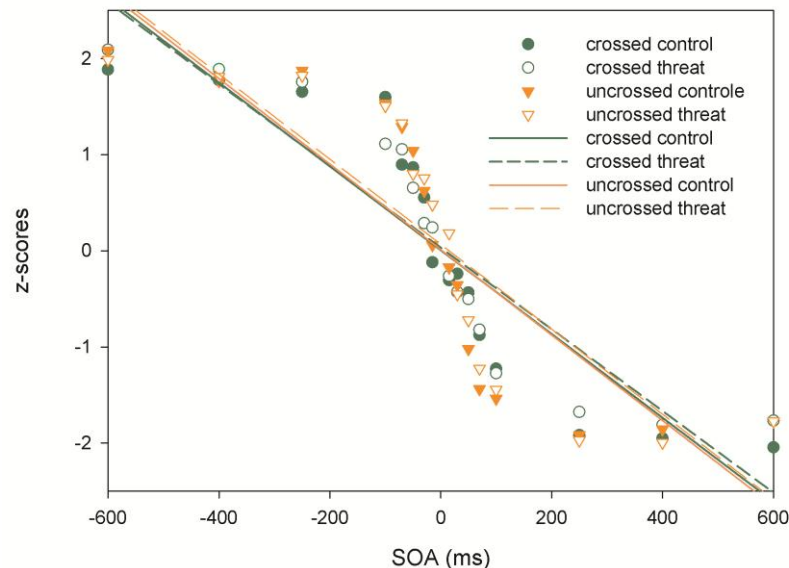


Figure 10. Temporal order judgment (TOJ) data for Experiment 2: average of the fitted data for all participants. The data are plotted after the proportion of ‘threatened hand first’ responses were converted to z-scores. The corresponding best fitting straight lines were added for each condition (see legend).

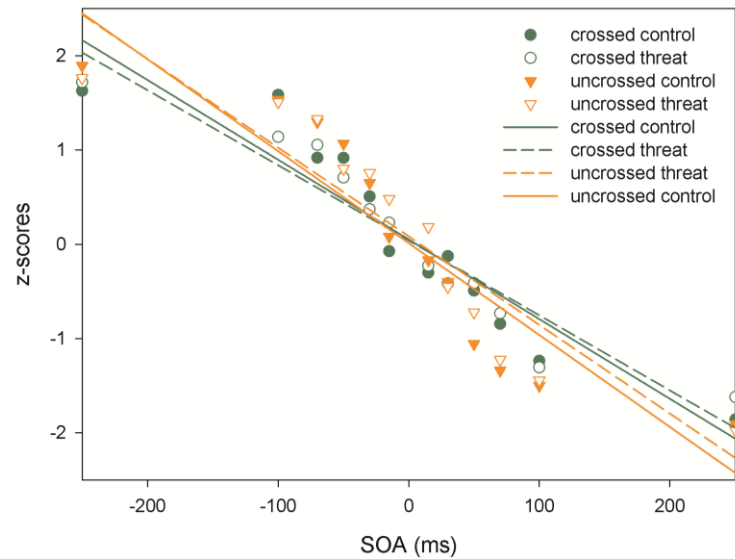


Figure 11. Temporal order judgment (TOJ) data for Experiment 2 without data points of the longest intervals (± 600 ms and ± 400 ms): average of the fitted data for all participants. The data are plotted after the proportion of ‘threatened hand first’ responses were converted to z-scores. The corresponding best fitting straight lines were added for each condition (see legend).

Data-analysis

Four participants (3 women and one male; all right-handed) had an accuracy of less than 80% on those trials with the largest SOA tested (± 250 ms).

PSS

The main effect of Cue was not significant ($F(1,26) = 1.18, p = 0.29$), with no significant differences between threat trials ($M = 9.62$ ms, $SD = 54.72$) and control trials ($M = 2.19$ ms, $SD = 41.26$) ($d = 0.15$ [95% CI: -0.24, 0.54]). The main effect of Condition was not significant ($F(1,26) = 0.19, p = 0.67; d = 0.12$ [95% CI: -0.40, 0.64]), meaning that, on average, the PSS was not different between the crossed and uncrossed conditions ($M = 3.47; SD = 33.82$ and $M = 8.34; SD = 45.77$, respectively) (see Figure 12). *T*-tests revealed that, in both the crossed and uncrossed condition, none of the PSS values in control and threat trials were significantly different from 0, respectively, $t_{crossedcontrol}(27) = 0.52, p = 0.61$, $t_{crossedthreat}(27) = 0.36, p = 0.72$, $t_{uncrossedcontrol}(27) = -0.05, p = 0.96$, and $t_{uncrossedthreat}(27) = 1.29, p = 0.21$. Of particular interest, there was no significant interaction between Cue and Condition ($F(1,26) = 2.03, p = 0.17; d = 0.36$ [95% CI: -0.22, 0.94]), indicating that threat effects were not different between the

crossed ($M = -2.41$ ms, $SD = 47.26$) and the uncrossed conditions ($M = 17.28$ ms, $SD = 60.78$). Note that there was again a significant effect of the Pain Side ($F(1,26) = 11.03$, $p < 0.01$), larger PSS values were observed in subjects who attended the pain on the left side ($M = 22.45$ ms, $SD = 54.94$) as compared to PSS values in subjects who attended pain on the right side ($M = -8.43$ ms, $SD = 36.67$) ($d = 0.65$ [95% CI: 0.09, 1.39]).

In a next step, only the uncrossed condition was analyzed again, to check whether the attentional prioritization effect of previous studies (Vanden Bulcke et al., 2013, 2014) was replicated. One subject had a PSS higher than the highest SOA (± 250 ms) tested and was therefore excluded for further analysis. A repeated measures ANOVA with Cue (threat vs. control; within) and Pain Side (left vs. right; between) showed no significant main effect of Cue ($F(1,29) = 1.16$, $p = 0.29$), showing on average no significant differences in PSS values in threat trials ($M = 13.42$ ms, $SD = 70.89$) compared to control trials ($M = 1.51$ ms, $SD = 35.47$) ($d = 0.19$ [95% CI: -0.16, 0.55]). The interaction Cue x Side of Pain nor the main effect of Pain Side were significant (all $F < 1$).

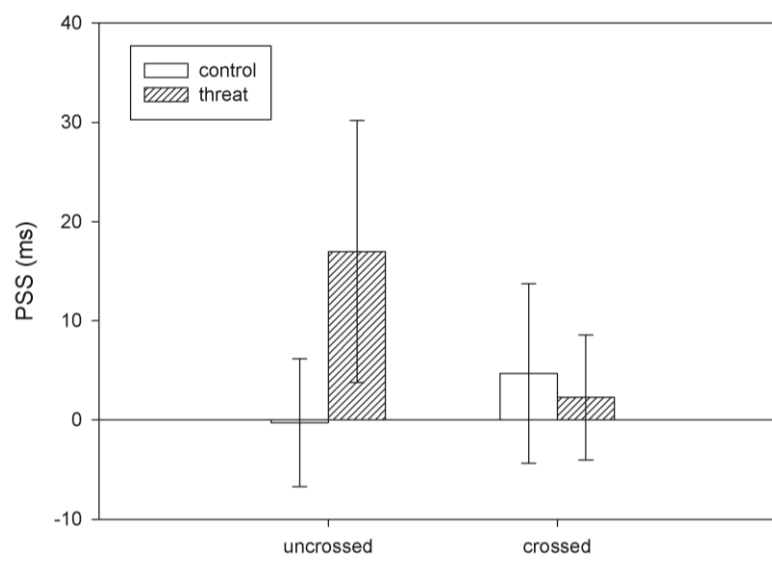


Figure 12. Index for attentional prioritization (PSS) without data points of the longest intervals (± 600 ms and ± 400 ms) for the uncrossed and crossed condition (in ms and with standard errors) in control and threat trials. Positive values indicate that stimuli on the threatened hand were perceived more rapidly than those presented to the other hand, whereas negative values indicate that stimuli on the neutral hand were perceived more rapidly than those presented to the threatened hand.

JND

The main effect of Cue was significant ($F(1,26) = 5.99, p = 0.02$), showing larger JND values in threat trials ($M = 88.81$ ms, $SD = 28.41$) than in control trials ($M = 76.34$ ms, $SD = 19.10$) ($d = 0.37$ [95% CI: 0.02, 0.72]). The main effect of Condition was significant ($F(1,26) = 4.51, p = 0.04; d = 0.39$ [95% CI: 0.02, 0.76]), meaning that, on average, the JND was larger in the crossed condition ($M = 88.95$; $SD = 37.50$) than in the uncrossed conditions ($M = 76.21$; $SD = 21.20$) (see Figure 13). Furthermore, there was a significant interaction between Cue and Pain Side, $F(1,26) = 5.65, p = 0.03$. Follow-up analyses showed a significant main effect of Cue when pain was presented at the left arm ($F(1,12) = 6.45, p = 0.03, d = 0.59$ [95% CI: 0.10, 1.08]), meaning that, on average, the JND was larger in the threat trials ($M = 98.91$; $SD = 43.84$) compared to control trials ($M = 72.50$; $SD = 11.39$). When pain was presented at the right arm, no significant main effect of Cue was found ($F(1,14) = 0.006, p = 0.94, d = 0.01$ [95% CI: -0.29, 0.32]).

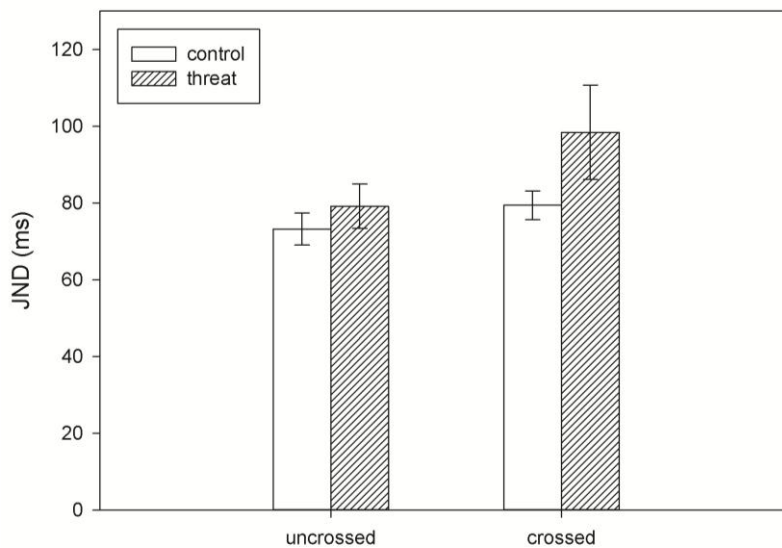


Figure 13. Index for accuracy (JND) in Experiment 2 without data points of the longest intervals (± 600 ms and ± 400 ms) for the uncrossed and crossed condition (in ms and with standard errors) in control and threat trials.

Discussion

In the second experiment, we adapted some parameters of the tactile TOJ task due to poor performance in the crossed condition in experiment 1. The range of SOAs was enlarged ($\pm 600, \pm 400, \pm 250, \pm 100, \pm 70, \pm 50, \pm 30, \pm 15$ ms) and the

same range of SOAs was used both in the crossed and uncrossed condition. Moreover, a short practice block was included before each experiment block and both types of blocks were not alternated anymore. However, again we found no evidence for a threat-related attentional prioritization effect, neither in the uncrossed nor in the crossed condition. A closer look at the data showed evidence for a ceiling effect of the longest SOAs for both the crossed and uncrossed condition. Therefore, a second data analysis strategy was reported in which the largest SOAs (± 600 ms and ± 400 ms) were excluded. Although this resulted in a better fit of the data, yet again no evidence was found for any threat-related attentional prioritization effect.

General discussion

In the two studies presented here, it was investigated by means of a TOJ task whether the effect of threat of pain on one arm is due to somatosensory input occurring at the ipsilateral hand of the threatened body part (i.e. somatotopic reference frame of threat localization) or rather because of corresponding spatial encoding of somatosensory input and pain independent of the body part on which they occur (spatiotopic reference frame of threat localization). The effect of threat of pain to one arm on somatosensory processing at the ipsilateral and contralateral hand was compared between two body postures conditions: uncrossed versus crossed arms. Participants made temporal order judgments of pairs of tactile stimuli presented on the left and the right hands, while occasionally experiencing a painful stimulus on one arm. If the effect of threat of pain on one arm was due to enhanced processing of somatosensory input occurring on the threatened body part (somatotopic reference frame of threat localization), tactile stimuli would be perceived more rapidly on the hand ipsilateral to the threatened arm in both conditions. In contrast, if the threat-related prioritization effect was the result of corresponding spatial encoding of somatosensory input and pain independent of the body part on which they occurred (spatiotopic reference frame of threat localization), tactile stimuli in the crossed condition would be perceived more rapidly on the hand contralateral to the threatened arm than on the hand ipsilateral to the threatened arm.

The results of the presented studies indicated that there was no prioritization effect of the threatened arm for tactile stimuli at neither the ipsilateral, nor the contralateral hand. The data of the uncrossed condition followed the pattern of findings of previous studies (Vanden Bulcke et al., 2013; 2014) in which an analogous range of SOAs was used (± 120 , ± 60 , ± 30 , ± 15 , ± 5 ms). Though, statistically significant effects were only obtained in experiment 1, after analyzing the uncrossed condition separately. This allowed us to include more participants, thereby increasing statistical power to replicate the attentional prioritization effect of previous studies. The results in the uncrossed condition of experiment 2 followed the same pattern as the findings in the uncrossed condition of experiment 1, but the results did not reach statistical significance, even when data points of the largest SOA were excluded to improve fit.

We can speculate about possible reasons why we did not find evidence in both experiments in the crossed condition for any threat-related attentional prioritization effect. First of all, as already mentioned earlier, it was very difficult for the participants of our first experiment to perform a tactile TOJ task when crossing the hands over the midline. This finding was rather surprising, as previous studies with a crossed hands TOJ task using a range of smaller SOAs did not have such a loss of subjects based on accuracy level (see e.g. Shore et al., 2002; Spence, Baddeley, Zampini, James, & Shore, 2003, SOAs ranging from ± 10 ms to ± 200 ms; Moseley, et al., 2009, SOAs ranging from ± 5 ms to ± 120 ms; Moseley, Gallagher, & Gallace, 2012, SOAs ranging from ± 10 to ± 240 ms). Although we already used a larger range of SOAs compared to these previous studies, we still had to exclude too many participants not attaining performance criteria in the crossed condition. Consequently, a lack of power might be a reason why we did not found any significant main effect of Cue in our first experiment. Second, and in consequence to the first point, it must be noted that we cannot fully compare our design with the design of previous studies, as an extra manipulation with painful stimuli was added in our studies. It might be expected that bodily threat may have a negative influence on performance. The expectation of bodily threat might add an additional burden on working memory, as a new attentional priority is imposed. As such, this might have resulted in poorer performance (e.g. Crombez, Eccleston, Baeyens, & Eelen, 1998b), more exclusion of participants and less power. Third, and probably the most important reason, is

that in both experiments very large standard deviations were observed. Standard deviations are ranging from 50 till 90, which is twice or even three times higher than standard deviations found in our previous studies (Vanden Bulcke et al., 2013, 2014). This points to the fact that there was a lot of interindividual variability. We may assume that theoretically relevant variables such as pain-related fear and pain catastrophizing might play an important role in the top-down attentional prioritization of somatosensory sensations at a threatened body part. Several theoretical models have formulated specific hypotheses that catastrophizing thoughts of pain and pain-related fear are supposed to facilitate the processing of pain-related information (Eccleston & Crombez, 2007; Vlaeyen and Linton, 2000). Unfortunately, the sample size of our study was too low to allow reliable interpretation of an analysis of individual differences in pain-related fear and/or pain catastrophizing. A fourth and last argument for explaining the zero-effects in the crossed condition is that by crossing the arms over the body midline effects of somatotopic and spatiotopic frames of reference may have cancelled each other out. The somatotopic frame of reference contains a spatially organized representation of the cutaneous surface of the body (Harris, Harris & Diamond, 2001; Kuroki, Watanabe, Kawakami, Tachi, & Nishida, 2010; Penfield and Boldrey, 1937) and as such, allows the detection of which part of the body is potentially threatened. The spatiotopic frame of reference is using external space as coordinate system to identify the spatial position of the threatened object and as such, we are able to recognize that the right hand, that crosses the midline of the body, is stimulated, despite the fact that somatosensory inputs are sent to the left hemisphere (Ehrsson, Spence, & Passingham, 2004; Graziano, 1999; Kitazawa, 2002). According to our findings, it might be suggested that the mapping of the perception of bodily threat did not provide benefits for experiencing somatosensory sensations presented on the same body part as where threat is expected (i.e. somatotopic frame of reference), neither for somatosensory input on a different body part that is located closer in space to bodily threat (i.e. spatiotopic frame of reference). As such, it might be possible that in our study both frames of reference might have cancelled each other out, which might have caused the zero effects.

Previous studies using a crossed hands TOJ task have mainly focused on decreases in performance by relying on the 'just noticeable difference' (JND)

measure. The JND, which provides a measure of the sensitivity of participants' temporal perception, normally has average values between 40 and 70 ms in 'normal' hand postures. This JND value doubles or triples when hands were crossed over the midline (Sambo, et al., 2013; Shore, et al., 2002, Yamamoto & Kitazawa, 2001). Although we had no specific hypotheses concerning the JND, analysis of the JND data in experiment 1 and experiment 2 (analyses with the exclusion of the largest data points) revealed that participants are less accurate in making tactile TOJs when their arms were crossed over the midline compared with an uncrossed hands posture. These results are in line with previous studies demonstrating the 'crossed hands deficit', a decrease in performance when adopting a crossed hands position (Sambo et al., 2013; Shore et al., 2002; Yamamoto & Kitazawa, 2001). To the best of our knowledge, this is one of the first studies with a crossed hands TOJ design that is investigating biases in spatial attention and therefore analyzing the PSS as primary outcome. In a study of Moseley, Gallace and Spence (2009), it was already demonstrated by means of a crossed hands TOJ task that patients with complex regional pain syndrome (CRPS) are characterized by a type of spatial neglect. Participants with CRPS on one arm performed temporal order judgments of tactile stimuli, one delivered to each hand under a crossed and uncrossed arms condition. While participants prioritized stimuli from the unaffected limb over those from the affected limb in the uncrossed arms condition, the reverse pattern was found in the crossed arms condition. These results demonstrated that CRPS is associated with a deficit in tactile processing that is defined by the space in which the affected limb normally resides (spatiotopic reference frame) and not by the affected limb itself (somatotopic reference frame). Since previous studies investigating the dominance of different frames of reference on the threat-related prioritization effect are scarce, more research is recommended in healthy volunteers by means of the induction of experimental pain as well as in clinical pain populations.

Some issues deserve further consideration. First, analyzing techniques different from the one used in our study are recommended. According to the approach used in our studies, the S-shaped performance curve was linearized by probit-transforming right-first response probabilities at each SOA, and PSS and JND values were calculated on the best fitting *straight* line. This approach has the advantage that linearization of response values allows the use of regular

regression analysis. However, the disadvantage is that this technique is less adequate for analyzing large SOAs, as the psychometric functions asymptote at higher SOAs. Indeed, it has been demonstrated in experiment 2 that if the larger SOAs were included, the TOJ probabilities resembled a typical S-shaped curve and were better fitted with a cumulative Gaussian function. Therefore, it would be better to analyze TOJ tasks with larger SOAs using logistic function techniques (for a similar approach see Azañón & Soto-Faraco, 2007; Sambo et al., 2013; Yamamoto & Kitazawa, 2001). Second, several studies have already demonstrated that the spatiotopic frame of reference prevails when visual information is involved. Spence, Pavani, and Driver (2000) demonstrated that crossmodal links between vision and touch get fully remapped when the hands are crossed. Similar results were found by Kennett, Eimer, Spence, and Driver (2001) who found that visual judgments are better on the same side of external space as the preceding touch, even when the hands are crossed. When the hands of the participants are unseen, tactile judgments are better at the same side of external space as a visual cue (Kennett, Spence, & Driver, 2002). Moreover, the crossed hands deficit is absent in blind people (Röder, Rösler, & Spence, 2004), reduced in a space individuals cannot see (e.g. crossing their arms behind the back) (Kóbor, Füredi, Kovács, Spence, & Vidnyánszky, 2005) and is even found when feet are crossed over the midline (Schicke & Röder, 2006). Since no visual information was integrated in our study, it would be interesting to investigate the effect of visual input on the attentional prioritization of the threatened bodily location. In extension to our study, a threatening visual cue (e.g. picture of physical threat, see Van Damme et al., 2009) might be presented before the two tactile stimuli were administered. As visual information emphasizes more the external-spatial coordinates, we should expect that participants would prioritize tactile stimuli on the hand that is laying in the same hemifield of the threatening cue, compared to the other hand. In sum, further research is needed to validate the current results and investigate the dominance of different frames of reference of threat localization.

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Part II

Do patients with unilateral knee pain prioritize bodily sensations at the painful knee?¹**Abstract**

Research has shown that the expectation of pain at a particular location of the body results in the prioritization of somatosensory information at that location. Since previous studies experimentally manipulated threat of pain by the induction of painful stimulation in healthy volunteers, it is yet unclear whether the attentional prioritization of somatosensory sensations on a threatened body part is also displayed in individuals experiencing clinical pain. Here, we investigated, using a temporal order judgment (TOJ) task, whether patients with unilateral (sub)acute knee pain prioritized somatosensory sensations on the painful knee compared to the non-painful knee. Patients judged which one of two tactile stimuli, one presented to either knee, had been presented first. In order to maximize threat of pain, patients were led to believe that they would have to perform several stressful knee movements immediately after the task. We found no support for the hypothesis that patients would be more quickly aware of somatosensory input on the affected knee than on the other knee. Potential explanations for these findings, as well as suggestions for future research are discussed.

¹ Vanden Bulcke, C., Crombez, G., Steyaert, A., Danneels, L., Van Damme, S. (in preparation). Do patients with unilateral knee pain prioritize bodily sensations at the painful knee?

Introduction

Pain is an evolutionarily programmed warning signal that activates an adaptive defensive system involving a range of protective responses including sympathetic activation, muscle contractions, withdrawal, fear, and heightened attention for potential bodily threats (Bolles & Fanselow, 1980; Chapman, Tuckett, & Song, 2008; Eccleston & Crombez, 1999). Because successful adaptation is also promoted by the ability to predict pain and undertake preventive actions, such as avoidance, it has been proposed that the defensive system may already be activated in situations where pain or bodily harm is anticipated (Moseley & Vlaeyen, 2015; Van Damme, Crombez, Eccleston, 2004).

In the present study we specifically focus on how anticipation of pain influences attentional processes. According to recent models of attention to pain (Legrain et al., 2009; Van Damme et al., 2010), pain-induced worries and goals may result in top-down attentional prioritization of pain-related information. Such prioritization is thought to occur through the activation of an attentional set, i.e. the collection of stimulus features that a person is keeping in working memory to identify goal-relevant information. Because an important feature of pain is its location on the body, one would expect the anticipation of pain to result in prioritized processing of somatosensory input sharing its spatial coordinates with the imminent pain. Several studies experimentally inducing pain anticipation in healthy volunteers are in line with this view. It has been shown that the threat of pain on a particular location of the body resulted in heightened somatosensory processing on the anticipated pain location (e.g., Durnez & Van Damme, 2015; Vanden Bulcke, Van Damme, Durnez, & Crombez, 2013; Van Hulle, Durnez, Crombez, & Van Damme, 2015).

Although these studies offered us valuable findings regarding pain-related top-down attentional prioritization, they are limited in the conclusions that can be drawn with regard to clinical pain. All individuals who participated in those experiments were healthy undergraduate students, and pain anticipation was experimentally induced by the regular administration of electrocutaneous stimulation on one body location. Caution is thus required in generalizing these findings to "real life" or "clinical" pain, which is likely to differ on a number of qualities and parameters. For instance, the experimental pain stimuli administered in the previously mentioned studies were short, phasic,

stimulations, whereas clinical pain is often more tonic, which could have differential effects on attention (Sinke, Schmidt, Forkmann, & Bingel, 2015). We are not aware of any studies investigating attentional prioritization of somatosensory input at a body part that is threatened by clinically relevant pain. Individuals experiencing clinical pain are likely to have specific worries or concerns related to their pain problem, especially in situations that they perceive as threatening.

We aimed to test this idea in unilateral knee pain patients. The need for investigating the relationship between cognitive factors and knee pain was recently highlighted (Urquhart et al., 2015), since structural changes alone do not fully account for this problem (Symmons, 2001). In the present study, a sample of patients with (sub)acute unilateral knee pain made temporal order judgments regarding which one of two tactile stimuli, administered to each knee, had been presented first. This task has successfully been used to assess heightened attention for somatosensory input at a threatened body location (Van Damme, Gallace, Spence, Crombez, & Moseley, 2009; Vanden Bulcke et al., 2013). In order to maximize threat of pain, and thus to activate pain features in patients' attentional control settings, they were led to believe that immediately after the task, they would have to execute three stressful movements with the affected knee. We hypothesized that tactile stimuli on the pain-relevant knee would be perceived more rapidly than tactile stimuli presented on the pain-irrelevant knee, indicating prioritization of attention toward the threatened knee. Furthermore we explored the potential role of individual differences in bodily threat appraisal, both situational (fear and expected pain of anticipated knee movements) and dispositional (pain catastrophizing and vigilance).

Method

Participants

The participants were recruited through the department of Physical Medicine and Sports Rehabilitation of Ghent University Hospital. Inclusion criteria included a diagnosis of acute (less than 6 weeks) or subacute (more than 6 weeks, but less than 12 weeks) unilateral knee pain determined by the physician, an age between 18 and 65 years, and Dutch speaking. Postoperative patients were

excluded for participation, because of the risk of reduced somatosensory sensitivity. Potential participants were informed about the possibility of participating by means of a poster in the waiting room, flyers and information given by their physician. When they agreed to participate, they received a phone call from the researcher providing more detailed information about the study. Forty-six patients were initially willing to participate. Two participants who did not fulfill the criteria were excluded for participation (one woman was younger than 18 years old, one man had already undergo surgery). Later on, a further eleven patients decided not to participate due to lack of time (2 women, 3 men) or reported having no more knee pain complaints (5 women, 1 men). The final knee pain sample consisted of thirty-three individuals. However, two of them were excluded for further analysis, due to incomplete data. The main age of the remaining thirty-one patients (15 females) was 31 years ($SD = 9.86$, ranging from 19-52 years). Thirteen patients (5 females) experienced pain on the left knee, whereas eighteen patients had right knee pain (10 females). Participants included both individuals who just had their first consultation behind (55%), as persons who already were treated for a longer period (45%). The mean duration of the treatment for this second group was 9 weeks ($SD = 2.88$, ranging from 4-12 weeks). Most knee pain patients were singles (65%). The other ones were married or lived together with their partner (35%). All participants but three (9%) finished their studies at the high school or university (91%). All participants received the diagnosis of (sub)acute knee pain. Though, further diagnostic tests are performed in five patients (16%), in order to determine the underlying cause of their knee pain. None of the participants took pain medication at the moment of the study. Furthermore, patients experienced an average intensity of knee pain of 1.53 ($SD = 0.91$), assessed by means of the pain severity subscale of the Multidimensional Pain Inventory (MPI-DV, Kerns, Turk, & Rudy, 1985). Seven of the participants (22%) reported having pain symptoms other than knee pain at the moment of testing, but the average rating of the intensity of the pain for these seven participants was low ($M = 2.86$; ranging from 1 to 5, $SD = 1.77$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'.

The study was approved by the Medical Ethical Committee of the Ghent University Hospital. At the end of the experiment, all participants received a monetary reward as reimbursement for their expenses. The experimental session

lasted for approximately 1 hour and a half. A detailed overview of the demographic characteristics for the 31 participants selected for analysis is provided in Table 1.

Table 1
Demographic characteristics of participants.

	Patients		
	M ± SD	Range	N (%)
Men			16 (52%)
Women			15 (48%)
Age (in years)	29.87 ± 9.86	19-52	
Family situation			
single			20 (65%)
living together			8 (26%)
married			3 (9%)
widow(er)			0
Educational level			
primary education			0
lower secondary education			0
higher secondary education			3 (9%)
higher education			11 (36%)
higher education: university			17 (55%)
Profession			
housemen/housewife			0
laborer			0
employee			18 (58%)
professional			0
senior manager			0
disabled			0
student			11 (36%)
jobseeker			2 (6%)
Number of consultations			
first consultation			17 (55%)
several consultations			13 (45%)
Duration of treatment (weeks)	8.83 ± 2.88	4-12	
Pain severity (MPI-PS)	1.53 ± 0.91		

Apparatus and stimulus material

Tactile stimuli (10 ms duration; 200Hz) were presented by means of two resonant-type tactors (C-2 TACTOR, Engineering Acoustics, Inc., Florida, <http://www.eaiinfo.com/>) consisting of a housing of 3.05 cm diameter and 0.79 cm high, with a skin contactor of 0.76 cm diameter. Prior to the start of the experiment, the perceived stimulus intensities at both tactor locations were

individually matched (Weinstein, 1968). This was done by means of a double random staircase procedure, based on the ‘simple up-down method’ of Levitt (Levitt, 1971). In a first phase, 24 stimuli presented on the left knee were judged relative to a reference stimulus with maximum intensity (power = 0.21 Watt) on a 5-point Likert scale ranging from 1 (‘no sensation’) to 5 (‘maximum intensity’). The intensity that elicited an averaged rating of 3 was used as the stimulus intensity for the left knee, and was the reference stimulus for the second phase. In the second phase 24 stimuli on the right knee were judged relative to the reference stimulus on the left knee on a 5-point Likert scale (1 = ‘more than less strong’, 2= ‘less strong’, 3= ‘equally strong’, 4= ‘stronger’, 5= ‘much stronger’). The intensity that elicited an averaged rating of 3 was used as the intensity of the stimulus at the right knee.

The task was programmed and controlled by the INQUISIT Millisecond software package (Inquisit 3.0, Millisecond Software LLC, Seattle, WA, <http://www.millisecond.com/>) on a laptop (Dell Vostro 3550).

Tactile Temporal Order Judgment (TOJ) paradigm

In a tactile TOJ task (Piéron, 1952), two tactile stimuli were administered, usually one on either hand, separated by one of 10 randomly assigned stimulus onset asynchronies (SOAs). We adapted the ‘traditional’ TOJ paradigm by administering the tactile stimuli on each knee, separated by 10 SOAs ranging from -200 ms to 200 ms (-200, -90, -55, -30, -10, +10, +30, +55, +60, +200 ms; negative values indicate that the left knee was stimulated first; see Shore, Gray, Spry, & Spence, 2005 for a similar range of SOAs)². Participants were instructed to report aloud the knee on which the first tactile stimulus was presented, and the experimenter registered the answers using a keyboard. A trial started with the presentation of a fixation cross (2000ms) in the middle of the screen. Following this, the two tactile stimuli were presented to each knee. Participants wore noise-cancelling headphones (PXC 350 Sennheiser) in order to prevent any interference from environment noise.

² Based on a pilot study with healthy volunteers (see chapter 6, experiment 2), a range of larger SOAs was used compared to those used in studies with undergraduate students.

Self-report measures

Socio-demographic information was obtained by means of a general questionnaire including age, sex, and educational level. Participants pain prior to the experiment was assessed by means of the Dutch version of the Multidimensional Pain Inventory (MPI-DV, Kerns et al., 1985). This questionnaire consists of 28 items rated on a 7-point scale measuring severity of the pain problem (e.g. *'Rate the level of your pain at the present moment'*), interference with daily-life activities (e.g. *'In general, how much does your pain interfere with your day-to-day activities?'*), perceived control (e.g. *'During the past week how much control do you feel you have had over your life?'*), affective anxiety (e.g. *'During the past week how irritable have you been?'*) and social support (e.g. *'How supportive or helpful is your significant other to you in your relation to your pain?'*). The reliability and validity of the MPI have been well established (Rudy, 1989). Only the pain severity subscale of the MPI (MPI-PS; three items) was reported in the study. Cronbach's alpha of the MPI severity subscale in this study was 0.67.

Dispositional bodily threat appraisal was assessed by three questionnaires. The Dutch version of the Pain Vigilance and Awareness Questionnaire (PVAQ, McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002) constitutes of 16 items that represent two subscales: 'attention to pain' (e.g. *"I focus on sensations of pain"*) and 'attention to changes in pain' (e.g. *"I quickly realize when pain gets worse or less worse"*). This questionnaire assesses the frequency of behavior of the past two weeks and is scored on a 6-point scale ([1 = "never", 5 = "always"]). The PVAQ shows a good internal consistency between both subscales 'attention to pain' and 'attention to changes in pain' (Cronbach's alpha is 0.83, 0.85 and 0.80 respectively). The PVAQ has been shown to be valid and reliable in both healthy populations and chronic pain patients (Roelofs et al., 2002, Roelofs, Peters, McCracken, & Vlaeyen, 2003). Cronbach's alpha of the PVAQ in this study was 0.77. The Body Vigilance Scale (BVS; Schmidt, Lerew, & Trakowski, 1997) is a four-item questionnaire measuring on a 11-point numerical rating scale the degree of attentional focus to bodily sensations (e.g., *'I am the kind of person who pays close attention to internal bodily sensations'* [0 = "not at all like me, 10 = extremely like me]), perceived sensitivity to changes in bodily sensations (e.g., *'I am very sensitive to changes in my internal bodily sensations'* [0 = "not at all

like me, 10 = extremely like me]) and the average amount of time spent attending to bodily sensations (*'On average, how much time do you spend each day 'scanning' your body for sensations'* [0 = "no time", 10 = "all of the time"]). The last item is an average of the awareness scores of 15 non-specific body symptoms (e.g., *Rate how much attention you pay to each of the following ... heart palpitations, dizziness, nausea, ... sensations* [0 = "none", 10 = "extreme"]). Cronbach's alpha of the BVS in this study was 0.89. The Dutch version of the Pain Catastrophizing Scale (PCS-DV; Sullivan, Bishop, & Pivik, 1995; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove, 2002) measures the degree of pain catastrophizing, an exaggerated negative orientation to noxious stimuli. This questionnaire consists of 13 items rated on a 5-point scale measuring rumination (e.g., *'I can't stop thinking about how much it hurts'* [0 = "not at all", 10 = "all the time"]), magnification (e.g. *'I am afraid that something serious might happen'* [0 = "not at all", 10 = "all the time"]) and helplessness to manage the pain (e.g. *'There is nothing I can do to reduce the intensity of my pain'* [0 = "not at all", 10 = "all the time"]). Cronbach's alpha of the PCS in this study was 0.70.

Situational bodily threat appraisal was assessed by means of three self-report items with regard to each of the anticipated knee movements (*'How much pain do you expect that this exercise will cause?'*, *'How afraid are you to perform this exercise?'*, *'To what extent would you avoid to perform this exercise?'*) on eleven-point numerical rating scales (anchored 0 = not at all and 10 = very strongly). The participants also had to rate several questions about concentration (*'To what extent have you made an effort to perform this task?'*, *'To what extent did you concentrate on this task?'*), attention to tactile stimuli (*'To what extent did you pay attention to the tactile stimuli?'*), intensity of the tactile stimuli (*'How intense did you experience the stimuli on your left/right knee?'*), pain experience (*'How painful did you find the task?'*), anxiety (*'How anxious were you during this block?'*), fatigue (*'To what extent did you find this task tiring?'*) on eleven-point numerical rating scales (anchored 0 = not at all and 10 = very strongly).

Procedure

Pre-experimental phase. Participants were informed about the nature of the stimuli that would be administered and gave their informed consent. Then, patients were asked to fill in a number of questionnaires: the general socio-demographic questionnaire, the Multidimensional Pain Inventory, and the dispositional bodily threat appraisal questionnaires (PCS, PVAQ, BVS). Next, in order to induce anticipation of pain, participants were informed that immediately after the attention task, they had to perform three knee movements. A video was shown wherein those three knee movements were demonstrated: (1) squat, i.e. a posture where the weight of the body was on the feet but the knees were fully bent, (2) duck walk, i.e. performed by going in the squatting position and walk forward and (3) a patella exercise, i.e. the patella was pressed up by the patient, while the experimenter provided resistance against the patella. It is believed that these movements are considered as painful for individuals who experience knee pain. Finally, participants' individual perceptual thresholds were determined by means of the double random staircase.

Experimental phase. Participants were seated in front of the experimental apparatus. The tactors were placed in the middle of the patella on each knee. Participants were informed that they have to decide on each trial which tactile stimulus had been presented first. The accuracy of participants' responses was emphasized, rather than the speed. To become familiar with the task, participants first performed a practice phase of twenty trials (2 trials per SOA). Next, four blocks of 70 trials (7 trials per SOA) were presented.

Post experimental phase. After the TOJ task, participants were informed that we were interested in their thoughts about executing the knee movements. For each movement they were asked to fill in the three items regarding situational bodily threat appraisal. After completing these items, they were informed that they did not actually have to execute the knee movements. They were debriefed and received their compensation.

Results

TOJ data handling

In TOJ studies, it is common practice (Shore et al., 2005; Spence, Shore, & Klein, 2001) to exclude those participants from statistical analysis when (1) any of the PSS values is greater than the highest SOA (± 200 ms) tested, (2) participants have less than 80% accuracy on the trials with the largest SOA tested (± 200 ms). No participants had to be excluded for these reasons. Though, two participants had to be excluded for further analysis due to incomplete data collection.

The analyses were based on a procedure that has been commonly described in the literature (Shore et al., 2005; Spence et al., 2001; Van Damme et al., 2009). The proportions of 'left-knee-first' and 'right-knee-first' responses for the painful and non-painful knee, respectively, for all trials at each SOA, were converted into the corresponding z-scores using a standardized cumulative normal distribution (probits). The best-fitting straight line was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS) values for the subsequent statistical analyses. The PSS refers to the point at which observers report the two events (right hand first and left knee first) equally often. This is commonly taken to be equivalent to the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time and such equivalent to the SOA value corresponding to a proportion of left/right hand first responses of 0.5. The PSS is computed as the opposite of the intercept divided by the slope from the best-fitting straight line. We recoded the PSS data so that a positive value indicates that the stimulus contralateral to the painful knee had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS indicates that stimuli on the painful knee are perceived more rapidly than those presented to the other knee. In sum, the PSS provides information concerning biases in spatial attention to the painful knee. A one sample *t*-test with 0 as test value was performed on the PSS data.

Self-report measures

Average and standard deviation scores on self-report measures among participants are provided in Table 2. Self-reported intensities did significantly differ between tactile stimuli on the left knee ($M = 3.27$, $SD = 2.44$) compared to

the right knee ($M = 3.71$, $SD = 2.79$), $t(30) = -2.66$, $p = 0.013$. No significant differences appeared in perceived intensities between tactile stimuli presented on the painful knee ($M = 3.43$, $SD = 2.44$) and tactile stimuli presented on the non-painful knee ($M = 3.54$, $SD = 2.57$), $t(30) = -0.61$, $p = 0.554$. Furthermore, Table 3 provides the average and standard deviation scores for self-reported expectation ('How much pain do you expect that this exercise will cause?'), fear ('How afraid are you to perform this exercise?') and avoidance ('To what extent would you avoid to perform this exercise?') for each knee movement separately.

Table 2

Average and standard deviation of self-report measures among participants.

	M ± SD	Range
BVS	48.90 ± 28.40	14-111
PVAQ	34.87 ± 10.05	17-54
PCS	14.26 ± 5.75	4-25
Concentration	7.54 ± 1.87	2-10
Intensity stimulation left knee	3.27 ± 2.44	1-10
Intensity stimulation right knee	3.71 ± 2.79	1-10
Intensity stimulation painful knee	3.43 ± 2.44	1-10
Intensity stimulation non-painful knee	3.54 ± 2.57	1-10
Fatigue	3.18 ± 2.85	0-10

Table 3

Average and standard deviation scores for self-reported expectation, fear and avoidance among patients, for each knee movement individually.

	Expectation pain	Fear pain	Avoidance
Duck walk	4.25 ± 2.72	1.50 ± 1.83	4.06 ± 3.56
Squat	2.50 ± 1.98	0.94 ± 1.52	1.50 ± 2.00
Patella exercise	3.94 ± 3.22	2.19 ± 2.61	2.84 ± 3.23

³ Physical factor intensities did not significantly differ between the left ($M = 26.61$, $SD = 2.72$) and right knee ($M = 25.16$, $SD = 4.63$), $t(30) = 1.99$, $p = 0.06$

⁴ No significant differences appeared in physical intensities between tactile stimuli presented on the painful knee ($M = 25.90$, $SD = 3.99$) and tactile stimuli presented on the non-painful knee ($M = 25.87$, $SD = 3.74$), $t(30) = 0.04$, $p = 0.97$.

PSS

The one sample *t*-test revealed that the average PSS value ($M = 1.93$; $SD = 26.98$) was not significantly different from the actual point of simultaneity (0), $t(30) = 0.40$, $p = 0.69^5$. Table 4 represents the PSS values for each patient individually.

Table 4

Single-subject PSS values (in ms). Positive values indicate that stimuli on the pain-relevant knee were prioritized, whereas negative values indicate that stimuli on the pain-irrelevant knee were prioritized.

Patient	PSS
1	2.83
2	-28.21
3	-4.26
4	3.25
5	60.20
6	-7.57
7	3.83
8	-34.35
9	-20.60
10	-76.05
11	2.58
12	-27.47
13	28.35
14	-19.02
15	-7.64
16	3.60
17	-1.90
18	16.00
19	3.71
20	20.02
21	22.24
22	-12.42
23	12.87
24	9.60
25	-16.39
26	60.26
27	8.44
28	49.15
29	7.10
30	4.65

⁵ When excluding the five left-handed patients (1 woman with right knee pain; 4 men from who 3 with left knee pain), the results remained the same, $t(25) = 0.39$, $p = 0.70$ ($M = 2.17$, $SD = 28.73$)

Correlations

Pearson correlations were calculated between self-reported measures of dispositional and situational bodily threat, and the TOJ outcome measure (PSS). Regarding threat value of the knee movements, an average score⁶ over the three questions (expectation, fear, avoidance) was individually calculated, separately for the *squat*, *duck walk* and *patella exercises*. An overview of all correlations is provided in Table 5. First, no significant correlations were observed between any of the self-report measures and prioritization of the pain-relevant knee (PSS). Second, a significant correlation was observed between the PCS and the threat value of the patella exercise. The more patients tended to have catastrophic thoughts about pain in general, the higher the threat value of the patella exercise. Last, the PCS was significantly positively correlated with the PVAQ and the BVS.

Table 5
Correlation coefficients.

	1	2	3	4	5	6	7
1. PSS	-	0.07	0.05	0.26	-0.04	0.02	-0.02
2. PVAQ		-	0.27	0.37*	0.09	-0.08	0.05
3. BVS			-	0.42*	0.17	0.20	0.27
4. PCS				-	0.04	0.28	0.47**
5. duck walk					-	0.22	0.26
6. squat						-	0.67**
7. patella exercise							-

Note. * $p < 0.05$, ** $p < 0.01$

Discussion

The present study aimed at examining the top-down prioritization of somatosensory sensations at a pain-relevant bodily location in individuals experiencing clinical pain. A sample of patients with unilateral (sub)acute knee

⁶ Results remained the same when the maximum score over the three questions was calculated instead of the average score

pain was selected to take part in the experiment. Tactile stimuli were presented on both knees with a variable inter-trial-interval and participants judged which tactile stimulus had been presented first. In order to induce anticipation of pain, patients were led to believe that at the end of the experiment, they would have to execute several exercises, which were thought to be stressful for the knee. It was expected that patients would be more quickly aware of somatosensory sensations at the pain-relevant knee than at the other knee. The results, however, revealed that tactile sensations at the pain-relevant knee were not prioritized, indicating no support for our hypothesis. Moreover, no significant positive associations were observed between prioritization of the pain-relevant knee and any of the self-report measures of dispositional, neither situational, bodily threat.

With respect to these results, we wish to point out that when observing the single-subject PSS data, there was considerable inter-individual variability in displaying the attentional prioritization effect. A number of possible explanations for this heterogeneity could be discussed. First, the possibility arises that theoretically relevant moderators, such as bodily threat appraisal might play a crucial role. Given the presence of bodily threat appraisal in several theoretical models attempting to explain pain perception and pain-related disability (Eccleston & Crombez, 2007; Sullivan, Rodgers, & Kirsch, 2001; Vlaeyen & Linton, 2000), it may be assumed that the prioritization of somatosensory sensations on the pain-relevant bodily location might be more pronounced in individuals who have the tendency to experience bodily sensations as threatening. However, no significant positive associations between pain-related prioritization and dispositional bodily threat appraisal (assessed by PCS, PVAQ, and BVS) were found. With regard to situational bodily threat, it might be expected that patients who found the knee movements more threatening would display a larger attentional prioritization effect, but such effect did not emerge from the data. Importantly, since the results of the self-report measures indicated that the average level of bodily threat appraisal of performing the knee exercises was rather low, we might speculate that these knee movements were not as stressful in this sample as we might have expected. Second, due to the lack of specificity of the knee pain problem, a diversity of pain diagnoses could be observed (e.g. chondromalacia patellae syndrome, i.e. inflammation of the underside of the patella; patellofemoral pain syndrome, i.e. pain originating from the contact of

the posterior surface of the patella with the thigh bone; iliotibial band syndrome). This heterogeneity may have had an influence on the effects, but the small sample size rendered further examination of this issue in the present study impossible. Third, in previous studies that investigated the effect of anticipating *experimental* pain on the attentional prioritization of a particular body part in healthy volunteers, the intensity of painful stimuli was determined for each participant individually, such that all participants perceived the pain as equally intense. Since the intensity of clinical pain is often more variable from moment to moment and differences in pain intensity appear between individuals with similar pain complaints, experimental control over pain intensity is lacking in this study. Overall, a more systematic approach is needed to further examine the possible explanations for the heterogeneity of the prioritization effect in the current study.

There is some evidence for the idea that the perception of non-painful tactile stimuli at the affected body part is less accurate in pain patients. It has already been shown that somatosensory perception may be reduced by actual pain, either experimentally (Apkarian, Stea, & Bolanowski, 1994; Bolanowski, Maxfield, Gescheider, & Apkarian, 2000) or chronic (Moseley, 2008). Such decrease of sensitivity for somatosensory information in the affected region may have interfered with the possible prioritization effect on the painful body part. Though, in our study, this might be less likely to have an influence on the results, as the perceived stimulus intensities at both tactor locations were individually matched by means of a double random staircase procedure, in order to maximize the chance that the tactile stimuli were perceived as equally intense on both knees. The results of the self-report measures indeed showed that there were no differences in perceived tactile intensities between the painful and non-painful knee.

One important issue deserves further consideration. According to the neurocognitive model of attention to pain (Legrain et al., 2009), top-down attentional prioritization is driven by one's current worries and concerns, as these might have an influence on which features might become activated in the attentional set. We assumed such worries and concerns to be present in our sample of knee pain patients, especially because we attempted to maximize situational bodily threat by letting them expect to have to perform stressful knee movements. One plausible explanation why the results did not support our

hypothesis, could be that the pursued goals or concerns of (sub)acute knee pain patients were not sufficiently related to pain, in order to activate pain-related features in their attentional set. Pain-related attention has been proposed to be malleable by current goal focus (Durnez & Van Damme, 2015; Van Damme et al., 2010). For instance, Schrooten and colleagues (2012) demonstrated that attention to pain-related cues was inhibited when participants were engaged in the pursuit of another salient but non-pain goal. Since the majority of the patients in our sample are active individuals who frequently practice sports, it is not unlikely that they were strongly focused on non-pain goals, such as the good accomplishment of the task, which might have reduced attention effects. Different effects may be found in more chronic pain populations with higher levels of disability and a stronger focus on pain-related goals. Finally, most patients reported that their pain symptoms only emerge in particular situations, such as running and climbing stairs. This underlines the importance of contextual factors, and urges investigation of attentional prioritization in more ecologically valid situations.

It should be noted that the present study has some limitations. First, we did not recruit a matched control group. Although there is no reason to believe that healthy controls would demonstrate prioritized attention to one of the knees, future studies are recommended to include a matched control group. Second, although prior to the start of the experiment, the perceived stimulus intensities at both tactor locations were individually matched by means of a staircase procedure, we observed that during the course of the experiment, participants reported the perceived intensity of tactile stimuli on the right knee as more intense than on the left knee, regardless of the affected knee. This might have affected how often participants reported 'left-knee-first' and 'right-knee-first', although this could not have systematically biased the results because there was a fairly equal proportion of patients with pain on the left knee and on the right knee. Last, because the sample size of the present study was rather small, it is possible that small and medium effects remained undetected.

The current findings provided insights in whether attention may influence the processing of information on the painful knee. In sum, the present study did not support the hypothesis that patients with unilateral knee pain would prioritize somatosensory sensations at the painful knee than on the non-painful

knee. Before any firm conclusions can be drawn, however, future research is needed to investigate the attentional prioritization of somatosensory sensations in more ecologically valid situations.

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Keeping pain in mind: investigating hypervigilance for somatosensory sensations in patients with chronic unilateral orofacial pain¹

Abstract

It is often assumed that chronic pain patients are characterized by hypervigilance, or heightened attentional processing, of painful and/or somatosensory information, but convincing evidence is currently lacking. This study aimed investigating whether patients with chronic unilateral temporomandibular joint dysfunction (TMD), i.e. pain on one side of the orofacial region, prioritized somatosensory sensations on the painful orofacial region compared to the non-painful orofacial region. For this purpose we developed a Temporal Order Judgment (TOJ) task in which participants judged which one of two tactile stimuli, presented on each jaw, had been stimulated first. We report three studies. As a first step, we conducted two pilot experiments in undergraduate students (experiment 1) and healthy volunteers from the general population (experiment 2) to test whether threat of experimental pain on one side of the jaw resulted in attentional prioritization of tactile stimuli on that side of the jaw. Next we investigated whether the presence of unilateral pain on one side of the jaw in a sample of TMD patients resulted in prioritized somatosensory processing on that side of the jaw, in comparison with a matched healthy control sample without pain on the jaw (experiment 3). The results of the pilot studies displayed the hypothesized pattern, although statistical significance was only obtained in the first experiment. Results of experiment 3 did not statistically confirm the hypothesis of prioritized somatosensory processing on the affected side of the jaw, despite scores on self-reported pain vigilance being higher in TMD patients than in healthy controls. Possible explanations for these findings, as well as suggestions for further research are discussed.

¹ Vanden Bulcke, C., Crombez, G., Van den Berghe, L. & Van Damme, S. (in preparation). Keeping pain in mind: investigating hypervigilance for somatosensory sensations in patients with chronic unilateral orofacial pain.

Introduction

Chronic pain, defined as pain that has lasted longer than three months, is a highly prevalent global health problem. Chronic pain can take both a physical and emotional toll on the individual (Krismer & Van Tulder, 2007), and may furthermore have major personal impacts (e.g. through work absenteeism, see Dagenais, Caro, & Haldeman, 2008). Unfortunately such pain often remains medically unexplained, and there is increasing consensus that psychosocial variables may play an important role in the initiation and maintenance of chronic disability (Gatchel, Peng, Peters, Fuchs, & Turk, 2007). One such psychosocial factor is attention. The importance of attentional processes has increasingly been highlighted in attempting to explain amplified pain perception, disability and distress in chronic pain sufferers (Crombez, Van Damme, & Eccleston, 2005; Legrain et al., 2009; Sullivan, Rodgers, & Kirsch, 2001; Vlaeyen & Linton, 2000). Attentional prioritization of pain and pain-relevant information is, intrinsically, an adaptive mechanism, fulfilling a protective function (Eccleston & Crombez, 1999). According to the neurocognitive model of attention to pain (Legrain et al., 2009), such attentional prioritization of pain and pain-related information is driven by the current concerns or goals of the individual, and occurs through the activation of the attentional set, i.e. the set of stimulus features that participants keep in working memory to identify goal-relevant information. All stimuli that are relevant to one's current concerns or goals, will be more likely to be selected for further processing (Legrain et al., 2009; Van Damme, Legrain, Vogt, & Crombez, 2010). When the current concerns or goals of an individual are pain-related, the expectation of pain may activate pain-related features in the attentional set, resulting in the prioritization of stimuli that share features with pain, such as its location.

In chronic pain patients, the interplay between pain and attention does no longer fulfill a protective function, but rather represents a maladaptive condition with devastating effects on quality of life. It is typically assumed that chronic pain patients are characterized by hypervigilance, or excessive attentional processing, of painful and/or somatosensory information. Individuals who appraise bodily sensations as dangerous and who have more fearful beliefs for possible (re)injury, are thought to be more likely to scan the body for threatening sensations (Vlaeyen & Linton, 2000). Despite its potential utility, many studies failed to detect

differences in attentional allocation to pain and somatosensory input between chronic pain patients and healthy volunteers (Peters, Vlaeyen, & van Drunen, 2000; Peters, Vlaeyen, & Kunnen, 2002; Tiemann et al., 2012; Van Damme, et al., in press). Yet, previous studies largely neglected the potential importance of the *specific body location* of somatosensory input. According to the attentional set hypothesis, somatosensory stimulation is expected to be prioritized especially when it occurs at a pain-relevant bodily location, as such input would match an important feature of pain, i.e. its bodily location.

In this respect, the attentional set idea might provide us fruitful new insights and allow developing interesting new hypotheses concerning hypervigilance in chronic pain patients. It might be assumed that chronic pain patients maintain features of excessive somatosensory expectations for the pain-relevant bodily location within their attentional set. Consequently, it is more likely that bodily sensations presented on the pain-relevant location will be prioritized, as these match with their attentional set features. For example, imagine a person with low back pain, who recently recovered from a serious back injury. Being fearful of re-injury, this person might continuously scan the back in order to detect signals of potential harm. As such, features of excessive somatosensory sensations on the pain-relevant body part (back) might become activated in the attentional set. Stimuli that share one or more features defined by the attentional set, might be prioritized by attention. It is likely that this individual might become more quickly aware of somatosensory sensations at the painful region compared to a pain-irrelevant region.

The aim of the present study was to investigate hypervigilance in chronic pain patients within the context of the attentional set hypothesis. Three experiments were reported here in which participants made judgments regarding which of two tactile stimuli administered to each orofacial region had been presented first (Temporal Order Judgment; TOJ). In the first experiment, we tested whether the paradigm was feasible to investigate attentional prioritization processes on the jaw. It was examined in undergraduate students whether experimentally induced bodily threat on the jaw resulted in the prioritization of tactile stimuli on that orofacial region. While performing the TOJ task, participants were led to expect a painful stimulus on one jaw (threat trials) or no painful stimulus (control trials). In line with previous studies (Vanden Bulcke,

Van Damme, Durnez, & Crombez, 2013; Vanden Bulcke, Crombez, Spence, & Van Damme, 2014), it might be expected that in threat trials, participants become more rapidly aware of tactile stimuli presented on the threatened jaw than on the other jaw. In a second experiment, the same approach was used in a group of healthy volunteers from the general population with an age ranging between 18 and 65 years, to determine whether the paradigm was feasible in non-student populations. In the third and last experiment, we examined somatosensory hypervigilance in patients with unilateral chronic temporomandibular joint dysfunction (TMD), i.e. chronic unilateral pain in the orofacial region. A sample of TMD patients and a matched sample of healthy volunteers performed a tactile TOJ on the jaws, without any experimental pain induction. Hypervigilance in TMD patients should be reflected by prioritization of tactile stimuli in the pain-relevant compared to the pain-irrelevant region of the body. As such, we expected that TMD patients might become more quickly aware of tactile sensations presented on the painful jaw compared to the non-painful jaw, whereas such effect was not expected in the group of healthy controls.

Experiment 1

Method

Participants

Twenty-four undergraduate students (all female; mean age = 20.04 years; all white Caucasian) participated to fulfill course requirements. All of the participants had normal or corrected-to-normal vision and normal hearing. All but three of the participants reported being right-handed. The participants rated their general health on average as 'very good' and none of the participants reported to have a current medical or mental disorder. Although a student group is often described as healthy, pain can be a prevalent symptom amongst this group, and is therefore best documented. Nineteen of the participants reported having experienced pain during the last six months (average of 17.72 days in 6 months). Seven of these participants reported feeling pain at the moment of testing, but the average rating of the intensity of this pain was low ($M=1.86$, $SD=1.07$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'.

All of the participants gave their informed consent and were free to terminate the experiment at any time should they so desire. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experimental session lasted for approximately 1 hour.

Apparatus and stimulus material

Tactile stimuli (10 ms duration; 200Hz) were presented by means of two resonant-type tactors (C-2 TACTOR, Engineering Acoustics, Inc., Florida, <http://www.eaiinfo.com/>) consisting of a housing of 3.05 cm diameter and 0.79 cm high, with a skin contactor of 0.76 cm diameter. Prior to the start of the experiment, the perceived stimulus intensities at both tactor locations were individually matched (Weinstein, 1968). This was done by means of a double random staircase procedure, based on the 'simple up-down method' of Levitt (Levitt, 1971). In a first phase, 24 stimuli presented on the left jaw were judged relative to a reference stimulus, which was defined as the maximum intensity (power = 0.21 Watt) on a 5-point Likert scale ranging from 1 ('no sensation') to 5 ('maximum intensity'). The intensity that elicited an averaged rating of 3 was used as the stimulus intensity for the left jaw, and was the reference stimulus for the second phase. In the second phase, 24 stimuli on the right jaw were judged relative to the reference stimulus on the left jaw on a 5-point Likert scale (1 = 'much weaker', 2 = 'weaker', 3 = 'equally strong', 4 = 'stronger', 5 = 'much stronger'). The intensity that elicited an averaged rating of 3 was used as the intensity of the stimulus at the right jaw.

Painful stimuli were electrocutaneous stimuli delivered by constant current stimulators (Digitimer DS5 2000, Digitimer Ltd, England, <http://www.digitimer.com/index.htm>). They consisted of trains of 20 ms sinusoid pulses with a frequency of 50 Hz, and were delivered via two lubricated Fukuda standard Ag/AgCl electrodes (1 cm diameter) for 200 ms. The intensity of the electrocutaneous stimuli was determined for each participant individually by means of a random staircase procedure. For each jaw, on the superficial head of the musculus masseter, 20 electrocutaneous stimuli were presented to participants (starting intensity between 0 and 1.5 mA) and self-reports were collected on an 11-point Likert scale (0 = 'no sensation'; 10 = 'unbearable pain'). The pain intensity that elicited an average rating of 7 was selected as the pain

stimulus for the main experiment (Arntz, Dreessen, & De Jong, 1994; Vanden Bulcke, et al., 2013).

The task was programmed and controlled by the INQUISIT Millisecond software package (Inquisit 3.0, Millisecond Software LLC, Seattle, WA, <http://www.millisecond.com/>) on a laptop (Dell Vostro 3550).

Tactile Temporal Order Judgment paradigm

In a TOJ task (Piéron, 1952), two tactile stimuli were administered, one on either jaw, separated by one of 10 randomly assigned stimulus onset asynchronies (SOAs) ranging from -120 to 120 ms (-120, -60, -30, -15, -5, +5, +15, +30, +60, +120 ms; negative values indicate that the left jaw was stimulated first) (see also Vanden Bulcke et al., 2013). The participants were instructed to report aloud, the jaw on which the tactile stimulus was presented first, and the experimenter registered the answers using a keyboard. There were two different types of trials (control vs. threat trials) based on the color of the cue. More specifically, a trial started with a fixation cross (1000 ms) in the middle of the screen, followed by a colored cue (either blue or yellow, of 1000 ms duration), indicating whether or not a painful electrocutaneous stimulus could follow on one jaw (control vs. threat trials). Which color of cue was associated with threat was counterbalanced across participants. Before the start of each block of trials, the participants were told on which location (left or right jaw) they should expect the painful stimulation to be delivered. In 10% of the threat trials, the pain stimulus was actually delivered instead of the two tactile stimuli (pain trials), but the participants were not informed about this contingency (see Figure 1). The participants were informed that no response had to be given in such trials.

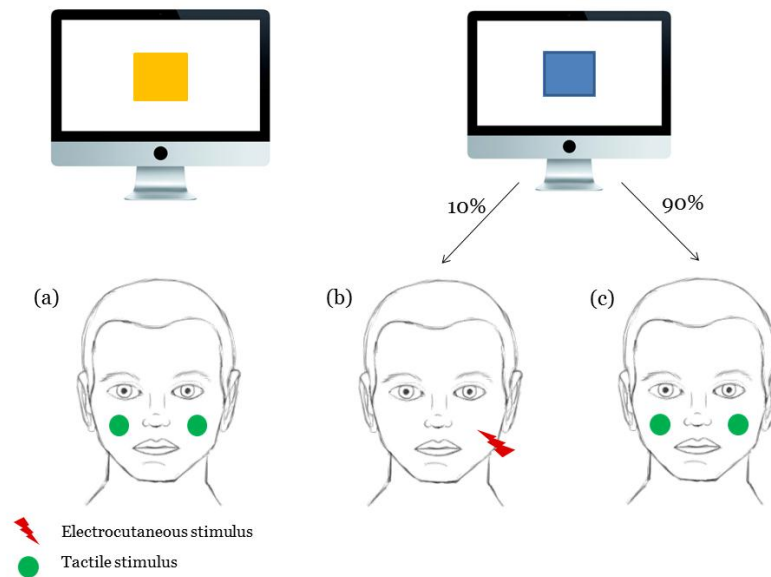


Figure 1. Experimental setup with (a) example of a control trial (b) example of a threat trial in which the electrocutaneous stimulation was presented on the right jaw and (c) example of a threat trial without electrocutaneous stimulation.

Self-report measures

After each test phase, the participants had to rate several questions about concentration (“To what extent have you made an effort to perform this task?”, “To what extent did you concentrate on this task?”), attention to painful/tactile stimuli (“To what extent did you pay attention to the painful/tactile stimuli?”), pain experience (“How painful did you find the electrocutaneous stimuli?”), anxiety (“How anxious were you during this block?”), fatigue (“To what extent did you find this task tiring?”) on eleven-point numerical rating scales (anchored 0 = not at all and 10 = very strongly). As a manipulation check, we were especially interested in the participant’s ratings of fear (“To what extent were you afraid that a painful stimulus would be administered by the blue/yellow cue?”) and expectations (“To what extent did you expect that a painful stimulus would be administered by the blue/yellow cue?”). The participants were also asked to complete the Pain Vigilance and Awareness Scale (PVAQ) (McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002) and the Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove, 2002). These data were collected for meta-analytical purposes and are not reported in detail here.

Procedure

Upon arrival at the laboratory, the participants received the task instructions and were told that an electrocutaneous stimulus would be used during the experiment and that “most people find this kind of stimulation unpleasant” (Crombez, Eccleston, Baeyens, & Eelen, 1998; Van Damme, Crombez, & Eccleston, 2004). After the participants had given their written informed consent, they were seated in front of the experimental apparatus. Their forearms were positioned symmetrically on the table. The tactors were placed in the middle of the superficial head of the *musculus masseter* of each jaw. The two electrodes were attached beside the tactors on the jaw. To visualize the *musculus masseter*, participants were asked to put their teeth together. The skin at the electrode sites was first abraded with a peeling cream (Nihon Kohden, Tokyo, Japan) to reduce the resistance of the skin. The participants were informed that they have to decide on each trial which stimulus had been presented first. The accuracy of participants’ responses was emphasized, rather than the speed. Participants wore headphones (Wesc, Conga) during the experiment. Pink noise (42.2 dB) was presented continuously through headphones to mask the noise resulting from the operation of the tactors. The participants were not given any feedback about their performance.

The session began with a practice block of twenty-three trials (1 trial per SOA for control trials; 1 trial per SOA for threat trials; 3 pain trials). Following this, four blocks of 105 trials (5 trials per SOA for control trials; 5 trials per SOA for threat trials, 5 pain trials) were presented. The experimental pain side (left or right jaw) was counterbalanced between participants.

Results

Self-report data and manipulation check

Participants reported being more afraid during the threat trials ($M = 5.86$, $SD = 2.69$) than during the control trials ($M = 0.12$, $SD = 0.24$) ($t_{18} = 9.49$, $p < 0.01$; $d = 2.18$ [95% CI: 1.36, 3.01]). Furthermore, the participants expected a painful electrocutaneous stimulus more during the threat trials ($M = 6.30$, $SD = 2.36$) than during control trials ($M = 0.28$, $SD = 0.55$) ($t_{18} = 11.24$, $p < 0.01$; $d = 2.58$ [95% CI: 1.64, 3.51]). Finally, the participants rated the electrocutaneous

stimuli as moderately painful ($M = 5.82$, $SD = 2.04$). Mean questionnaire scores were 8.42 ($SD = 6.09$) for the PCS and 38.42 ($SD = 7.88$) for the PVAQ.

TOJ data handling

In a TOJ task, it is common practice (Shore, Gray, Spry, & Spence, 2005; Spence, Shore, & Klein, 2001) to exclude those participants from statistical analysis when (1) any of the PSS values is greater than the highest SOA (± 120 ms) tested, (2) participants have less than 80% accuracy on the trials with the largest SOA tested (± 120 ms). Four participants (women, all right-handed) had to be excluded for the first reason, one participant (woman, right-handed) for the second reason. Trials following trials with electrocutaneous stimulation were removed from data analysis to avoid the possibility that (1) potential effects would be mainly driven by trials directly following painful stimulation or (2) after-effects of pain would interfere with the tactile TOJ (max. 10% of all trials).

The analyses were based on the procedure that has been commonly described in the literature (Shore, et al., 2005; Spence, et al., 2001; Van Damme, Gallace, Spence, Crombez, & Moseley, 2009). The proportions of 'left-jaw-first' and 'right-jaw-first' responses for threat presented on the left and right side, respectively, for all trials at each SOA, were converted into the corresponding z-scores using a standardized cumulative normal distribution. The best-fitting straight line was computed for each participant and the derived slope and intercept values were used to compute the point of subjective simultaneity (PSS). The PSS refers to the point at which observers report the two events (right jaw first and left jaw first) equally often. This is commonly taken equivalent to the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time and such equivalent to the SOA value corresponding to a proportion left/right jaw first responses of 0.5. The PSS is computed as the opposite of the intercept divided by the slope from the best-fitting straight line. The sign of the PSS in which threat was presented on the right jaw was reversed. Subsequently, for each participant the final PSS values were calculated by taking the average of the PSS values for threat presented on the left side and the reversed PSS values for threat presented on the right side. Hence, a positive value indicated that the stimulus contralateral to the side of threat had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS means

that stimuli on the threatened jaw are perceived more rapidly than stimuli on the other jaw. In sum, the PSS provides information concerning biases in spatial attention resulting from the presentation of bodily threat. A repeated measures analysis of variance (ANOVA) with the factors Cue (within; threat versus control), and Pain Side (between; left versus right) was performed on the PSS. For ease of comparison with the norms of Cohen (Cohen, 1988), we calculated effect sizes for independent samples using the formula of Dunlap and colleagues (Dunlap, Cortina, Vaslow, & Burke, 1996). We determined whether Cohen's d was small (0.20), medium (0.50), or large (0.80) (Cohen, 1988). We also report the 95% confidence intervals (95% CI) of the effect sizes.

PSS

The main effect of Cue was significant ($F(1,17) = 8.97, p < 0.01$), with threat trials ($M = 24.83$ ms, $SD = 22.16$) showing a larger PSS than control trials ($M = 10.56$ ms, $SD = 16.26$) ($d = 0.71$ [95% CI: 0.21, 1.21]) (see Figure 2). The main effect of Pain Side was not significant ($F(1,17) = 0.33, p = 0.58, d = 0.21$ [95% CI: -0.66, 1.07]), meaning that, on average, the PSS was similar when experimental pain was presented on the left jaw ($M = 20.04$; $SD = 24.15$) as compared to the right jaw ($M = 15.59$; $SD = 16.89$). None of the interactions were significant.

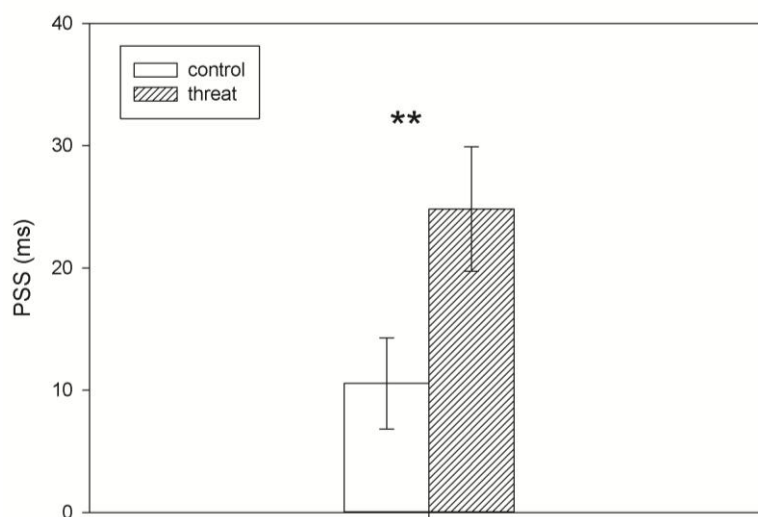


Figure 2. Index for attentional prioritization (PSS) (in ms and with standard errors) in control and threat trials for experiment 1. Positive values indicate that stimuli on the threatened jaw were perceived more rapidly than those presented to the other jaw, whereas negative values indicate that stimuli on the neutral jaw were perceived more rapidly than those presented to the threatened jaw (** $p < 0.01$).

Interim discussion

The results of the first experiment demonstrated that when participants made judgments regarding which of two tactile stimuli had been presented first, stimuli presented on the side of the jaw on which pain was expected were perceived more rapidly than stimuli presented on the other jaw. Thus, when participants anticipated pain at one jaw, they became more quickly aware of innocuous somatosensory sensations in that jaw. These findings are in line with previous studies showing somatosensory prioritization of body locations where pain is anticipated (Vanden Bulcke et al., 2013; 2014). In addition, the findings are the first to demonstrate a bodily threat induced attentional prioritization effect in the orofacial region, and thus show that such effect is not limited to clearly spatially separated joints (hands, arms, legs).

It is generally known that a student group is not representative for the general population. Furthermore, the paradigm should be suitable to use in chronic pain patients, entailing a broader range of the population (e.g., more variable age range) as compared with a more homogeneous student group. Importantly, previous studies have already shown that adults have more difficulties in performing cognitive tasks (e.g. Craik, 1994; Grady & Craik, 2000; Salthouse, 1996). For these reasons, we conducted a second experiment, in which the same hypothesis as in experiment 1 was tested, but now within a sample of healthy volunteers from the general population with an age ranging between 18 and 65 years. In order to make the TOJ task less difficult for an adult population, the range of SOAs was enlarged to a minimum of 10 ms and a maximum of 200 ms (-200, -90, -55, -30, -10, +10, +30, +55, +60, +200 ms; see Shore et al., 2005 for similar SOAs).

Experiment 2

Method

Participants

Healthy volunteers from the general population were recruited by means of a database (<http://www.healthpsychology.ugent.be/vrijwilligers/>). Participants who wish to participate on scientific studies could register on this website.

Potential participants were contacted by the researcher who provided more details about the study. Twenty-one healthy volunteers participated in the experiment. One participant (female, 29 years old) was excluded, due to poor performance. The mean age of the 20 remaining participants (all female; 19 right-handed) was 41.9 years (ranging from 25 to 60 years). All of the participants had normal or corrected-to-normal vision and normal hearing. The participants rated their general health on average as 'very good' and none of the participants reported having a current medical condition or mental disorder. Eleven of the participants reported having experienced pain during the last six months (average of 16 days in 6 months). Three of these participants reported feeling pain at the moment of testing, but the average rating of the intensity of this pain was low ($M = 2$, $SD = 1.73$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'. All of the participants gave their informed consent and were free to terminate the experiment at any time should they so desire. The study protocol was approved by the Ethics Committee of the Faculty of Psychology and Educational Sciences of Ghent University. The experimental session lasted for approximately 1 hour and the participants were given 20 euro in return for their participation.

Apparatus and stimulus materials

The same apparatus and stimulus characteristics were used as in Experiment 1.

Tactile Temporal Order Judgment paradigm

The task was identical to Experiment 1, with the exception that higher SOAs were used (-200, -90, -55, -30, -10, +10, +30, +55, +60, +200 ms; negative values indicate that the left jaw was stimulated first).

Self-report measures

The questionnaires and self-report measures were the same as in Experiment 1.

Procedure

The procedure was identical to that used in Experiment 1.

Results

Self-report data and manipulation check

Participants reported to be more afraid during threat trials ($M = 3.41$, $SD = 2.58$) than during the control trials ($M = 0.25$, $SD = 0.64$) ($t_{19} = -4.50$, $p < 0.001$; $d = 1.12$ [95% CI: 0.55, 1.69]). Furthermore, the participants reported a higher expectation of a painful electrocutaneous stimulus during the threat trials ($M = 4.18$, $SD = 2.68$) than during the control trials ($M = 0.56$, $SD = 1.62$) ($t_{19} = -4.68$, $p < 0.001$; $d = 1.05$ [95% CI: 0.49, 1.61]). Finally, the participants rated the electrocutaneous stimuli as being moderately painful ($M = 4.85$, $SD = 2.12$). Mean questionnaire scores were 2.55 ($SD = 4.16$) for the PCS and 35.15 ($SD = 8.69$) for the PVAQ.

TOJ data handling

Exclusion criteria were the same as described in Experiment 1. One participant (female, right-handed) had an accuracy of less than 80% on those trials with the largest SOA tested (± 200 ms) and was therefore removed from data analysis.

PSS

Although the pattern of results was in the expected direction (see Figure 3), the main effect of Cue was not significant ($F(1,18) = 2.53$, $p = 0.13$, $d = 0.36$ [95% CI: -0.09, 0.81]), meaning that on average, there was no significant difference in PSS values between threat ($M = 15.13$ ms, $SD = 39.51$) and control trials ($M = 5.68$ ms, $SD = 34.98$). The main effect of Pain Side was not significant ($F(1,18) = 0.69$, $p = 0.42$, $d = 0.34$ [95% CI: -0.51, 1.18]), meaning that, on average, no significant differences in PSS values appeared when bodily threat was presented on the left jaw ($M = 16.93$; $SD = 46.34$) as compared to the right jaw ($M = 3.88$; $SD = 24.38$). None of the interactions were significant.

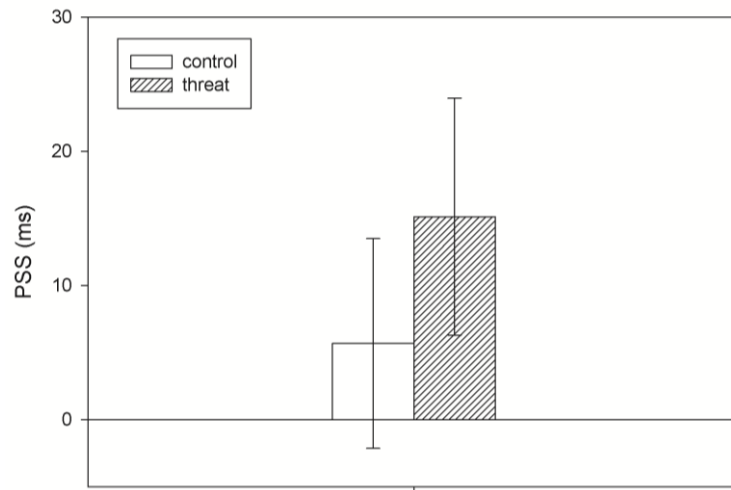


Figure 3. Index for attentional prioritization (PSS) (in ms and with standard errors) in control and threat trials for experiment 2. Positive values indicate that stimuli on the threatened jaw were perceived more rapidly than those presented to the other jaw, whereas negative values indicate that stimuli on the neutral jaw were perceived more rapidly than those presented to the threatened jaw.

Interim discussion

In the second experiment, we adapted the range of SOAs (-200, -90, -55, -30, -10, +10, +30, +55, +60, +200 ms) and conducted the experiment with healthy volunteers from the general population with an age ranging between 18 and 65 years. Only one participant had to be excluded for not attaining performance criteria, which indicates that the TOJ task with a larger range of SOAs is feasible to test hypervigilance in a non-student population. Furthermore, the data of the second experiment were in line with the hypothesized effect and followed the pattern of findings of experiment 1. Though, the results did not reach statistical significance. It must however be noted that in the second experiment, large standard deviations were observed, which were twice as high than standard deviations found in the first experiment. This points to the fact that there is a lot of inter-individual variability in displaying the threat-related prioritization effect for somatosensory sensations in healthy volunteers from the general population.

To test whether chronic pain patients might be characterized by hypervigilance, a third study was conducted with TMD patients, i.e. patients with a chronic unilateral pain problem on the orofacial region. Experimental pain was no longer induced, since we assumed that the clinical problem would be sufficient to activate the affected location in the attentional set.

Experiment 3

Participants

TMD patients were recruited through the department of dentistry of Ghent University Hospital. Inclusion criteria included a diagnosis of unilateral chronic TMD (longer than 3 months) determined by the dentist, an age between 18 and 65 years, and Dutch speaking. Potential participants were informed about the possibility of participating by means of a flyer and information given by their dentist. When they agreed to participate, they received a phone call from the researcher providing more detailed information about the study. Twenty-one patients participated in the experiment. Later on, one woman (40 years, right-handed) was excluded from analysis because she reported to have fibromyalgia, i.e. chronic widespread pain. The age of the remaining 20 participants TMD patients (17 females) was 36.8 years (SD = 11.6, range = 22-59 years). The TMD group included both people who have only had one consultation (70%), as persons who already were treated for a longer period (30%). The mean duration of the treatment for this second group was 14 months (SD = 11.3 months, range 4-36). Most TMD patients were married or lived together with their partner (65%), the other ones were singles (20%) or widowed (15%). 60% of the TMD patients finished their studies at the high school or university. The others have an education level not higher than the secondary school (40%). Three patients were not able to work anymore due to their pain symptoms and received a monthly allowance. Nine patients (45%) reported having pain symptoms other than orofacial pain at the moment of testing, but the average rating of the intensity of the pain for these nine participants was low ($M = 3.67$; ranging from 1 to 7, $SD = 2.12$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'. Furthermore, patients reported a mean pain level of 1.90 ($SD = 1.12$), assessed by means of the pain severity subscale of the Multidimensional Pain Inventory (MPI-DV; Kerns, Turk, & Rudy, 1985).

The patient group was matched for age, sex and educational level with a control group of healthy volunteers. The control participants were recruited by means of a database (<http://www.healthpsychology.ugent.be/vrijwilligers/>). Participants who wish to participate in scientific studies of the Ghent Health Psychology Research Group could register on this website. Potential participants

were contacted by the researcher who provided more details about the study. Inclusion criteria for the control participants were the absence of chronic pain complaints or neurological or psychiatric conditions, Dutch speaking, and an age between 18 and 65 years. Twenty-one healthy volunteers were willing to participate. One men (23 years, right-handed) was excluded for further analysis due to not attaining performance criteria. The age of the remaining 20 participants was 36.9 years (range 20-63 years; SD = 13.9). Most of the control participants were single (60%), the other ones were married (20%) or in a relationship (20%). 55% of the control participants finished their studies at the higher education institute or university. The others have an education level not higher than the secondary school (45%). Although a control group is often described as healthy, pain can be a prevalent symptom among this group and is therefore best documented. Eighteen of the participants reported having experienced pain during the last six months (average of 19 days in 6 months). Seven of the participants reported feeling pain at the moment of testing, but the average rating of the intensity of the pain for these seven participants was low ($M = 2.57$; ranging from 1 to 5, $SD = 1.40$) on a Likert scale where 0 indicated 'no pain' and 10 'worst pain ever'. Furthermore, control participants reported a mean pain level of 1.07 ($SD = 1.13$), assessed by means of the pain severity subscale of the Multidimensional Pain Inventory (MPI-DV, Kerns, Turk, & Rudy, 1985). The study was approved by the Medical Ethical Committee of the Ghent University Hospital. At the end of the experiment, all participants received 25 Euro as reimbursement for their expenses. The experimental session lasted for approximately 1 hour and a half. A detailed overview of the demographic characteristics is provided in Table 1.

Statistical analyses showed no significant differences in the average number of men and women between both groups, $\chi^2(1) = 0.00$, $p < 0.001$, nor in average age between both groups, $t(38) = -0.03$, $p = 0.98$. Furthermore, there was no significant difference between both groups with regard to profession, $\chi^2(7) = 6.11$, $p = 0.41$ and educational level, $\chi^2(3) = 0.69$, $p = 0.87$. Both groups significantly differed with regard to family status, $\chi^2(3) = 8.44$, $p = 0.04$, and in mean pain level, $t(38) = 2.34$, $p = 0.02$.

Table 1
Demographic characteristics of the patient and control group.

	TMD patients		Control group	
	M ± SD	N (%)	M ± SD	N (%)
Men		3 (15%)		2 (10%)
Women		17 (85%)		18 (90%)
Age (in years)	36.8 ± 11.66 (range 22-59)		36.9 ± 13.90 (range 20-63)	
Family situation				
single		4 (20%)		12 (60%)
living together		5 (25%)		4 (20%)
married		8 (40%)		4 (20%)
widow(er)		3 (15%)		0
Educational level				
primary education		0		0
lower secondary education		2 (10%)		1 (5%)
higher secondary education		6 (30%)		8 (40%)
higher education		4 (20%)		4 (20%)
higher education: university		8 (40%)		7 (35%)
Profession				
housemen/housewife		1 (5%)		1 (5%)
laborer		2 (10%)		0
employee		10 (50%)		10 (50%)
professional		0		0
senior manager		0		1 (5%)
disabled		3 (15%)		1 (5%)
student		4 (20%)		5 (25%)
job seeker		0		2 (10%)
Number of consultations				
first consultation		14 (70%)		
several consultations		6 (30%)		
duration of treatment (months)	14 ± 11.3 (range 4-36)			
Pain severity (MPI-PS)	1.90 ± 1.12 (range 0-4.33)		1.07 ± 1.13 (range 0-4.33)	

Apparatus and stimulus materials

The same apparatus and stimulus materials for tactile stimulation were used as in Experiment 1 and 2. Experimental painful induction was not administered.

Tactile TOJ paradigm

Similar to the previous experiments, participants were instructed to report aloud the jaw on which the first tactile stimulus was presented. The SOAs that were used were the same as in Experiment 2 (-200, -90, -55, -30, -10, +10, +30, +55, +60, +200 ms; negative values indicate that the left jaw was stimulated first). A trial started with the presentation of a fixation cross (2000ms) in the middle of the screen. Following this, the two tactile stimuli were presented to each jaw. Participants wore noise-cancelling headphones (PXC 350 Sennheiser) in order to prevent any interference from environment noise.

Self-report measures

First, participants needed to fill in a general questionnaire including age, sex and education level. Furthermore, the MPI-DV, PVAQ, BVS and the PCS were completed by all participants, the TSK-TMD only by the patient group.

Participants pain prior to the experiment was assessed by means of the Dutch version of the Multidimensional Pain Inventory (MPI-DV, Kerns, et al., 1985). This questionnaire consists of 28 items rated on a 7-point scale measuring severity of the pain problem (e.g. *'Rate the level of your pain at the present moment'*), interference with daily-life activities (e.g. *'In general, how much does your pain interfere with your day-to-day activities?'*), perceived control (e.g. *'During the past week how much control do you feel you have had over your life?'*), affective anxiety (e.g. *'During the past week how irritable have you been?'*) and social support (e.g. *'How supportive or helpful is your significant other to you in your relation to your pain?'*). Only the pain severity subscale of the MPI (MPI-PS; three items) was reported in the study. Cronbach's alpha of the MPI severity subscale in this study was 0.73.

The Dutch version of the Pain Vigilance and Awareness Questionnaire (PVAQ, McCracken, 1997; Roelofs, et al., 2002) constitutes of 16 items that represent two subscales: 'attention to pain' (e.g. *"I focus on sensations of pain"*) and 'attention to changes in pain' (e.g. *"I quickly realize when pain gets worse or*

less worse”). This questionnaire assesses the frequency of behavior of the past two weeks and is scored on a 6-point scale ([1 = “never”, 5 = “always”]). The PVAQ shows a good internal consistency between both subscales ‘attention to pain’ and ‘attention to changes in pain’ (Cronbach’s alpha is 0.83, 0.85 and 0.80 respectively). The PVAQ has been shown to be valid and reliable in both healthy populations and chronic pain patients (Roelofs et al., 2002, Roelofs, Peters, McCracken, & Vlaeyen, 2003). Cronbach’s α of the PVAQ in this study was 0.92.

The Body Vigilance Scale (BVS; Schmidt, Lerew, & Trakowski, 1997) is a four-item questionnaire measuring on a 11-point numerical rating scale the degree of attentional focus to bodily sensations (e.g., *‘I am the kind of person who pays close attention to internal bodily sensations’* [0 = “not at all like me, 10 = extremely like me]), perceived sensitivity to changes in bodily sensations (e.g., *‘I am very sensitive to changes in my internal bodily sensations’* [0 = “not at all like me, 10 = extremely like me]) and the average amount of time spent attending to bodily sensations (*‘On average, how much time do you spend each day ‘scanning’ your body for sensations’* [0 = “no time”, 10 = “all of the time”]). The last item is an average of the awareness scores of 15 non-specific body symptoms (e.g., *‘Rate how much attention you pay to each of the following ... heart palpitations, dizziness, nausea, ... sensations’* [0 = “none”, 10 = “extreme”]). Cronbach’s α of the BVS in this study was 0.91.

The Dutch version of the Pain Catastrophizing Scale (PCS-DV; Sullivan et al., 1995; Van Damme et al., 2002) measures the degree of pain catastrophizing, an exaggerated negative orientation to noxious stimuli. This questionnaire consists of 13 items rated on a 5-point scale measuring rumination (e.g., *‘I can’t stop thinking about how much it hurts’* [0 = “not at all”, 10 = “all the time”]), magnification (e.g. *‘I am afraid that something serious might happen’* [0 = “not at all”, 10 = “all the time”]) and helplessness to manage the pain (e.g. *‘There is nothing I can do to reduce the intensity of my pain’* [0 = “not at all”, 10 = “all the time”]). Cronbach’s α of the PCS in this study was 0.94.

The Tampa Scale for Kinesiophobia for Temporomandibular Disorders (TSK-TMD; Visscher, Ohrbach, van Wijk, Wilkosz, & Naeije, 2010) consists of 12 items that need to be rated on a 4-point numerical rating scale [1 = “strongly disagree”, 4 = “strongly agree”]. The subscale ‘fear of movement’ (e.g. *‘I am afraid*

that I might injure myself if I move my jaw’) consists of 7 items, whereas the other subscale ‘Somatic focus’ (e.g. ‘If I would ignore my jaw complaints, then they would become worse’) consists of 5 items. Cronbach’s α of the TSK-TDM in this study was 0.81.

After each test phase, the participants had to rate several questions about concentration (‘To what extent have you made an effort to perform this task?’, ‘To what extent did you concentrate on this task?’), attention to tactile stimuli (‘To what extent did you pay attention to the tactile stimuli?’), intensity of the tactile stimuli (‘How intense did you experience the stimuli on your left/right jaw?’), pain experience (‘How painful did you find the task?’), anxiety (‘How anxious were you during this block?’), fatigue (‘To what extent did you find this task tiring?’) on eleven-point numerical rating scales (anchored 0 = not at all and 10 = very strongly).

Procedure

The procedure was identical to the one used in Experiment 1 and 2. Upon arrival at the laboratory, participants first needed to fill in a few questionnaires (see self-reported measures). Following this, the session began with a practice block of twenty trials (2 trials per SOA). Next, four blocks of 70 trials (7 trials per SOA) were presented.

Results

Self-report data

Table 2 represents the average scores and standard deviations for the self-reported measures for both TMD patients and healthy controls.

Independent samples *t*-tests revealed that the TMD group ($M = 43.80$, $SD = 13.16$) had significantly higher scores on the PVAQ as compared to the control group ($M = 31.55$, $SD = 16.24$; $t(38) = 2.62$, $p = 0.01$; $d = 0.83$, 95% CI [0.18, 1.47]). No significant differences between both groups were found on the Body Vigilance Scale ($t(38) = 0.69$, $p = 0.50$; $d = 0.22$, 95% CI [-0.40, 0.84]) and the Pain Catastrophizing Scale ($t(38) = 0.55$, $p = 0.58$; $d = 0.17$, 95% CI [-0.45, 0.80]). The mean questionnaire score for the TSK-TMD was 24.75 ($SD = 6.44$, range 14-40).

Table 2
Average and standard deviation of self-report measures among participants for each group.

	TMD pain patients	Control group
Body Vigilance Scale	51.70 ± 23.11 (range 18-112)	45.60 ± 32.15 (range 0-115)
Pain Catastrophizing Scale	18.35 ± 13 (range 0-44)	16.25 ± 10.99 (range 3-40)
Pain Vigilance Awareness Questionnaire	43.80 ± 13.16 (range 13-63)	31.55 ± 16.24 (range 0-56)
TSK-TMD	24.75 ± 6.44 (range 14-40)	
Concentration	8.20 ± 1.57 (range 3-10)	8.01 ± 1.53 (range 3-10)
Fear during experiment	1.19 ± 2.27 (range 0-9)	1.55 ± 2.27 (range 0-9)

Regarding the ratings on the post questions, both groups did not significantly differ in the level of concentration ($t(38) = -0.42$, $p = 0.68$; $d = 0.13$, 95% CI [-0.48, 0.75] and fear during the experiment ($t(38) = 0.53$, $p = 0.60$; $d = 0.17$, 95% CI [-0.46, 0.79]). No significant differences appeared between the mean level of self-reported intensity of the tactile stimuli on the left jaw ($M = 3.95$, $SD = 2.02$) and the right jaw ($M = 4.01$, $SD = 2.10$) for the control group, $t(19) = -0.62$, $p = 0.54$. For the patient group, the mean level of self-reported intensity of tactile stimuli on the left jaw ($M = 5.04$, $SD = 2.23$) differed significantly from the mean level of self-reported intensity of tactile stimuli on the right jaw ($M = 5.84$, $SD = 1.99$), $t(19) = -3.06$, $p = 0.01$. Though, no significant differences appeared in perceived intensities between tactile stimuli presented on the painful jaw ($M = 5.56$, $SD = 2.02$) and tactile stimuli presented on the non-painful jaw ($M = 5.31$, $SD = 2.27$), $t(19) = 0.80$, $p = 0.44$.

TOJ data handling

Exclusion criteria were the same as for Experiment 2. One participant of the control group (male, right-handed) had an accuracy of less than 80% on those trials with the largest SOA tested (± 200 ms) and was therefore removed from data analysis.

PSS

The average PSS of TMD patients ($M = 17.59$, $SD = 41.51$) was positive, indicating biased attention towards the pain-relevant orofacial region, but did

only marginally differ from the actual point of simultaneity (0 ms), $t(19) = 1.90$, $p = 0.07$. In line with our hypothesis, the average PSS of healthy controls ($M = -0.12$, $SD = 27.40$) did not significantly differ from the actual point of simultaneity, $t(19) = -0.02$, $p = 0.98$. The average PSS was, however, not significantly larger in the patient group than in the healthy control group, despite a medium effect size, $t(38) = 1.59$, $p = 0.12$, $d = 0.50$, 95% CI [-0.13, 1.13] (see Figure 4).

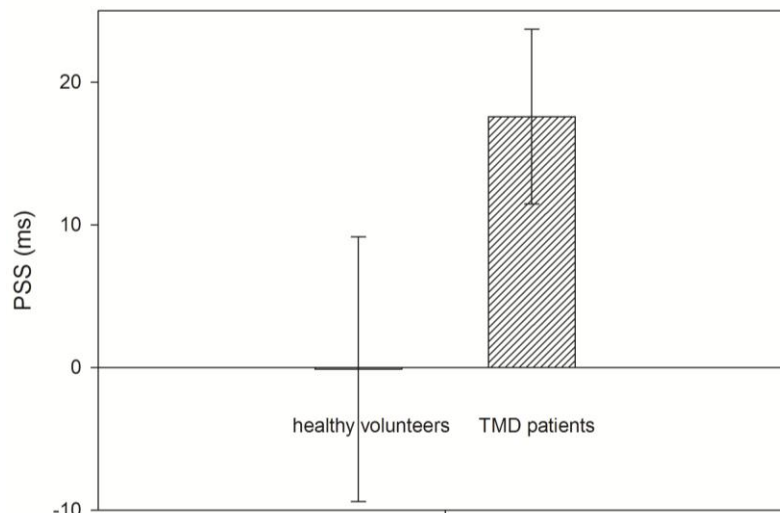


Figure 4. Index for attentional prioritization (PSS) (in ms and with standard errors) for healthy volunteers and TMD patients. In the patient group, positive values indicate that stimuli on the painful jaw were perceived more rapidly than those presented to the other jaw, whereas negative values indicate that stimuli on the non-painful jaw were perceived more rapidly than those presented to the painful jaw. In the control group, positive values indicate that stimuli on the left jaw were perceived more rapidly than those presented to the right jaw, whereas negative values indicate that stimuli on the right jaw were perceived more rapidly than those presented to the left jaw.

Correlations

Pearson correlations were calculated between self-report measures and the TOJ outcome measure (PSS) for the patient and the control group. An overview of all these correlations is provided in Table 3. First, scores on the PVAQ were positively associated with the PSS in the TMD patient group, although this relationship was only marginally significant. Second, a marginally significant relationship was observed between the PCS and the PSS in the matched control group. Last, there was a significant, positive relationship between the PCS and self-reported fear during the experiment in TMD pain patients. The higher the score on the PCS, the more TMD pain patients reported to be fearful during the experiment. None of the other correlations proved to be significant.

Table 3

Correlations between self-report measures and the TOJ outcome measure (PSS) for the TMD patient group and the control group.

	TMD patient group						Control group				
	1	2	3	4	5	6	1	2	3	4	5
1. PSS	-	-0.26	0.41 ^o	0.35	0.19	-0.02	-	0.08	0.05	0.41 ^o	0.25
2. BVS		-	0.00	0.20	0.07	0.05		-	0.21	0.22	-0.03
3. PVAQ			-	0.42	0.17	0.36			-	0.35	-0.12
4. PCS				-	0.46 [*]	0.43				-	0.06
5. fear					-	0.30					-
6. TSK-TMS						-					

Note. * $p < 0.05$, ^o $p < 0.10$

Discussion

Hypervigilance, i.e. heightened attentional processing, of pain and/or pain-related information is omnipresent in various theoretical models attempting to explain the experience of chronic pain. However, convincing evidence for the presence of hypervigilance in chronic pain patients is lacking. The current study aimed to investigate hypervigilance in chronic pain patients with unilateral TMD within the framework of the attentional set idea. It was assumed that chronic unilateral TMD pain patients have in their attentional set excessive somatosensory expectations for the pain-relevant location of the body, i.e. the affected jaw. Hypervigilance should be reflected by the prioritization of somatosensory sensations at the painful jaw compared to the non-painful jaw. A matched control group was expected not to display such effect. Beforehand, two pilot experiments were conducted to examine whether the TOJ paradigm was feasible to test attentional prioritization processes on the jaw in undergraduate students (Experiment 1) and in healthy volunteers from the general population (Experiment 2). Participants made temporal order judgments regarding tactile stimuli that were presented on each jaw. Crucially, they could expect a painful stimulus on one jaw (in accordance with the painful orofacial region of TMD patients; threat trials), or no painful stimulus was expected (control trials). The results in undergraduate students (Experiment 1) indicated that the anticipation of pain resulted in the prioritization of tactile stimuli on the threatened jaw compared to the other jaw. Although the results in healthy volunteers from the general population (experiment 2) followed the same pattern, they failed to reach statistical significance. Of particular interest to our hypothesis, the results of experiment 3 showed that the average PSS in TMD pain patients was positive, indicating biased attention towards the pain-relevant orofacial region, whereas such bias of attention was not found in the matched control group. Although these results were in line with our hypothesis, the PSS in TMD pain patients did only marginally differ from the actual point of simultaneity (i.e. 0 ms; point where no attentional bias is expected), and was not significantly larger than in the healthy controls.

The findings of the two pilot studies replicated the findings of previous experiments (Vanden Bulcke et al., 2013; 2014), demonstrating that

somatosensory sensations at a bodily location where experimental pain is expected were prioritized, although statistical significance was only obtained in the first experiment. The results not only confirm the robustness of the threat-related prioritization effect, but extend previous findings by demonstrating that the effect is not limited to clearly spatially distinguished joints such as the hands or arms.

Despite the fact that the data pattern of the TOJ task in experiment 3 was in line with our hypothesis, the results did not statistically support our hypothesis that differences in attentional prioritization of the painful jaw would be observed between patients with unilateral chronic pain and healthy controls. Though, our results were not so remarkable as previous studies also failed to detect differences in attention to pain and pain-related information between chronic pain patients and healthy volunteers. Peters and colleagues operationalized hypervigilance as the detection of weak electrical stimuli in combination with a second attention-demanding task, and assumed that hypervigilance for somatosensory sensations should be reflected by the allocation of attention on the detection task. The results revealed no indication for hypervigilance for non-noxious somatosensory signals in fibromyalgia patients (Peters et al., 2000) and patients with chronic low back pain (Peters et al., 2002) in comparison to control subjects. Likewise, other studies showed that patients with fibromyalgia consider themselves hypervigilant towards pain and pain-related information as compared to healthy controls, but this was not confirmed by the results of behavioral measures (Tiemann et al., 2012; Van Damme et al., in press). Though, in these studies, the importance of the specific body location of somatosensory input was largely neglected.

Interesting are the findings of the self-report measures in experiment 3, demonstrating that the mean level of self-reported hypervigilance for pain, assessed by the PVAQ, was significantly higher for chronic unilateral TMD pain patients as compared to healthy controls, thereby replicating the results of several other studies in patients with chronic fibromyalgia (Crombez, Eccleston, Van den Broeck, Goubert, & Van Houdenhove, 2004; Peters et al., 2000; Roelofs et al., 2003; Tiemann, et al., 2012; Van Damme et al., in press). Though, self-reported measures were proven less adequate to examine hypervigilance (e.g., Crombez et al., 2004), since the continuous presence of pain in chronic pain patients might rather reflect the presence of multiple somatic complaints than an excessive

attentional focus on these sensations, which might confound the self-reported scores (Crombez, Eccleston, Van den Broeck, Goubert, & Van Houdenhove, 2004). Therefore, it is recommended to rely on behavioral measures that are less susceptible to report bias.

One can question whether chronic pain patients are actually characterized by hypervigilance as most of previous research found no consistent differences in excessive attentional processing of pain-related information between patients and controls. However, several important issues should be clarified in future research before firm conclusions can be drawn. Most importantly, we observed substantial individual differences in displaying the prioritization effect of somatosensory sensations at the threatened or painful orofacial region. Two plausible explanations for this heterogeneity can be put forward. First, a look at the standard deviations in experiment 2 and experiment 3 showed that the standard deviations of TMD patients and those of healthy volunteers were much larger than the one's observed in the more homogeneous group of undergraduate students. We may assume that other relevant variables, such as bodily threat appraisal (e.g. catastrophic thoughts about pain, pain-related fear) might play an important role in the top-down attentional prioritization of somatosensory sensations at the threatened/painful region of the body. Several theoretical models (Eccleston & Crombez, 2007; Vlaeyen & Linton, 2000) have highlighted the importance of bodily threat appraisal in the facilitation of pain-related information. Yet, it might be hypothesized that the prioritization of somatosensory sensations on the threatened/painful region of the body might only emerge in individuals who have the tendency to experience bodily sensations as threatening. Correlational analyses between self-reported bodily threat appraisal (catastrophic thoughts about pain, vigilance to pain) and the TOJ outcome measure (PSS), confirmed that in TMD pain patients, the PVAQ was positively related to the attentional prioritization effect on the affected orofacial region, although this relationship was only marginally significant. Though, it must be noted that a marginally significant and positive relationship between the PSS and PCS was also found in the matched control group: the more healthy volunteers catastrophize about their pain, the more they prioritized somatosensory sensations on the right jaw. Further research is needed to allow a reliable interpretation concerning the effect of individual differences. Second,

with regard to the chronic pain group, the duration of the treatment individually differed. This might play a mediating role to what extent bodily threat appraisal might influence the prioritization of somatosensory sensations on the painful bodily location. Previous research has already demonstrated that the phase of treatment in which the patient was currently situated was an important indicator for experiencing catastrophizing thoughts (Brown et al., 1993). Specifically, it might be that chronic pain patients in a later phase of the treatment experienced less catastrophic thoughts, since the positive influence of psycho-educational advices given by the dentist. Unfortunately, the sample size of the patient group was too low to differentiate individuals based on the duration of their treatment.

Another important issue that needs further consideration is the assumption that hypervigilance may vary depending on the context. In our pilot studies, the anticipation of pain was experimentally induced by means of phasic experimental pain stimuli. In experiment 3, we hypothesized that individuals experiencing clinical pain may have thoughts or concerns related to their pain problem, which in turn might have resulted in the spontaneous activation of pain-related features concerning the painful bodily location in the attentional set of pain patients. As such, we expected that bodily sensations on the pain-relevant location would be prioritized. Though, it is plausible that we might have overestimated the impact of clinical pain in chronic pain patients as a trigger for the activation of pain-related features in the attentional set. It might be that a situation without an active anticipation of pain is not experienced as threatening for TMD pain patients. In consequence to this, features in the attentional set might not be (sufficiently) activated, which in turn might have resulted in the absence of the prioritization of somatosensory sensations on the painful orofacial region. Self-reported measures indeed demonstrated that the mean level of pain at the moment of testing for the patient group was rather low and patients appeared not to be more fearful during the experiment than controls. Future research is recommended in which a threatening context is induced for chronic pain patients, such as requiring TMD patients to perform movements with their mouth (e.g. biting into an apple).

It is certainly worth mentioning that our study marks a shift in the operationalization and conceptualization of hypervigilance, by taking into account limitations of previous studies. It is of critical importance that

hypervigilance is not confused with other central mechanisms that account for hyperalgesia, allodynia, and hyperresponsivity (Crombez et al., 2005, González et al., 2010; Hollins et al., 2009; Maixner, Fillingim, Booker, Sigurdsson, 1995; Maixner, Fillingim, Sigurdsson, Kincaid, & Silva, 1998). Therefore, it is necessary to demonstrate that *cognitive attentional* processes are involved. As such, hypervigilance in our study was operationalized as the prioritization of attention to certain (pain-related) information. Furthermore, concerning the operationalization of hypervigilance, most studies have been limited to paradigms measuring *visual* attention, i.e. the measurement of attention to pain-related visual stimuli such as words, pictures, or conditioned cues (for a review, see Van Damme et al., 2010) and paradigms using reaction times as outcome measure. First, the use of pain-related words as valid pain stimuli has been questioned, as these are only semantic representations of pain which are barely capable of activating bodily threat (Crombez et al., 2000). Second, reaction times as outcome measure for attentional bias are believed to be not sufficiently suitable in clinical pain populations, as these populations are typically characterized by slower response speed or delayed psychomotor movements (Van Damme, Crombez, & Notebaert, 2008). Our study offers an important benefit in respect to these previous studies since we made use of a somatosensory paradigm that focused on accuracy rather than on response speed.

The present study has a number of limitations that the reader should be made aware of. First, it should be noted that the sample size of our experiment 2 and experiment 3 was rather low, resulting in the detection of large effects, but leaving undetected differences with small and even medium effect size. Second, unilateral TMD pain patients are only a subgroup within the group of chronic pain patients, and one might ask whether the same results might occur in other unilateral chronic pain populations. It should certainly be interesting for further research to investigate this phenomenon in chronic pain patients with different unilateral pain problems, to increase the generalizability of our findings. Last, although TMD pain is more usually unilateral than bilateral, our findings are only applicable to TMD patients experiencing pain on one side of the face which limits the generalizability to the entire population of TMD pain patients.

In conclusion, chronic pain patients with unilateral TMD reported to be more attentive for pain and pain-related information than matched controls.

Although the data of the somatosensory paradigm was in line with the hypothesized effect that differences in attentional prioritization of the painful jaw would be observed between chronic unilateral pain patients and healthy controls, the results did not reach statistical significance. Further research is needed that will examine hypervigilance in more ecologically valid situations.

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Part III

Is threat-related attentional prioritization more pronounced in individuals with a tendency to experience bodily sensations as threatening?¹

Abstract

This paper reports secondary analyses on a set of our previous published and unpublished studies in which it was demonstrated that the expectation of pain at a particular location of the body resulted in the prioritization of somatosensory input at that threatened bodily location. Because within each study, substantial inter-individual variability was observed, the main objective was to investigate whether this heterogeneity could be accounted for by differences in bodily threat appraisal, both in a general trait-like manner (pain catastrophizing and hypervigilance) and in an experiment-specific state-like manner (fear and expectation of painful stimulation). Both data of the self-report measures and the behavioral measure of threat-related prioritization (Temporal Order Judgment (TOJ) task) were merged and analyzed across studies. Correlational analyses demonstrated no significant associations between threat-related prioritization effects and trait-like bodily threat variables. Significant positive associations between prioritization of the threatened location and state-like bodily threat appraisal were found for the threat trials. When we performed a regression analysis controlling for trait bodily threat and prioritization of the threatened location in neutral trials, however, these associations were no longer significant. Implications for the theoretical framework in which top-down threat-related attentional prioritization of somatosensory sensations is supposed to be driven by bodily threat appraisal are discussed, as well as methodological issues in assessing threat-related somatosensory prioritization.

¹ Vanden Bulcke, C., & Van Damme S. (unpublished manuscript). Is threat-related attentional prioritization more pronounced in individuals with a tendency to experience bodily sensations as threatening?

Introduction

The top-down modulation of attentional capture by pain is assumed to be driven by threat appraisal, that is, one's current beliefs and/or cognitions about bodily threat. According to the neurocognitive model of attention to pain (Legrain et al., 2009), pain-related information might be prioritized or inhibited by attention, driven by the current concerns or goals of the individual. Habits to attend to bodily sensations in general, fear of pain and catastrophic thoughts about pain are likely to shape such concerns, which in turn might influence top-down facilitation of pain-related stimulus features. The idea that bodily threat appraisal modulate pain-related attention is central in several pain theories (Crombez, Van Damme, & Eccleston, 2005; Sullivan, Rodgers, & Kirsch, 2001; Van Damme, Legrain, Vogt, & Crombez, 2010; Vlaeyen & Linton, 2000).

The majority of experimental research that examined the effect of individual differences in bodily threat appraisal (e.g. catastrophic thoughts about pain, vigilance to pain, pain-related fear) on pain-related attention has focused on top-down *inhibition*, more specific the ability to direct attention away from pain (distraction). For example, Van Ryckeghem Crombez, Van Hulle and Van Damme (2012) showed that people who initially experienced pain as more severe benefited less from a distraction task during pain. Crombez, Eccleston, Baeyens, and Eelen (1998a) and Van Damme, Crombez, and Eccleston (2004a; 2004b) showed that individuals with a higher level of pain catastrophizing had more difficulties in disengaging from pain. Moreover, in a study of Verhoeven and colleagues (2010), it was shown that distraction effects were influenced by the level of catastrophic thinking about pain. For low catastrophizers, executing a distraction task while experiencing pain, resulted in less pain as compared to a control group (to which no distraction task was given). Though, for high catastrophizers, executing a distraction task while experiencing pain, resulted in less pain, only when the distraction task was motivationally relevant (e.g. receiving a monetary reward for good task performance). Increasing the motivational relevance of the distraction task increased the effects of distraction, especially for high pain catastrophizers.

Considerably less studies have investigated the influence of individual differences in bodily threat appraisal on top-down attentional *facilitation/prioritization* of pain and pain-related information (e.g. Van Damme,

et al., 2004a; 2004b). A series of studies reported in this PhD thesis has investigated the effect of threat of pain at a particular location of the body on somatosensory processing at that location. A robust finding across all the studies in healthy volunteers was a threat-induced attentional prioritization of somatosensory sensations at the anticipated pain location. Nevertheless, within each study, substantial inter-individual heterogeneity was observed in displaying this threat-related prioritization effect. Therefore, the aim of the present study was to investigate whether individual differences in bodily threat appraisal (e.g. pain catastrophizing, vigilance to pain and pain-related fear) might account for the inter-individual variability in displaying the threat-related attentional prioritization effect that was observed in our previous described studies. We explicitly differentiated between *trait-related* bodily threat appraisal (i.e. individual differences in the disposition to perceive bodily sensations as threatening) and *state-related* bodily threat appraisal (i.e. situation-specific; individual differences in bodily threat appraisal in the specific context of the experiment).

All studies of this PhD thesis in which *healthy* volunteers performed a *tactile* TOJ task and in which pain expectation was experimentally induced at one of the locations where tactile stimuli were presented, were selected for secondary analyses. Both data of self-reported state-related and trait-related (Pain Catastrophizing Scale; PCS; Sullivan et al., 1995; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove, 2002; Pain Vigilance and Awareness Questionnaire; PVAQ; McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002) bodily threat appraisal, together with the behavioral measure of threat-related prioritization (TOJ task) were merged and analyzed across studies. We expected that if individual differences in bodily threat appraisal played a role in the threat-related attentional prioritization of somatosensory sensations in healthy volunteers, there would be positive associations between our behavioral and self-report measures.

Method

Inclusion criteria²

The following criteria were used to select the data for the analysis:

- 1) Studies performed with healthy volunteers, i.e. conditions in which one location was threatened by occasionally inducing painful stimulation, the other location was unthreatened
- 2) Conditions consisting of *tactile* temporal order judgments
- 3) Conditions in which “*normal*” body postures were adapted, i.e. the left side of the body operating in the left side of space and the right side of the body operating in the right side of space
- 4) Conditions with SOAs ranging from -120 ms to 120 ms (-120, -60, -30, -15, -5, +5, +15, +30, +60, +120 ms)
- 5) Conditions where the painful stimulation was occasionally induced at one of the locations where tactile stimuli were presented

Based on these criteria, the following data were included in the analysis.

- Experiment of chapter 1: full data
- Experiment 1 of chapter 2: only the two trial types (control and threat) in which painful stimuli were occasionally presented on the hand
- Experiment 2 of chapter 2: only the two trial types (control and threat) in which painful stimuli were occasionally presented on the hand
- Experiment chapter 3: only the two trial types (control and threat) in which tactile temporal order judgments were performed
- Pilot experiment with undergraduate students of chapter 5: full data

The remaining data were excluded for the analysis:

- Experiment 1 of chapter 2: the two trial types (control and threat) in which tactile stimuli (hand) were presented on a different location than the painful stimuli (arm)
- Experiment 2 of chapter 2: the two trial types (control and threat) in which tactile stimuli (hand) were presented on a different location than the painful stimuli (leg)

² All of these criteria were selected to obtain consistency over studies.

- Experiment chapter 3: the two trial types (control and threat) in which visual temporal order judgments were performed
- Experiment 1 of chapter 4: all data: conditions where arms were crossed over the midline were excluded for analysis. Painful stimuli were occasionally presented on the arm which was a different location than the location where the tactile stimuli were presented (hand). As such, uncrossed hands conditions were also removed from analysis.
- Experiment 2 of chapter 4: all data: similar reasons as experiment 1 of chapter 2
- Pilot experiment with healthy volunteers of chapter 5: the SOAs that were used (-200 ms to 200 ms) were different from the SOAs (-120 ms to 120 ms) included as a criteria for analysis.

TOJ paradigm

In the TOJ task (Piéron, 1952), two tactile stimuli were administered, on two different bodily locations, separated by one of 10 randomly assigned stimulus onset asynchronies (SOAs) ranging from -120 to +120 ms (-120, -60, -30, -15, -5, +5, +15, +30, +60, +120 ms; negative values indicate that the left side was stimulated first). The participants were instructed to report aloud the location on which the first tactile stimulus was presented, and the experimenter registered the answers using a keyboard. A trial started with the presentation of a fixation cross (1000 ms) in the middle of the screen, followed by a colored cue (either blue or yellow, of 1000 ms duration), indicating whether or not a painful stimulus could follow on one specific location (threat and control trial, respectively). Which color of cue was associated with threat was counterbalanced across the participants. Before the start of each block of trials, the participants were told on which bodily location they should expect the painful stimulation to be delivered. In 10% of the threat trials, the pain stimulus was actually delivered instead of the two tactile stimuli (pain trials), but the participants were not informed about this contingency. The participants were informed that no response had to be given in such trials.

The TOJ outcome measure, that is the Point of Subjective Simultaneity (PSS), refers to the point at which observers report the two events (right hand first and left hand first) equally often. This is commonly taken to be equivalent to

the (virtual) SOA at which participants perceive the two stimuli as occurring at the same time and such equivalent to the SOA value corresponding to a proportion of left/right hand first responses of 0.5. We recoded the PSS so that a positive value indicated that the stimulus contralateral to the side of threat had to be presented first in order for both stimuli to be perceived as simultaneous. As a result, a positive PSS indicates that stimuli on the threatened bodily location are perceived more rapidly than those presented to the other location. In sum, the PSS provides information concerning biases in spatial attention resulting from the presentation of bodily threat.

Self-report measures

Two questionnaires assessing trait-related bodily appraisal, i.e. individual characteristics to perceive bodily sensations as threatening, such as catastrophic thinking about pain (PCS) and vigilance to pain (PVAQ) were included in the analysis. Furthermore, self-reported scores on questions about fear and expectations in the specific context of the experiment (state-related bodily threat appraisal) were also taken into account in the analysis.

The Dutch version of the Pain Vigilance and Awareness Questionnaire (PVAQ, McCracken, 1997; Roelofs, et al., 2002) contains 16 items rated on a 6-point scale measuring self-reported vigilance for pain sensations (e.g. *'I focus on sensations of pain'* [1 = "never", 5 = "always"]). The PVAQ has been shown to be valid and reliable in both healthy populations and chronic pain patients (Roelofs et al., 2002, Roelofs, Peters, McCracken, & Vlaeyen, 2003).

The Dutch version of the Pain Catastrophizing Scale (PCS-DV; Sullivan et al., 1995; Van Damme et al., 2002) measures the degree of pain catastrophizing, an exaggerated negative orientation to noxious stimuli. This questionnaire consists of 13 items rated on a 5-point scale measuring rumination (e.g., *'I can't stop thinking about how much it hurts'* [0 = "not at all", 10 = "all the time"]), magnification (e.g. *'I am afraid that something serious might happen'* [0 = "not at all", 10 = "all the time"]) and helplessness to manage the pain (e.g. *'There is nothing I can do to reduce the intensity of my pain'*[0 = "not at all", 10 = "all the time"]).

Ratings of fear and expectations were calculated based on the questions 'To what extent were you afraid that the blue/yellow cue would be followed by a

painful stimulus?’ and ‘To what extent did you expect that the blue/yellow cue would be followed by a painful stimulus?’ respectively. Participants had to fill in these questions on an eleven-point numerical rating scale (anchored 0 = not at all and 10 = very strongly) after each test phase.

Results

Data- analysis and self-reported data

The PSS scores for threat and control trials were obtained for each individual of the selected studies. Furthermore, a PSS difference score which provides information of the threat bias, was calculated for each individual in each study. The PSS difference score was obtained by subtracting the PSS in control trials from the PSS in threat trials. Table 1 provides an overview of the PSS values and standard deviations for control trials, threat trials and PSS difference scores, averaged amongst participants for each selected study together with the corresponding Cohen’s *d* effect size and 95% confidence intervals (CI) of the effect sizes (Cohen, 1988).

Table 1

*Average PSS values and standard deviations among participants for control and threat trials, PSS difference scores and corresponding Cohen’s *d* effect sizes and confidence intervals for the effect sizes for each study.*

Study	N	PSS control	PSS threat	PSS difference	Effect size and 95% CI
Chapter 1	20	8.71 ± 11.15	25.37 ± 20.48	16.66 ± 23.91	<i>d</i> = 0.70 [0.21-1.19]
Chapter 2: experiment 1	29	9.49 ± 25.30	22.78 ± 29.64	13.28 ± 26.16	<i>d</i> = 0.51 [0.12-0.89]
Chapter 2: experiment 2	31	0.24 ± 27.31	13.96 ± 31.43	13.73 ± 24.37	<i>d</i> = 0.56 [0.18-0.94]
Chapter 3	31	-0.49 ± 20.69	11.71 ± 31.90	12.20 ± 35.10	<i>d</i> = 0.35 [-0.01-0.71]
Chapter 5	19	10.56 ± 16.26	24.83 ± 22.16	14.26 ± 20.12	<i>d</i> = 0.71 [0.21-1.21]
All data	130	4.94 ± 22.16	18.73 ± 28.65	13.79 ± 26.76	<i>d</i> = 0.51 [0.33-0.70]

Figure 1 represents an overview of the inter-individual variability of the attentional prioritization effect across all selected studies. Data were plotted as the PSS for threat trials (in which participants occasionally expected a painful stimulus; y-axis), as a function of the PSS for control trials (in which no painful stimulation was expected; x-axis) for each individual of the selected studies. Positive PSS values indicate that stimuli on the threatened bodily location were perceived more rapidly than stimuli on the neutral bodily location, indicating a bias of attention towards the threatened body part. Based on the ideal scenario of the threat-related prioritization effect, we expected that in most individuals the PSS in control trials should fluctuate around zero, whereas the PSS in threat trials should be positive (bias towards threat), indicated as the red line in Figure 1.

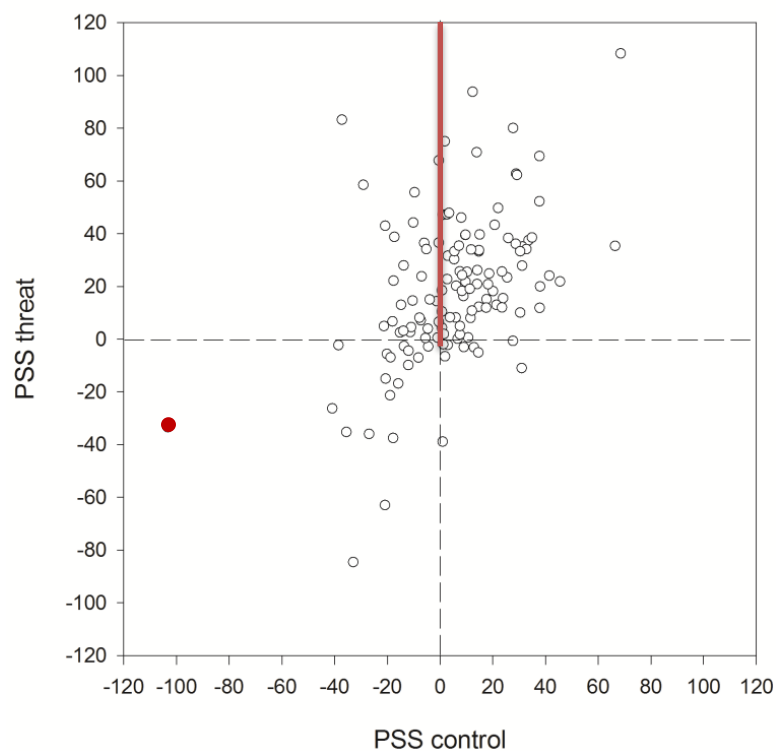


Figure 1. Representation of the inter-individual variability of the attentional prioritization effect across all selected studies ($N = 130$). We expect that in most individuals the PSS in control trials should fluctuate around zero, whereas the PSS in threat trials should be positive (bias towards threat). According to our interpretation of the threat-related prioritization effect, it is assumed that individuals display a prioritization effect when the PSS in threat trials is higher than the PSS in control trials. A person with a negative PSS threat score, but whose PSS control score is even more negative (e.g. see the red dot), might be interpreted as an outlier, although this person meets our criteria for displaying the prioritization effect.

The total sum score³ on the PCS and the PVAQ (trait-related bodily appraisal), together with expectation/fear scores for threat and control trials (state-related bodily appraisal) were obtained for each individual of the selected studies. Again, an expectation/fear difference score was calculated by subtracting the expectation/fear score in control trials from the expectation/fear score in threat trials. The expectation/fear difference score provides information concerning the expectation/fear of a painful stimulus on a particular bodily location. Average and standard deviation scores on self-report measures among participants for each study are provided in Table 2.

Table 2

Average and standard deviation of self-report measures among participants for each study.

Study	PCS	PVAQ	Expectation difference	Fear difference
Chapter 1	11.16 ± 10.90 (range 0-39)	36.30 ± 8.96 (range 17-52)	6.04 ± 1.77 (range 1.75-8.50)	5.81 ± 1.75 (range 1.75-9.00)
Chapter 2: experiment 1	9.90 ± 9.52 (range 0-47)	37.86 ± 8.18 (range 23-53)	5.09 ± 2.37 (range 1.25-9.00)	5.21 ± 2.44 (range 1.75-9.75)
Chapter 2: experiment 2	9.18 ± 7.55 (range 0-37)	33.10 ± 14.15 (range 1-54)	4.84 ± 2.13 (range 1.50-9.00)	4.80 ± 2.60 (range 0.50-8.75)
Chapter 3	6.25 ± 8.87 (range 1-23)	7.61 ± 40.84 (range 27-56)	5.04 ± 2.20 (range 1.25-9.75)	4.35 ± 2.39 (range 0.25-9.25)
Chapter 5	6.09 ± 8.42 (range 0-21)	38.42 ± 7.88 (range 27-54)	6.03 ± 2.34 (range 2.25-9.50)	5.74 ± 2.64 (range 0.25-9.50)
All data	8.95 ± 8.64 (range 0-47)	37.28 ± 10.13 (range 1-56)	5.20 ± 2.44 (range 1.25-9.75)	4.96 ± 2.67 (range 0.25-9.75)

Correlations

Correlational analyses over studies were performed between the PSS scores for threat and control trials and individual difference measures. An overview of these correlations is provided in Table 3. First, as expected, self-reported fear and expectation scores about the painful stimulation in threat trials were significantly and positively associated with the PSS in threat trials. Second, and contrary to our hypothesis, associations between trait-like bodily threat variables and the PSS in

³ Previous studies have demonstrated that the three latent factors of the PCS and the two latent factors of the PVAQ were moderately to highly correlated (Roelofs, Peters, Muris, & Vlaeyen, 2002; Van Damme, Crombez, Bijttebier, Goubert, Van Houdenhove, 2002). As such, total sum scores were used in the analysis.

threat trials were not significant. Third, there were several interesting correlations between self-report variables. The higher the score on the PCS, the more participants reported to expect and be more afraid of the painful stimulation in the threat trials. Surprisingly, there was also a significant positive association between the PCS and self-reported fear of pain in control trials, and between the PVAQ and expectation and fear scores in the control trials. Last, significant positive relations were observed between expectation scores in control/threat trials and fear scores in control/threat trials, as well as between the PSS in threat trials and control trials.

Table 3
Correlation coefficients.

	1	2	3	4	5	6	7	8
1. PSS control	-	0.44**	-0.04	0.01	-0.09	0.12	-0.10	0.12
2. PSS threat		-	0.08	0.05	-0.04	0.20*	-0.11	0.22*
3. PCS			-	0.12	0.13	0.29**	0.20*	0.39**
4. PVAQ				-	0.26**	0.11	0.22*	0.17
5. expectation control					-	0.11	0.79**	0.08
6. expectation threat						-	0.12	0.91**
7. fear control							-	0.10
8. fear threat								-

Note. * $p < .05$, ** $p < .01$

Regression analysis

A linear regression analysis was conducted with *PSS difference scores* as dependent variable. *PVAQ score*, *PCS score*, *Expectation difference score*, *Fear difference score* and *Study* were included as predictors. The categorical predictor *Study* was recoded into the respective dummy variables. Table 4 provides an overview of the standardized beta values, *t*-values and *p*-values of the regression analysis. The linear regression analysis showed that none of the variables was a

significant predictor, $F(8,121) = 0.45$, $p = 0.89$ (all $p > 0.05$) ($R = 0.17$, adjusted $R^2 = 0.03$).

Table 4
Standardized beta values, *t*-values and corresponding *p*-values for the linear regression.

	Beta value	T value	P value
PCS	0.069	0.725	0.470
PVAQ	0.005	0.057	0.954
Expectation difference score	-0.256	-1.080	0.282
Fear difference score	0.320	1.312	0.192
Study chapter 5	-0.023	-0.195	0.846
Study chapter 4	-0.029	-0.223	0.824
Experiment 2 chapter 2	-0.037	-0.287	0.775
Experiment 1 chapter 2	-0.060	-0.476	0.635

Discussion

It has repeatedly been demonstrated in this PhD thesis that the anticipation of a painful stimulus resulted in the prioritization of somatosensory sensations in the region of the body where healthy volunteers expect to feel pain. This threat-related prioritization effect appeared to be a robust finding when averaged across all studies. Nevertheless, a lot of inter-variability in PSS values within each experiment was observed. The main objective of this study was to investigate whether individual differences in trait-related (i.e. catastrophic thoughts about pain and vigilance to pain) and state-related (i.e. fear and expectations about the painful stimulation in the experiment) bodily threat appraisal might account for the inter-individual variability in the top-down prioritization of somatosensory sensations at a threatened body part. The data of all previous studies in which *tactile* temporal order judgments were performed and where painful stimulation was occasionally induced at one of the locations where tactile stimuli were presented, were selected for secondary analysis. Both data of the self-report

measures and the behavioral measure of threat-related prioritization (TOJ outcome measure) were merged and analyzed across studies. It was hypothesized that threat-related attentional prioritization effects would be positively associated with both trait and state bodily threat appraisal.

The findings of the correlational analyses revealed that state-related bodily threat appraisal was positively correlated with the PSS in threat trials. The more participants reported to be fearful and to expect the painful stimulation in threat trials, the higher the PSS in those trials. Nevertheless, the results of the regression analysis showed that when both threat and control trials for both types of threat appraisal as well as for the prioritization effects were taken into account, by means of the differences scores, neither state-related nor trait-related bodily threat appraisal was significantly related to the threat-related attentional prioritization effect. We may speculate about possible explanations for this finding. Important to note is that, for many individuals, the PSS in control trials differed from the actual point of simultaneity (0 ms), that is, the PSS in control trials did not fluctuate always around zero. In other words, even when participants were cued that no painful stimulus would follow, they perceived tactile stimuli on the threatened body part more rapidly than on the other body part, suggesting that also in these trials attention was prioritized –to some extent– to the threatened body part. This indicates that control trials were not for everyone considered as neutral, which implicates that some participants in a so called safe situation still fear that a painful stimulus would follow. This is confirmed by the statistically significant positive correlations between both PCS and PVAQ on the one hand, and self-reported expectation and fear in the control trials on the other hand. It is not unlikely that, due to the random order of control and threat trials within each block, prioritization of the threatened bodily location generalized, to some extent, to control trials. Note that there was a significant positive association between the PSS in threat and control trials. It may be interesting for future studies to use a block-wise manipulation of control and threat trials, and see if that might nullify the generalization effect observed here. Nevertheless, this generalization effect is an interesting phenomenon in its own right. Specifically, reduced ability to learn differentiating between threat and safety cues has been proposed to be a potential maintaining factor of pain-related disability (Moseley & Vlaeyen, 2015).

Despite the significant associations between state bodily threat appraisal and threat-related prioritization effects on the one hand, and between trait and state variables of bodily threat on the other hand, no significant associations between the trait-related bodily threat variables, i.e., pain catastrophizing and hypervigilance, and prioritization of the threatened body location in threat trials were found. We may speculate that a general tendency for catastrophic thinking about pain might indirectly influence the PSS in threat trials through increased fear for the painful stimulation during the experiment. The lack of effect of trait-related bodily threat appraisal is not in line with hypotheses drawn from current theoretical models (Crombez et al., 2005; Sullivan et al., 2001; Van Damme et al., 2010; Vlaeyen & Linton, 2000). Nevertheless, this finding is in line with a recent meta-analysis of Crombez, Van Ryckeghem, Eccleston and Van Damme (2013), who demonstrated that attentional bias to pain-related information was not significantly associated with individual differences in pain-related fear and catastrophizing about pain. Yet, we should be careful in comparing our experiments with the studies that were included in that meta-analysis. The meta-analysis was based on studies that used linguistic or pictorial stimuli whereas our studies made use of a somatosensory attentional paradigm. Despite this, the absence of robust correlations between individual differences in trait-related bodily threat appraisal and pain-related attention is remarkable. A possible explanation lies in the use of questionnaires. Scores on trait-related questionnaires such as the PCS depend on the ability to sufficiently and accurately remember the pain (Roelofs, Peters, Patijn, Schouten & Vlaeyen, 2004). When completing these questionnaires, healthy individuals who are not daily confronted with pain, must rely on memory of pain they have experienced in the past, possibly resulting in bias and inaccurate measurement. Furthermore, with regard to the PVAQ, Crombez, Eccleston, Van den Broeck, Goubert and Van Houdenhove (2004) believe that questionnaires querying attention to bodily sensations are often measuring the presence of physical symptoms rather than the attentional focus on these sensations. These arguments might suggest that scores on self-report measures as the PVAQ and the PCS might not provide a perfect reflection of individual characteristics in trait-related bodily threat appraisal. It might also be that there was too little dispersion regarding the scores on self-reported measures in healthy volunteers to detect reliable associations

between bodily threat appraisal and threat-related prioritization effects. With respect to these points, we may assume effects of trait-related bodily threat appraisal on pain-related attention to be more pronounced in individuals with clinical pain disorders. Although we have conducted two studies with pain patients, which are reported in this PhD thesis but were not included in this meta-analysis, sample sizes were too low to reliably draw conclusions concerning individual differences in bodily threat appraisal on the threat-related prioritization effect. It would be interesting to further explore the influence of bodily threat appraisal on the prioritization of somatosensory sensations at a pain-relevant bodily location in clinical pain populations.

Obviously, the current study is not without limitations. First, all studies that were included in the analysis are cross-sectional, thus causal effects cannot be determined. Second, not all data of the studies reported in this PhD thesis could be included in the analysis and only a limited number of questionnaires were administered. As such, this limits the generalizability of our results. Third, due to the experimental design we were only able to collect retrospective ratings of fear and expectation of pain after each block. Online ratings, or use of psychophysiological measures such as heart rate variability and skin conductance, may provide a more objective measure of bodily threat in the specific experimental context.

In conclusion, since the sample size of each study described in this PhD thesis was too low to allow reliable interpretation from an analysis of individual differences in bodily threat appraisal, we merged and analyzed both the data of the self-report measures and the behavioral measure of threat-related prioritization across all studies. Correlational analyses highlighted the importance of state-related bodily threat appraisal in the top-down threat-related attentional prioritization of somatosensory sensations. Though, future research on this issue is recommended to further explore whether top-down threat-related attentional prioritization of somatosensory sensations is driven by bodily threat appraisal.

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Preface

There is increasing evidence that psychological variables such as attention may play an important role in a better understanding of the experience of pain. The enhanced processing of pain-related information is intrinsically an adaptive mechanism which fulfills a protective function (Eccleston & Crombez, 1999). Despite its potential importance, studies that investigated this top-down attentional prioritization of pain and pain-related information are scarce. This doctoral dissertation provides new insights concerning pain-related attentional prioritization. According to the neurocognitive model of attention to pain (Legrain et al., 2009), current goals or concerns might direct attention through the activation of a set of stimulus features kept in mind (attentional set) to identify goal-relevant information. All stimuli relevant to one's current concerns/goals are believed to be facilitated by attention. Here, we assumed that the *expectation* of pain may activate *pain-related* features in the attentional set, resulting in the prioritization of stimuli that share features with pain, such as its spatial coordinates (location).

The aim of this PhD thesis was threefold. First, we aimed to investigate the effect of anticipating pain at a particular region of the body on the top-down prioritization of attention. Second, we tested the hypothesis whether patients suffering from pain at a specific body part prioritize bodily sensations at that specific location. Finally, we aimed to examine whether threat-related attentional prioritization of bodily sensations is more pronounced in individuals who have the tendency to experience bodily sensations as threatening. In this general discussion, the main research findings will first be highlighted, interpreted and integrated. Also theoretical and clinical implications of the current set of studies will be discussed. Finally, possible avenues for future research will be highlighted.

Main findings

In **part I**, we investigated in healthy volunteers the effect of expecting pain at a particular bodily location on the top-down prioritization of attention. In **chapter 1**, participants made tactile temporal order judgments of pairs of tactile stimuli presented to each hand. Occasionally, a painful stimulus was administered on one hand to induce bodily threat at one particular bodily location. It was found that tactile stimuli on the threatened hand were perceived earlier in time than stimuli on the other hand. This finding suggests that the anticipation of pain at a particular location of the body resulted in the prioritization in time of somatosensory sensations at that location, indicating biased attention toward the threatened body part.

In **chapter 2**, we tested whether the spatial features of bodily threat were limited to the exact location of pain. Two experiments were reported in which participants performed a tactile temporal order judgment (TOJ) task on the hands while occasionally experiencing a painful stimulus. The distance between the pain and tactile locations was manipulated (near: hand versus far: arm or leg). The results of both the near and far condition were in line with the results of chapter 1. We can conclude that in this study the encoding of spatial features of bodily threat was not limited to the exact location where pain was anticipated, but rather generalized to the entire body part and even to different body parts at the same side of the body.

In **chapter 3**, participants performed both tactile and visual TOJ tasks while expecting a painful stimulus on one of the hands or expecting no painful stimulus. With this study, we wanted to determine whether the threat-related prioritization effect was limited to somatosensory information or generalized to other sensory modalities. The results revealed that, while expecting pain, both tactile and visual stimuli were perceived more rapidly on the threatened hand than on the neutral hand. These findings suggest that attentional prioritization of the threatened location is not limited to the somatosensory modality, but rather is a multisensory phenomenon.

In **chapter 4**, the effect of threat of pain to one arm on somatosensory processing at the ipsilateral and contralateral hand was compared between two body postures: uncrossed versus crossed arms. This allowed us to investigate whether the threat-related prioritization effect was due to somatosensory input

occurring at the same body part as pain (somatotopic reference frame of threat localization) or rather because of corresponding spatial encoding of somatosensory input and pain, independent of the body part on which they occur (spatiotopic reference frame of threat localization). When arms were uncrossed, results were largely in line with previous findings. Yet, no threat-related prioritization effect was observed in the crossed arms condition.

In **Part II** two chapters were described in which the idea was investigated whether patients suffering from pain at a specific bodily location prioritized bodily sensations on the painful region of the body compared to the non-painful region of the body. The tactile TOJ task was performed in samples of unilateral (sub)acute knee pain patients (chapter 5) and patients with unilateral chronic temporomandibular joint dysfunction (TMD; chapter 6). In contrast to all previous studies of part I, no experimental pain was induced.

In **chapter 5**, the idea was tested whether the attentional prioritization of somatosensory sensations on a pain-relevant body part was also displayed in individuals experiencing clinical, “real-life” pain. Patients with (sub)acute unilateral knee pain performed temporal order judgments of tactile stimuli presented on each knee. In order to maximize threat, patients were led to believe that they would have to perform several stressful knee movements immediately after the task. We found no support for the hypothesis that patients would be more quickly aware of somatosensory input on the painful knee as compared to the pain-irrelevant knee, indicating no bias of attention toward the pain-relevant region of the body.

In **chapter 6**, chronic unilateral TMD pain patients and matched control participants engaged in a tactile TOJ task without the induction of experimental pain stimulation. Beforehand, two pilot studies in undergraduate students (experiment 1) and healthy volunteers from the general population (experiment 2) were conducted to test whether the TOJ paradigm was feasible to examine attentional prioritization processes on the jaw. Results of the pilot studies were in line with previous studies demonstrating the prioritized somatosensory processing on the threatened region of the body, although statistical significance was only obtained in the first experiment. Although the data of experiment 3 were in line with the hypothesized effect that differences in attentional prioritization of

the painful jaw would be observed between chronic unilateral pain patients and healthy controls, the results did not reach statistical significance.

In **part III**, one chapter is described (**chapter 7**), in which it was investigated whether the threat-related top-down attentional prioritization was more pronounced in individuals with the tendency to experience bodily sensations as threatening. Both data of the self-report measures and the behavioral measure of threat-related prioritization (TOJ task) were merged and analyzed across studies with healthy volunteers. Although correlational analyses demonstrated positive associations between prioritization of the threatened location and state-like bodily threat appraisal (i.e. fear and expectation of painful stimulation during the experiment for threat trials), these associations were no longer significant when performing a regression analysis controlling for trait bodily threat and prioritization of the threatened location in neutral trials.

Theoretical implications

Do healthy individuals prioritize information at the location of the body where experimental pain was expected?

In the first part of this PhD thesis it was aimed to systematically investigate the effect of *anticipating* pain at a particular region of the body on the top-down *prioritization* of attention. Recently, an increasing number of behavioral studies has investigated the effect of anticipating pain on the modulation of attention (Notebaert et al., 2011; Ploghaus et al., 1999; Porro et al., 2002; Schrooten et al., 2012; Spence, Bentley, Phillips, McGlone, & Jones, 2002; Van Damme, Crombez, & Eccleston, 2004b; Van Damme, Crombez, Eccleston, & Roelofs, 2004d; Van Damme, Crombez, Eccleston, & Koster, 2006). In the introduction of this doctoral dissertation, we proposed that if the scope of the neurocognitive model of attention to pain (Legrain et al., 2009) is broadened, it may allow us to develop several interesting new hypotheses. In its current form, the model only allows statements about the amount of attention allocated to *painful* stimuli. Expecting pain to occur, might induce thoughts or concerns that are related to pain, which in turn might activate *pain-related* features in the attentional set. We can elaborate the current view by assuming that also *non-painful* stimuli that share

one or more of the pain-related features in working memory, such as the somatosensory modality or the pain location (spatial coordinates), will be facilitated by attention.

The findings of the current set of studies of part I provided evidence for this assumption. Overall, we found that anticipating experimental pain resulted in the prioritization of *somatosensory* sensations at the location of the body where pain was expected. We may conclude that due to the expectation of pain at a particular region of the body, location features (spatial coordinates of bodily threat) were activated in participants' attentional set. The findings are consistent with the results of a study of Crombez, Eccleston, Baeyens and Eelen (1998) who already provided indirect, preliminary evidence for this idea. In their study, participants were threatened with the fact that a very intense, painful stimulus could occur at one particular location of the body. The results demonstrated that a mildly painful stimulus at that particular location interfered more with the performance on a cognitive task, than painful stimuli at another location. However, in this study the focus of investigation was on attentional *interference* during the anticipation of threatening stimuli at a particular body part, as a result of which it is not possible to draw conclusions about top-down attentional *facilitation* of pain and pain-related information. Our findings extend the findings of Crombez and colleagues (1998) by demonstrating that the anticipation of pain results in the *prioritization of non-painful somatosensory* information in the threatened body part relative to other body parts.

The results of chapter 2 extended the findings of chapter 1, indicating that the boundaries of the threat-related prioritization effect were wider than the exact location where pain is expected. The results demonstrated that top-down prioritization of somatosensory sensations is generalized to the entire body part and even to different body parts at the same side of the body. Our findings were in line with a recent study of Van Hulle, Durnez, Crombez, & Van Damme (2015), using a tactile change detection paradigm. In their study, participants had to detect changes between two consecutively presented patterns of tactile stimuli at various bodily locations (8 possible locations of the body). In half of the trials the same pattern was presented twice. In the other half of the trials, one of the stimulated locations in the first pattern was no longer stimulated in the second pattern, and another location was stimulated instead. Similar to the set-up of our

studies, bodily threat was induced by occasionally administering a painful stimulus to the arm. Tactile changes on the threatened arm were better detected than tactile changes on other limbs. Particularly interesting and similar to our findings, was the finding that tactile changes were not only better detected at the exact pain location, but a heightened attention to tactile stimuli was also found for the whole body part involving the threatened location. Based on our findings and those of Van Hulle and colleagues (2015), it seems that participants became more attentive for somatosensory sensations not only at the expected pain location, but also at other locations of the same body part/half. This intriguing finding calls for an explanation. First, it may be suggested that the encoding of spatial features of bodily threat in the attentional set generalized to the entire threatened body part and even to different body parts at the same side of the body. Second, one could argue that individuals may use a better safe than sorry strategy. The ‘precautionary avoidance’ of potentially threatening stimuli may occur for the entire body part/half of the body, such that somatosensory sensations in the whole half of the body might become more salient. As a result, participants might become more quickly aware of somatosensory sensations presented at the entire body part/whole half of the body. Third, the more general encoding of the spatial features of bodily threat in the attentional set may also be the result of the response characteristics of the TOJ task. Since participants must encode targets on a left-right dimension (‘left-side first’ or ‘right-side first’), this may have led to encoding of bodily threat in the attentional set in the same manner (on the left or right side of the body). One possible solution to address this issue would be conducting a similar TOJ task in which the response dimensions of the stimulus are orthogonal to the coding dimensions of bodily threat. A TOJ task with four possible tactile locations (two on the left and two on the right hand), placed one above the other is recommended in which participants have to indicate which one of two tactile stimuli administered to each hand was presented first (the upper or the lower one) (Gallace, Soto-Faraco, Dalton, Kreukniet, & Spence, 2008). On one of these locations, a painful stimulus might occasionally be administered. We predict that participants would now probably encode bodily threat on an upper-lower distinction. Therefore, we expect similar results, i.e., stimuli on the threatened location will be prioritized. A preferred alternative might the simultaneity judgment (SJ) task (Axelrod, Thompson, &

Cohen, 1968; Zampini, Shore & Spence, 2005), in which participants have to judge whether or not two tactile stimuli delivered to the left and right hand were presented simultaneous. As such, participants do not need to compute the location of the tactile stimuli. If attended stimuli are perceived earlier, as hypothesized, this should affect the SOA between the target stimuli at which individuals maximally report them as simultaneous (i.e. the PSS). More research is clearly needed which systematically varies several different graduations on a spatially-defined dimension in order to draw more reliable conclusions about the specificity of this generalization effect.

The characteristics of the threat-related attentional prioritization effect were further explored in chapter 3, where it was demonstrated that not only the perception of *somatosensory* stimuli was biased in favor of the threatened location, but also stimuli of other modalities, such as visual information. This finding was rather unexpected based on what was found in a previous study of Van Damme, Gallace, Spence, Crombez and Moseley (2009). They showed that physical threat shifts attention to somatosensory rather than to auditory information at its location. Though, the results of chapter 3 were not so perplexing as they contribute to the propositions made by neurocognitive theories. More specific, these theories have proposed that the brain possesses a *multisensory* salience detection system that orients and monitors attention to stimuli potentially threatening the integrity of the body (Haggard, Iannetti, & Longo, 2013; Legrain, Iannetti, Plaghki, & Moureaux, 2011; Moseley, Gallace, & Spence, 2012a). It would however be interesting for future research to demonstrate what kind of information is prioritized on the threatened body part when information of both modalities are competing with each other. A TOJ task could therefore be performed with mixed stimulus pairs, that is, a visual stimulus presented on one hand and a tactile stimulus presented on the other hand. Given the close correspondence between pain and touch, it may be assumed that somatosensory sensations in a body region where pain is expected will receive processing priority.

The findings of chapter 3 are also in line with the idea that a *multisensory* system monitors the space immediately surrounding our body and detects relevant sensory information. It is believed that there exists a *peripersonal* space that allows coding the position of somatosensory stimuli on the body surface and

the position of external, i.e. visual or auditory stimuli occurring close to the body part on which the somatosensory stimuli are applied (e.g. Holmes & Spence, 2004; Maravita, Spence, & Driver, 2003). Evidence for this idea comes from studies demonstrating that there exist crossmodal links between painful stimuli and proximal visual stimuli (De Paepe, Crombez, Spence, & Legrain, 2014; Favril, Mouraux, Sambo, & Legrain, 2014, Van Damme, Crombez, & Lorenz, 2007; Van Damme & Legrain, 2012; Van Ryckeghem et al., 2011).

The results of chapter 4 showed no evidence for any threat-related attentional prioritization effect when arms were crossed over the midline. No firm conclusions could be drawn whether the 'typical' attentional prioritization effect observed in an uncrossed arms posture might be due to the somatotopic reference frame of threat localization or rather because of the spatiotopic frame of reference of threat localization. Previous studies investigating the dominance of different frames of reference frames on the threat-related *prioritization* effect with a TOJ task are scarce. To the best of our knowledge, studies testing this idea by using the PSS as outcome measure in healthy volunteers are non-existent and only one study was reported in patients with complex regional pain syndrome (Moseley, Gallace, & Spence, 2009). Based on the findings of our study, several methodological issues need further investigation. Seemingly, the range of SOAs used in the first experiment in crossed arms blocks (-360, -180, -90, -45, -15, +15, +45, +90, +180, +360 ms) was too small as almost half of the participants had to be excluded due to poor performance. However, enlarging the range of SOAs in the second experiment ($\pm 600, \pm 400, \pm 250, \pm 100, \pm 70, \pm 50, \pm 30, \pm 15$ ms) resulted in ceiling effects of the longest intervals. As a consequence, the analyzing technique used in our studies has proven less adequate for analyzing large SOAs, as the psychometric functions asymptote at higher SOAs. These methodological issues, i.e. the appropriate range of SOAs and the most adequate analyzing techniques, should be clarified in further research.

It is noteworthy that in the studies of this PhD thesis, we specifically examined the effects of *anticipated* pain on attention, rather than the influence on the pain experience itself. Interestingly in this regard is the phenomenon of 'touch gating', the attenuation of tactile sensitivity in the presence of experimental pain. It is a well-documented phenomenon in healthy subjects. For instance, it has been shown that tactile thresholds on the hand were elevated by

co-occurring, tonic pain stimulation (Apkarian, Stea, & Bolanowski, 1994; Bolanowski, Maxfield, Gescheider, & Apkarian, 2000). In contrast, Ploner, Pollok and Schnitzler (2004) have found that short, phasic pain stimulation on the hand facilitated processing in the somatosensory cortices of tactile stimuli applied 500 ms later. Though, two fundamental differences can be mentioned with regard to our studies. First, we were interested in the cognitive effects of anticipated pain rather than the sensory effects of actual pain. Harper and Hollins (2012) have shown that the phenomenon of ‘touch gating’ is a purely sensory rather than a cognitive effect. Second, we were interested whether tactile stimuli at a threatened body part were perceived earlier in time than tactile stimuli at the other hand. This is fundamentally different from studies investigating tactile acuity (spatial discriminability of tactile stimuli) at a threatened body part. The underlying mechanism of the latter is altered body representation, whereas we were more interested in attentional prioritization. Nevertheless, the studies reported here investigated the effect of *anticipating* pain on the prioritization of attention on the threatened body part. Therefore, we opted also to exclude all trials from analysis in which a pain stimulus was administered.

Since the main focus of this PhD thesis was to investigate attentional prioritization effects, the point of subjective simultaneity (PSS) was used as primary outcome measure. Yet, we also observed effects on another parameter of TOJ tasks, namely the just noticeable difference (JND) (see Shore, Gray, Spry, & Spence, 2005; Van Damme et al., 2009). Analysis of the JND data revealed that participants in our studies were less accurate in making tactile TOJ on trials in which bodily threat was induced as compared to control trials. The finding of reduced accuracy when making tactile temporal order judgments following the anticipation of pain is similar to the findings of studies showing that painful somatosensory stimuli interfere with task performance (Crombez et al., 1998; Van Damme, et al. 2004b; Van Ryckeghem, Crombez, Eccleston, Liefoghe, & Van Damme, 2012). Furthermore, the results regarding the JND in chapter 4 revealed that participants were less accurate when their arms were crossed over the midline compared with an uncrossed arms posture. These findings provide further evidence for the ‘crossed hands deficit’, a decrease in performance when adopting a crossed hands position (Sambo, et al., 2013; Shore, Spry & Spence, 2002; Yamamoto & Kitazawa, 2001).

Taken together, these results offered us valuable knowledge regarding the effect of anticipating pain at a particular location of the body on the top-down attentional prioritization. Furthermore, the present studies have provided new insights for the neurocognitive model of attention to pain as theoretical framework (Legrain et al., 2009). In its current form, the neurocognitive model may only make statements concerning the prioritization of *painful* stimuli. In fact, the model currently states that top-down facilitation of pain occurs when pain stimuli share active pain features in the attentional set. Furthermore, the model does not allow to draw straightforward conclusions under which circumstances the prioritization of attention is displayed and it is limited in the definition of which features are exactly activated in the attentional set when expecting or experiencing pain at a particular region of the body. Based on the results of our studies, it may be considered to corroborate the model by stating that *non-painful somatosensory* sensations, and even input of other modalities (e.g. visual information) might be prioritized on the region of the body where pain is expected. It may even be added to the model that the spatial features of bodily threat are not encoded in the attentional set in terms of the exact location, although alternative explanations for this finding should first be clarified in future research.

Hypervigilance in patients suffering from clinical pain

In the second part of this PhD dissertation, it was investigated whether patients suffering from pain at a particular location of the body prioritized bodily sensations at that specific location. As a valuable extension of the studies with healthy volunteers, we wanted to examine whether individuals experiencing clinical pain prioritize somatosensory sensations on the pain-relevant body part as compared to a pain-irrelevant body part. In line with the results of chapter 1 to 4, demonstrating that the threat of pain on a particular location of the body resulted in heightened somatosensory processing on the anticipated pain location, we assumed that patients suffering from pain at a particular body part would become more quickly aware of somatosensory sensations at the pain-relevant body part as compared to a pain-irrelevant body part. According to the attentional set hypothesis, it was assumed that individuals experiencing clinical pain have specific worries or concerns related to their pain problem, which in

turn might have resulted in the activation of pain-related features concerning the painful bodily location in the attentional set of pain patients. As a result, we expected that bodily sensations on the pain-relevant location would be prioritized as compared to the pain-irrelevant body part.

The results of chapter 5 did not support the hypothesis that unilateral knee pain patients prioritized somatosensory sensations at the affected knee as compared to the other knee. The data pattern of the behavioral measure in chapter 6 was in line with our hypothesis. The results showed that the average PSS in TMD pain patients was positive, indicating biased attention toward the pain-relevant orofacial region, whereas such bias of attention was not found in the matched control group. However, the results did not statistically support our hypothesis of differences in attentional prioritization of the painful jaw between patients with unilateral chronic pain and healthy controls. The fact that the results of chapter 6 did not reach statistical significance might possibly be due to the small sample size, resulting in the lack of statistical power. Moreover, as statistical significance was also not obtained in the pilot study in healthy volunteers from the general population, we might speculate that the TOJ task is possibly not sensitive enough to detect attentional prioritization effects in non-student populations.

Interestingly, the results of the self-reported measure of vigilance to pain and non-pain sensations in chapter 6 indicated that individuals with chronic pain reported to be more attentive to painful sensations, as measured with the Pain Vigilance and Awareness Questionnaire (PVAQ; McCracken, 1997), as compared to healthy controls. Thereby, the results of several other studies in patients with chronic fibromyalgia were replicated (Crombez, Eccleston, Van den Broeck, Goubert, & Van Houdenhove, 2004; Peters, Vlaeyen, van Drunen, 2000; Roelofs, Peters, McCracken, & Vlaeyen, 2003; Tiemann, et al., 2012; Van Damme et al., in press). It has been argued that as a result of the continuous presence of pain in chronic pain patients, scores on self-report measures investigating hypervigilance rather reflect the presence of multiple somatic complaints than an excessive attentional focus on these sensations (Crombez et al., 2004). As such, it may be that the results of the self-report measures rather indicate report bias. Self-reported hypervigilance measured by the PVAQ was in line with the pattern of results of the behavioral measure, despite the non-significance of these results.

More research is needed concerning the validity of self-report measures of hypervigilance before any firm conclusions can be drawn.

To the best of our knowledge, we are not aware of any studies investigating attentional prioritization of somatosensory input at a body part that is threatened by clinically relevant (sub)acute pain. Yet, a few studies already aimed to investigate somatosensory hypervigilance in chronic pain populations. Similar to our results, they failed to detect differences in attention to pain and pain-related information between chronic pain patients and healthy volunteers. In a study of Peters and colleagues (2000), it was tested whether fibromyalgia patients displayed hypervigilance for innocuous somatosensory stimuli. Patients had to detect as fast as possible non-painful electrical stimuli that were administered to one of four different body locations, in combination with a second visual reaction time task. Results revealed no indication for hypervigilance for non-noxious somatosensory signals in fibromyalgia patients. Note however, that this study was based upon reaction time data, which has been criticized as being less suitable to study attentional prioritization in chronic pain populations (Van Damme, Crombez, & Notebaert, 2008). Likewise, the results of the study of Tiemann and colleagues (2012) and Van Damme and colleagues (in press) revealed no differences in attentional prioritization of somatosensory sensations between fibromyalgia patients and matched controls. However, these previous studies neglected the potential importance of the *specific body location* of somatosensory input. We extended previous research by investigating hypervigilance in chronic pain patients in the context of the attentional set idea. Importantly, caution is required for conclusions based on studies that equal hypervigilance to a heightened *sensitivity* for sensory information, i.e., perceptual amplification of painful and non-painful sensory information. Maixner, Fillingim, Booker and Sigurdsson (1995), demonstrated that chronic TMD pain patients had significantly lower pain thresholds and pain tolerance values as compared to healthy volunteers and thereby concluded that TMD patients were more sensitive to noxious stimuli than pain-free controls. Hypervigilance is only one mechanism that may account for research findings demonstrating hypersensitivity. Since other processes, such as central sensitization (Arend-Nielsen & Hendriksson, 2007; Staud, Robinson, & Price, 2007) might also account for lowered pain

threshold and tolerance levels in chronic pain patients, statements about hypervigilance cannot be drawn in such studies.

Can we conclude now that patients suffering from pain at a particular location of the body are not characterized by the attentional prioritization of somatosensory sensations at the painful body part as compared to the non-painful body part? We believe that several important issues should be taken into account and be clarified in further research before firm conclusions can be drawn. First, one important issue that has also been mentioned in our studies with healthy volunteers, is the observation of substantial individual differences in displaying the attentional prioritization effect. Given the presence of bodily threat appraisal in several theoretical models attempting to explain pain perception and pain-related disability (Eccleston & Crombez, 2007; Sullivan, Rodgers, & Kirsch, 2001; Vlaeyen & Linton, 2000), it may be assumed that the prioritization of somatosensory sensations on the pain-relevant bodily location might be more pronounced in individuals who have the tendency to experience bodily sensations as threatening. No positive correlations were found between pain-related prioritization and self-reported situational as well as dispositional bodily threat in sub(acute) knee pain patients. Yet, dispositional bodily threat appraisal, as measured by the PVAQ, was positively related to the attentional prioritization effect on the affected orofacial region in TMD pain patients, although this relationship was only marginally significant. It must however be mentioned that the sample size in both chapters with clinical samples was too low to allow further interpretation of the effect of individual differences. These findings highlighted the importance of systematically investigating the influence of individual characteristics of bodily threat appraisal on the prioritization effect in populations with a larger sample size. An interesting and worth mentioning observation with regard to situational bodily threat appraisal, is that self-reported fear during the experiment and pain expectancy ratings were rather low in both clinical populations. The fact that patients appeared not to be fearful during the experiment, makes us suspect that it may be necessary to create more threatening situations. This issue relates to the following argument.

Second, no experimental pain was induced in pain patients. According to the attentional set idea, it was assumed that individuals experiencing clinical pain may have worries or concerns related to their pain problem, which in turn might

have resulted in the spontaneous activation of pain-related features concerning the painful bodily location in the attentional set of pain patients. As such, we expected that bodily sensations on the pain-relevant location would be prioritized. Although both clinical samples consisted of patients suffering from a unilateral pain problem, these groups are not directly comparable. It may be assumed that chronic TMD pain patients have a stronger focus on pain-related goals and greater disability than (sub)acute knee pain patients.

Seemingly, we may have overestimated the impact of clinical pain on the presence of pain-related features in the attentional set. Because of the absence of imminent threat, features in the attentional set might not be (sufficiently) activated. Research would therefore benefit from maximizing the threat value of pain in both pain groups. In TMD pain patients, one way to achieve this is by making participants believe that they would have to perform stressful movements with their mouth (e.g. biting into an apple). Since most knee pain patients reported that their pain symptoms only emerge in particular situations, such as running and climbing stairs, we might assume that the attentional prioritization effect would only be displayed when knee pain patients are explicitly confronted with their pain in that particular threatening context. In sum, the results of our studies with clinical pain populations underline the importance of further investigation of attentional prioritization in more ecologically valid situations.

Previous studies in chronic pain patients already demonstrated that the experience of pain might result in a decreased somatosensory perception on the affected body part (Moseley, 2008; Moseley et al., 2009; Moseley, Gallagher, & Gallace, 2012b). Although one could argue such touch gating to have counteracted the possible attentional prioritization effect, this is not likely due to the calibration of the tactile intensities on both locations. A double random staircase procedure was used in our studies in order to maximize the chance that the tactile stimuli were perceived as equally intense on both locations of the body. Positively, the perceived intensity of tactile stimuli on the painful body part did not differ significantly from tactile stimuli presented on the non-painful body part. A disadvantage of the experimental set-up in the clinical studies, is the fact that experimental control over pain is lacking. To deal with this issue and in order to maximize the threat value of pain in pain patients, the paradigm in our clinical studies could be extended by the induction of experimental pain. We then might

expect a larger prioritization effect of the threatened body part in pain patients as compared to healthy volunteers.

Evaluating the operationalization of hypervigilance

Previous research made us aware of several limitations about investigating attentional processing of pain and pain-related information. The use of questionnaires for examining heightened attention toward pain and pain-related information has been criticized since a long time. Several questionnaires are believed not to reflect what they aimed to reflect, possibly resulting in bias and inaccurate measurement. It has been argued that the scores on these self-report measures in individuals with chronic pain may be, at least partly, confounded by the continuous presence of pain and other somatic symptoms, perhaps rather reflecting the presence of multiple somatic complaints than an excessive attentional focus on these sensations (Crombez et al., 2004). Furthermore, scores on questionnaires depend on the capacity to be able to sufficiently and accurately remember the pain (Roelofs, Peters, Patijn, Schouten, & Vlaeyen, 2004). This is especially problematic with regard to healthy volunteers, who are not daily confronted with pain and who must rely on memory of pain they have experienced in the past.

In order to avoid such report bias, behavioral paradigms that more directly measure attentional processes were put forward as an adequate solution. Although attentional bias paradigms demonstrated promising results with regard to the facilitation of pain and pain-related information, the findings were not always consistent. Within this PhD thesis, we have chosen to make use of a somatosensory attention paradigm, the temporal order judgment (TOJ) task, which has the benefit of administering *tactile* sensations.

Evaluation of the Temporal Order Judgment paradigm

From the results of our studies conducted with undergraduate students (chapter 1 to 4), it may be concluded that the tactile TOJ task in combination with a threat manipulation has proven to be successful in investigating the top-down attentional prioritization of pain-related information on a threatened body part. The finding that participants are becoming more quickly aware of tactile sensations presented on the threatened hand as compared to the other hand has repeatedly been demonstrated in several studies (chapter 1, chapter 2, chapter 3).

The adapted TOJ task has consistently demonstrated to be a useful tool to assess heightened attentional processing on a threatened region of the body.

When specifying hypervigilance as the prioritization of attention to certain information (Crombez, Van Damme, & Eccleston, 2005; Van Damme et al., 2009; Van Damme, Legrain, Vogt, & Crombez, 2010), we may conclude that the TOJ paradigm meets all our criteria to investigate hypervigilance. First, hypervigilance may be better studied in situations with competing attentional demands. In our version of the TOJ task, competition occurred between threat trials, in which participants expected a painful stimulus at a particular body part, and “safe”, neutral trials. Second, in the TOJ task, the accuracy of participants’ responses was emphasized, rather than their speed. Accuracy responses are assumed to be a better outcome measure for attentional bias in chronic pain populations, as these individuals are believed to be characterized by slower response speed and delayed psychomotor movements (Van Damme et al., 2008). Last, a recent meta-analysis by Crombez, Van Ryckeghem, Eccleston and Van Damme (2013) demonstrated that most studies attempting to examine attentional bias toward pain and pain-related information made use of *visual* attentional bias paradigms. These authors highlighted the use of visual stimuli (e.g. pain-related words) as a possible explanation for the rather disappointing results of the attentional bias effect toward acute pain, procedural pain and experimental pain. The use of pain-related words and pictures as valid pain stimuli might have proven less fruitful to activate pain schemata/memories, as these are only semantic representations of pain which are barely capable of activating bodily threat (Crombez, Hermans, & Adriaensen, 2000). Here, the TOJ task made use of somatosensory stimuli (tactile and pain stimuli) which are believed to have a higher ecological validity.

Although the TOJ task has proven to be a very useful tool to assess attentional prioritization processes throughout our studies, the paradigm is not without limitations. First, the TOJ task has proven less feasible to detect attentional prioritization effects in other populations than the student population, despite the fact that the parameters of the TOJ were adapted. Since more inter-individual variability was observed in healthy volunteers from the general population and clinical pain populations, it appeared that the TOJ task is less sensitive to detect effects in such heterogeneous populations. Second, in the studies of this PhD thesis, participants were instructed to report aloud which

stimulus was presented first (left or right stimulus). The experimenter registered the answers, instead of letting participants press a left or right button on a keyboard. This procedure was followed to avoid potential confound originating from the left-right correspondence of the task with the response characteristics. It might however be possible that not all responses of the participant were correctly entered by the experimenter, due to loss of concentration or fatigue. Therefore, a better option is to register the responses by means of a foot pedal, in which participants have to lift the toes versus the heel, respectively when the left or right stimulus is presented first. Third, as participants are forced in a TOJ task to choose one of both options ('left-side first' or 'right-side first'), it may be plausible that participants might guess when doubting about the correct answer. In order to minimize this 'guessing bias', the TOJ task might be adapted by adding an answer option 'simultaneously'. Fourth, it has already been shown that the outcome measure of the TOJ task, i.e., the PSS, can sometimes be modulated by the response that participants have to make. Particularly, some studies demonstrated that effects could be reversed simply by changing the judgment criteria from "which stimulus came first" to which stimulus came second" (Cairney, 1975; Drew, 1896; Spence, Shore, & Klein, 2001). Since participants only had to indicate which stimulus had been presented first in our studies, it is recommended for future research to add blocks in which response criteria were reversed (i.e., which stimulus had been presented second), to be able to control for any response bias. Fifth, the TOJ task appeared to be less suitable to investigate attentional prioritization processes in a crossed arms posture. The loss of participants who did not achieve performance criteria was problematic. Although several previous studies with a crossed arms TOJ did not have such a loss of subjects, the extra manipulation of bodily threat in our studies may have a negative influence on performance. Still, it remains remarkable how significant effects were obtained in the study of Moseley, and colleagues (2009), with a range of small SOAs (-120 ms to 120 ms) in a sample of only ten patients with complex regional pain syndrome. Last, when investigating whether the inter-individual variability in the threat-related attentional prioritization effect could be accounted for by differences in bodily threat appraisal (chapter 7), the effects were of smaller magnitude than expected. The outcome measure of the TOJ

might therefore not be sensitive enough to allow us to detect differences on the individual level.

Clinical implications

Current research may have several implications for clinical practice. Until now, no direct evidence has been found for the idea that pain patients are characterized by hypervigilance. Therefore, caution is required when targeting this heightened attention for pain and pain-related information in clinical practice. The fact that the prioritization of attention may only be present in certain individuals and certain contexts led us to suspect that therapeutic strategies, such as distraction or attention training techniques may not be applicable to all individuals. Individually tailored interventions are therefore recommended.

Distraction techniques are often used as a technique to control pain. Beneficial effects of distraction on pain perception were found in both experimental (Petrovic, Petersson, Ghatan, Stone-Elander, & Ingvar, 2000; Tracey et al., 2002; Van Damme, Crombez, Van Nieuwenborgh-De Wever, & Goubert, 2008; Van Ryckeghem, Crombez, Eccleston, Legrain, & Van Damme, 2013), as well as clinical studies (Elomaa, Williams, & Kalso, 2009; Morley, Shapiro, & Biggs, 2004). Though, a study of Van Ryckeghem and colleagues (2012) demonstrated that the presence of an attentional bias toward pain-related information may hinder the efficacy of distraction. This finding indicates that distraction may not always be effective.

Hypervigilance is generally considered to be a consequence of pain catastrophizing and pain-related fear (Vlaeyen & Linton, 2000; Eccleston & Crombez, 2007). It has been argued that due to the threatening appraisal of pain, it is difficult to ignore pain or direct attention away from it (Eccleston & Crombez, 1999; Van Damme et al., 2010). Furthermore, it has been shown that this is typically the case in high pain catastrophizers (Crombez et al., 1998, Van Damme et al., 2004a). Therefore, distraction techniques might be less suitable to diminish hypervigilance. An apparently opposing strategy that might be useful for targeting hypervigilance is mindfulness. Recently, this technique has become increasingly popular and requires patients to attend to bodily sensations in an accepting and

nonjudgmental way (Davis and Hayes, 2011; Kabat-Zinn, Lipworth, Burncy, & Sellers, 1986). In contrast to interventions (e.g. exposure, extinction) that target the fear system and the threat value of pain, mindfulness techniques may have an influence on the quality, rather than the quantity of pain-related attention. Mindfulness-based techniques may be especially helpful by blocking the automatic negative appraisals usually evoked by pain. This technique promotes focusing on what is happening in the present, as such reducing the future-orienting, ruminative style of thinking that is often associated with individuals who display hypervigilance. Consequently, mindfulness techniques may preferably be used in high pain catastrophizers. A number of studies investigated the effect of mindfulness training on pain experience during experimental pain in healthy volunteers. Individuals who acquired mindfulness skills showed lower pain sensitivity than individuals who were distracted, although this was only the case when pain was of low intensity (Liu, Wang, Chang, Chen, & Si, 2013) and when dispositional pain catastrophizing was high (Prins, Decuyper, & Van Damme, 2014). Furthermore, mindfulness-based interventions have shown to be promising for the treatment of chronic pain (Chiesa & Serretti, 2011; Veehof, Oskan, Schreurs, & Bohlmeijer, 2011).

Challenges for future research

The present results provide added value to the upcoming interest in studies investigating the effect of anticipating pain on the top-down attentional prioritization of pain and pain-related information in healthy volunteers as well as in clinical pain populations. Though, many questions are still unanswered. Based upon the current findings and a number of limitations, several recommendations for future research may be proposed.

First, we did not use a control condition in which a non-painful somatosensory stimulus at a specific location of the body was anticipated in our studies with healthy volunteers. As a result, we cannot rule out the possibility that the mere presentation of additional stimuli in a number of trials in the threat condition could have biased attention to some extent. Nevertheless, previous studies with other paradigms have already dealt with this issue, by demonstrating that visual cues signaling a painful stimulus attract more attention than visual

cues signaling a non-painful tactile stimulus (e.g., Van Damme, Crombez, & Eccleston, 2004a; 2004b; Van Damme & Legrain, 2012). Furthermore, the inclusion of a control condition would allow to examine whether the effect is pain-specific. However, we do not necessarily expect attention effects to be specific for pain. Pain has often been seen as the prototype of arousing information. Vogt, De Houwer, Koster, Van Damme and Crombez (2008) showed that other arousing stimuli, independent from their valence, are capable of biasing attention. Therefore, there is no reason to assume that our prioritization effect would be different when using other arousing, non-painful stimuli. When a similar attentional prioritization effect for somatosensory sensations would be found when expecting *non-arousing* tactile stimuli, our reasoning and assumptions would no longer hold true. Still, in that situation, we might consider that such effect is especially caused by the perceptual similarity between the expected (tactile) stimulus and the (tactile) target stimuli of the TOJ task. Thus, it is recommended that future studies wishing to investigate the issue of specificity are cautious in selecting control stimuli, and should consider using stimuli from other somatosensory sub-modalities (e.g., temperature).

Second, for many individuals, the PSS in control trials differed from the actual point of simultaneity (0 ms), and did not fluctuate always around zero. This finding suggests that also in control trials attention was prioritized -to some extent- to the threatened body part. As such, control trials were not for everyone considered as neutral, which implicates that some participants in a so called safe situation still fear that a painful stimulus would follow. Though, this appeared not to be the most important reason, as self-reported measures in all studies indicated that participants almost never expected a painful stimulus during control trials. Yet, the subtle expectations during the control trials might be neglected by the retrospective nature of these self-report measures. Importantly, due to the random order of control and threat trials within each block, it is not unlikely that there is some residual bias to the threatened bodily location even in control trials. Future studies may use a block-wise manipulation of control and threat trial, in order to investigate whether this manipulation might potentially nullify the generalization effect observed here.

Third, in all studies reported in this PhD thesis, participants received the explicit instruction to detect which tactile stimulus had been presented first. It is

plausible that this task goal may already have induced a state of vigilance for somatosensory information occurring at the body. This makes it more difficult to detect spontaneous differences in attentional prioritization of a threatened region of the body. This would not necessarily be problematic, as the results of our studies revealed an additional effect of threat manipulation as compared to the neutral condition. However, behavioral measures in combination with electroencephalography (EEG) research might be recommended, which might investigate cortical reactions on tactile, *task-irrelevant* stimuli. Furthermore, previous neuroimaging studies have revealed that the anticipation of pain activated similar brain areas that became active during the experience of actual pain (Ploghaus et al., 1999; Porro et al., 2002). Additionally, Langer and colleagues (2011) further demonstrated that expecting auditory, visual or tactile stimuli, in the absence of stimulation leads to selectively increased baseline activity in corresponding sensory regions and decreased activity in irrelevant ones, suggesting modality-specific effects. A functional magnetic resonance imaging (fMRI) study which investigates the brain areas relevant for the detection of somatosensory sensations on a threatened location of the body, would nicely supplement our findings. Important to mention is that the TOJ task may not be the most appropriate paradigm to combine with EEG and fMRI. As such, other behavioral tasks are required to investigate these issues.

Fourth, it has been argued that attention is mainly driven by the motivation to control pain (Notebaert et al., 2011; Van Damme et al., 2010). In threatening situations, it is plausible to assume that goals are activated to avoid the pain. However, in our set-up of the studies, we did not provide the opportunity to avoid or escape the pain. The hypothesis that the attentional prioritization on a threatened body part would be more pronounced in subjects attempting to control the pain, was investigated in recent work of Durnez and Van Damme (2015). The data of their study showed that participants who were cued to actively attempt to avoid the administration of pain stimuli, prioritized tactile stimuli at the anticipated pain location, also in 'safe' trials (i.e., when there was no risk of pain stimulation). In participants not attempting to avoid pain, the prioritization effect was only found when there was immediate threat, and not in safe trials. These findings suggest that trying to control the pain elicits a more pronounced, sustained attentional prioritization of pain-relevant body locations, or an over-

generalization of threat situations. Interesting for further research might be the investigation of the influence of motivational-affective characteristics in chronic pain populations. It has been proposed that hypervigilance will emerge especially in situations in which the goal to avoid pain is activated (Crombez et al., 2005; Van Damme et al., 2010). Consequently, it might be assumed that the purpose to avoid pain is more relevant to patients suffering from chronic pain, as such resulting in a larger attentional prioritization effect on the painful body part in chronic pain patients who have the opportunity to control the pain, as compared to a comparison group of chronic pain patients.

Fifth, increasing the ecological validity has often been discussed in our studies as an important avenue for further research. As previously mentioned, hypervigilance might especially emerge in threat-inducing contexts, for example when low back pain patients are performing back movements. Assessing hypervigilance in such context would be a new step forward (for a recent attempt, see Van Damme, Van Hulle, Danneels, Spence, and Crombez, 2014). With regard to our studies, a sport-related environment might be created for knee pain patients, whereas TMD pain patients might be asked to perform the behavioral task before their consultation with the dentist, in the context of the dentistry hospital (since TMD patients reported to be very afraid to go to the dentist). Moreover, research would benefit from the use of portable tactile stimulators that can be worn while participants behave in their normal context. At certain random moments of the day, participants may be beeped to report whether they have perceived the presence of a stimulus that may, or may not, have been presented shortly before. In combination with diary reports, this might be a useful tool to further investigate attentional prioritization processes in chronic pain patients.

Last, participants of many of our experiments were healthy undergraduate students (chapter 1 to 4). Since student samples are rather specific and homogeneous, they may not be representative for the general population. As such, this limits the generalizability of the findings of our first chapters to the entire population. The generalizability benefits from testing our hypotheses in the clinical population in two different groups of pain patients. Yet, only small subsets of sub(acute) and chronic pain patients were tested, all suffering from *unilateral* pain problems. Further research is needed which should investigate

hypervigilance in different pain populations as well as in patients suffering from bilateral pain problems.

Conclusion

The findings of the current PhD thesis offered us valuable knowledge regarding the effect of anticipating pain on the top-down attentional prioritization of a threatened region of the body. First, the anticipation of pain at a particular region of the body resulted in the prioritization of somatosensory information at that location. This attentional prioritization effect appeared to generalize to other sensory modalities and is not limited to the exact location of bodily threat. These findings have provided new insights for the neurocognitive model of attention to pain as theoretical framework (Legrain et al., 2009). Second, the clinical studies reported here did not support our hypothesis that patients suffering from pain at a specific body part would prioritize somatosensory sensations at that affected body part (although the results with chronic TMD pain patients were in line with the hypothesized effect, but did not reach statistical significance). However, more research in ecologically valid situations is needed. Third, several issues were discussed which first should be clarified in further research before firm conclusions can be drawn about the role of individual differences in bodily threat appraisal on the attentional prioritization effect. Nevertheless, the findings of this PhD thesis expand our understanding concerning the top-down attentional prioritization on a particular bodily location in healthy volunteers as well as in clinical pain populations.

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Nederlandstalige samenvatting

Inleiding

Pijn is niet alleen één van de meest voorkomende problemen in de gezondheidszorg, het heeft ook een grote persoonlijke en sociale impact (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006; Krismer & Van Tulder, 2007) en brengt vaak financiële problemen met zich mee, o.a. door ziekteverzuim (Dagenais, Caro, & Haldeman, 2008). Volgens het biopsychosociaal model (Gatchel, Peng, Peters, Fuchs, & Turk, 2007) dienen zowel biologische (medische en fysieke aspecten), als psychologische (mentale, emotionele en gedragsaspecten) en sociale factoren in rekening gebracht te worden in het begrijpen van de pijnervaring. Eén psychologische factor die een belangrijke rol speelt in het verklaren van acute of chronische pijn is *aandacht*. Een functioneel aandachtssysteem toont aan dat aandacht en pijn nauw met elkaar verbonden zijn (Allport, 1989). Enerzijds is het noodzakelijk dat in een mogelijks gevaarlijke situatie, onze aandacht gericht wordt naar de dreiging (bottom-up aandacht). Het aandachtsopeisende karakter van pijn wordt volgens het cognitief-affectief model van Eccleston en Crombez (1999) gezien als evolutionair adaptief: doordat mogelijke lichamelijke schade vroegtijdig kan gedetecteerd worden, kan een adequate (re)actie verdere letsels voorkomen. Heel wat onderzoek is reeds verricht naar de effecten van dit bottom-up richten van aandacht (bv. Crombez, Baeyens, & Eelen, 1994; Vancleef & Peters, 2006). Anderzijds zorgt aandacht ervoor dat onze huidige doelen vervuld worden zonder afgeleid te worden door minder belangrijke zaken (top-down aandacht). Huidige doelen, gedachten en intenties van een individu zorgen ervoor dat aandacht gericht wordt naar (top-down facilitatie) of weggericht van (top-down inhibitie) doelrelevante stimuli. Hoewel recent onderzoek voornamelijk toegespitst werd op top-down inhibitie mechanismen (o.a. distractie-effecten, Tracey & Mantyh, 2007; Van Ryckeghem, Crombez, Van Hulle & Van Damme, 2012; Veldhuijzen, Kenemans, de Bruin, Olivier, & Volkerts, 2006; Verhoeven et al., 2011; Roelofs, Peters, van der Zijden, & Vlaeyen, 2004; Goubert, Crombez, Eccleston, & Devulder, 2004; Keogh, Hatton, & Ellery, 2000), is de versnelde verwerking van mogelijks relevante

informatie (top-down facilitatie) een even belangrijk doel met betrekking tot protectief gedrag. Volgens het neurocognitief model van aandacht voor pijn (Legrain et al., 2009) spelen actieve kenmerken die individuen in het werkgeheugen opgenomen hebben, d.i. de aandachtsset, een belangrijke rol in de top-down facilitatie van aandacht. Wanneer een pijnlijke stimulus in de omgeving overeenstemt met één van de actieve kenmerken in de aandachtsset, is de kans groter dat deze pijnstimulus meer aandacht verkrijgt (Legrain et al., 2009; Van Ryckeghem, Crombez, Eccleston, Legrain & Van Damme, 2013, Zampini et al., 2007).

Niet enkel het ervaren van pijn zelf, maar ook het verwachten van pijn blijkt een belangrijke protectieve functie te hebben. Het verwachten van pijn kan ervoor zorgen dat stimuli die mogelijke dreiging met zich meebrengen, prioritair verwerkt worden. Op die manier laat dit het individu toe om verdere dreiging te vermijden en adequaat gedrag te stellen (Öhman, 1979). Hoewel er steeds meer interessant onderzoek naar het verwachten van pijn uitgevoerd wordt (Crombez, Baeyens, & Eelen, 1998a; Spence, Bentley, Phillips, McGlone, & Jones, 2002; Van Damme, Crombez, & Eccleston, 2002, 2004a; 2004b), blijft de evidentie toch schaars. Mits uitbreiding van het neurocognitief model van aandacht voor pijn (Legrain et al., 2009) kunnen heel wat interessante hypothesen geformuleerd worden. Het model laat in zijn huidige vorm enkel toe statements te maken omtrent de prioritering van *pijnlijke* stimuli. Er kan verondersteld worden dat ook *niet-pijnlijke stimuli*, die eigenschappen delen met de pijngerelateerde kenmerken in de aandachtsset van individuen, zoals locatie kenmerken, ook prioritair verwerkt zullen worden. Eén van de doelen in huidig proefschrift is nieuwe inzichten verwerven in de rol van het verwachten van pijn op het top-down prioriteren van aandacht binnen de context van het aandachtsset idee.

Wanneer pijn relevant blijkt te zijn voor de huidige doelen van een individu, kan aandacht gefocust worden op pijn. Bij sommige individuen blijft de pijn echter aanhouden, wat resulteert in de continue, angstige verwachting dat pijn zal optreden en/of verergeren. Hierbij wordt de hypothese vaak gesteld dat chronische pijnpatiënten hypervigilant zijn voor of overmatig aandacht besteden aan pijn en pijngerelateerde informatie (Chapman, 1978; Crombez, Van Damme, & Eccleston, 2005; Van Damme, Legrain, Vogt, & Crombez, 2010). Ondanks de bruikbaarheid van deze hypothese, is er geen eenduidigheid over de

conceptualisatie en operationalisatie van hypervigilantie (Van Damme et al., 2010). In huidig doctoraatsproject wordt hypervigilantie beschouwd als het prioritair verwerken van somatosensorische informatie in een context bestaande uit meerdere omgevingseisen (Crombez et al., 2005; Van Damme et al., 2009; Van Damme et al., 2010). Bovendien is het van cruciaal belang om aan te tonen dat er cognitieve aandachtsprocessen bij betrokken zijn. Voorts maakt deze visie een expliciet onderscheid met visies die hypervigilantie aanzien als een verhoogde sensitiviteit voor pijn (o.a. lagere pijndrempel en lager tolerantieniveau van pijn).

Ondanks de veelheid aan studies omtrent hypervigilantie is er nog steeds geen overtuigende evidentie dat chronische pijnpatiënten gekenmerkt worden door een overmatige aandacht voor somatosensorische informatie in vergelijking met gezonde vrijwilligers. Een recente meta-analyse van Crombez en collega's (2013), toonde aan dat chronische pijnpatiënten een aandachtsvertekening vertoonden voor pijngerelateerde informatie, maar dit effect was klein en niet verschillend van gezonde vrijwilligers. Een mogelijke verklaring voor deze eerder ontgoochelende resultaten is het feit dat vaak visuele, pijngerelateerde stimuli zoals woorden en figuren gebruikt werden voor het meten van pijngerelateerde aandacht. De vraag stelt zich of deze visuele aandachtsparadigma's voldoende effectief zijn in het oproepen van schemata met betrekking tot 'lichamelijke dreiging' (Crombez et al., 2013; Van Damme et al., 2010). Bovendien deden de meeste studies die hypervigilantie onderzochten, beroep op reactietijden als uitkomstmaat (Peters, Vlaeyen, & van Drunen, 2000; Peters, Vlaeyen, & Kunnen, 2002). Hoewel een dergelijke benadering bruikbaar is in homogene niet-klinische populaties, blijkt het gebruik ervan minder adequaat in patiëntenpopulaties (Van Damme, Crombez, & Notebaert, 2008). In huidig doctoraatsproject werd rekening gehouden met deze limitaties door gebruik te maken van een innovatief *somatosensorisch* aandachtsparadigma, de Temporal Order Judgment (TOJ) taak.

Doelstelling

Het doel van huidig doctoraatsproject was drievoudig. In een eerste onderzoekslijn werd het effect van het verwachten van pijn op een specifieke lichaamslocatie onderzocht op het top-down prioriteren van aandacht. In een

tweede onderzoekslijn werd nagegaan of patiënten met pijn op één specifieke lichaamslocatie gekenmerkt worden door hypervigilantie voor lichamelijke sensaties op dit pijnlijke lichaamsdeel. Tot slot werd in een derde onderzoekslijn getest of individuen die de neiging hebben om lichamelijke sensaties als bedreigend te ervaren een meer uitgesproken prioriteringseffect vertonen. Doorheen alle studies van dit doctoraatsproject werd gebruik gemaakt van de *Temporal Order Judgment* (TOJ) taak.

Bevindingen

In **deel 1** van deze doctoraatsthesis werd onderzocht wat het effect was van het verwachten van pijn op het prioriteren van aandacht aan de hand van vier studies, uitgevoerd bij gezonde vrijwilligers. In **hoofdstuk 1** dienden proefpersonen te oordelen welke van twee tactiele stimuli, aangeboden op iedere hand en met een variabel tijdsinterval tussen beide stimuli, eerst gevoeld werd. Bijkomend werd lichamelijke dreiging geïnduceerd op één hand door middel van de kleur van de cue. Proefpersonen verwachtten een pijnlijke prikkel op één hand bij de ene kleur (dreiging trials), terwijl geen pijnlijke prikkel op deze lichaamslocatie verwacht werd bij de andere kleur (controle trials). De resultaten toonden aan dat proefpersonen sneller lichamelijke sensaties gewaar werden op de locatie waar pijn verwacht werd, ten opzichte van de niet-bedreigde locatie. In **hoofdstuk 2** werd getest hoe specifiek de spatiale grenzen van dit dreigingsgerelateerd prioriteringseffect waren. Twee experimenten werden uitgevoerd waarbij de afstand gemanipuleerd werd tussen de pijnlocatie en de locatie waar tactiele stimuli aangeboden (handen) werden. Ofwel verwachtten proefpersonen pijn dichtbij de locatie van de tactiele stimuli (handen), ofwel werd de pijn verderaf aangeboden (arm of been). De bevindingen toonden aan dat het prioriteren van lichamelijke sensaties niet beperkt was tot de exacte locatie waar pijn verwacht werd, maar eerder generaliseerde naar het volledige bedreigde lichaamsdeel en zelfs naar de gehele bedreigde lichaamshelft. Proefpersonen in de studie van **hoofdstuk 3** oordeelden over de temporale orde van zowel tactiele als visuele stimuli aangeboden op elke hand, terwijl opnieuw al dan niet een pijnlijke prikkel op één hand verwacht werd. Op die manier kon nagegaan worden of het prioriteren van aandacht op een bedreigde lichaamslocatie enkel geldig was

voor somatosensorische sensaties of ook input uit andere sensorische modaliteiten geprioriteerd werd. Er werden geen verschillen gevonden in het prioriteren van tactiele en visuele stimuli op de bedreigde lichaamslocatie. Algemeen duiden deze resultaten op een multisensorische prioritering van informatie op het bedreigde lichaamsdeel. In **hoofdstuk 4** werd onderzocht of het dreigingsgerelateerde prioriteringseffect te wijten was aan somatosensorische input die aangeboden werd op hetzelfde lichaamsdeel als pijn (d.i. somatotopisch referentiekader van lichamelijke dreiging), of eerder het gevolg was van het overeenkomstig spatiaal coderen van somatosensorische input en pijn, onafhankelijk van het lichaamsdeel waarop beide soorten sensaties aangeboden worden (d.i. spatiotopisch referentiekader van lichamelijke dreiging). Om hierover een oordeel te kunnen vellen, werd het dreigingsgerelateerd prioriteringseffect onderzocht in situaties die een conflict veroorzaakten tussen beide referentiekaders. Proefpersonen dienden te beslissen welke van twee tactiele stimuli, aangeboden op iedere hand, eerst gevoeld werd. Op één arm kon al dan niet een pijnlijke prikkel verwacht worden. Verder werd aan proefpersonen gevraagd om in de helft van de blokken de armen symmetrisch op tafel te leggen (niet-gekruiste conditie). In de andere helft van de blokken werd gevraagd om de armen te kruisen over de middellijn van het lichaam, zodat de locatie waar de pijnlijke prikkel werd aangeboden (linker-of rechterarm), dichterbij in de ruimte gepositioneerd was bij de tactiele stimulus op de contralaterale hand dan bij de tactiele stimulus op de ipsilaterale hand (gekruiste conditie). Terwijl de resultaten in de niet-gekruiste conditie overeen kwamen met de resultaten van onze vorige studies, werd geen dreigingsgerelateerd prioriteringseffect gevonden in de gekruiste conditie.

In **deel 2** van dit proefschrift werd aan de hand van twee studies nagegaan of patiënten die pijn ervaren op één specifieke lichaamslocatie gekenmerkt worden door hypervigilantie voor lichamelijke sensaties op dit pijnlijk lichaamsdeel. In tegenstelling tot de studies vermeld in deel 1 werd geen experimentele pijn meer geïnduceerd. Het TOJ paradigma werd toegepast bij patiënten met unilaterale (sub)acute kniepijn en patiënten met chronisch unilaterale temporomandibulaire disfunctie (TMD), d.i. kaakpijn aan het scharnierpunt van het bovenste en onderste kaakgewricht. In **hoofdstuk 5** werd

onderzocht of unilaterale (sub)acute kniepijnpatiënten lichamelijke sensaties prioriteren op de pijnlijke knie ten opzichte van de niet-pijnlijke knie. Patiënten voerden de TOJ taak uit waarbij de tactiele stimuli op beide knieën werden toegediend. Lichamelijk dreiging werd verhoogd door proefpersonen te instrueren dat ze na het experiment drie pijnlijke knieoefeningen dienden uit te voeren. Onze hypothese dat patiënten sneller somatosensorische sensaties zouden gewaarworden op de geaffecteerde knie ten opzichte van de niet-geaffecteerde knie werd niet bevestigd door de resultaten. In **hoofdstuk 6** werd de TOJ taak, waarbij de tactiele prikkels op de kaak aangeboden werden, uitgevoerd door chronische unilaterale TMD patiënten en een vergelijkingsgroep van gezonde vrijwilligers. Hieraan voorafgaand werden twee pilootstudies uitgevoerd bij studenten (experiment 1) en bij gezonde vrijwilligers uit de algemene populatie (experiment 2) om na te gaan of de TOJ taak toelaat om aandachtsprocessen op de kaak te onderzoeken. In experiment 3 werd onderzocht of patiënten met chronische unilaterale TMD sneller lichamelijke sensaties gewaarworden op de pijn-relevante lichaamslocatie, d.i. de pijnlijke orofaciale regio, in vergelijking met de niet-pijn-relevante lichaamslocatie, d.i. de andere kaak en dit in vergelijking met een gezonde controlegroep. De resultaten van de pilootstudies toonden gelijkaardige resultaten aan als reeds gevonden in eerdere studies, namelijk een geprioriteerde verwerking van somatosensorische sensaties op de bedreigde lichaamslocatie, hoewel enkel de resultaten van de eerste pilootstudie statistisch significant waren. TMD patiënten rapporteerden meer aandacht te besteden aan lichamelijke sensaties in vergelijking met gezonde controles. Hoewel de data van de gedragsmaat overeenkwam met onze hypothese dat er verschillen dienden op te treden tussen het prioriteren van somatosensorische sensaties op de pijnlijke kaak tussen TMD patiënten en gezonde controles, waren de resultaten niet significant.

In **deel 3** werd in **hoofdstuk 7** onderzocht of het dreigingsgerelateerde prioriteringseffect voor somatosensorische sensaties meer uitgesproken is bij individuen die de neiging hebben om lichamelijke sensaties als bedreigend te ervaren. Enkele studies uit dit proefschrift waarbij gezonde vrijwilligers tactiele stimuli beoordeelden werden geselecteerd voor dit hoofdstuk. Hierbij werden zowel de vragenlijstdata als de uitkomstdata van de TOJ taak over alle studies

samengevoegd en geanalyseerd. Ondanks het feit dat correlatieanalyses positieve associaties aantoonde tussen het prioriteren van een bedreigde lichaamslocatie en situatie-specifieke beoordeling van lichamelijke dreiging, was dit resultaat niet langer significant bij het uitvoeren van een regressieanalyse die controleerde voor algemene beoordeling van lichamelijke dreiging en het prioriteren van een bedreigde lichaamslocatie in neutrale trials.

Algemeen besluit

In het huidig doctoraatsproject werd het top-down prioriteren van aandacht op een bedreigde lichaamslocatie meer in detail onderzocht bij een gezonde vrijwilligerspopulatie. Hierop aansluitend werd nagegaan of patiënten met een unilaterale pijnproblematiek gekenmerkt worden door hypervigilantie, d.i. een verhoogde aandachtsverwerking van pijnlijke en/of somatosensorische informatie op de pijnlijke lichaamslocatie. Algemeen suggereerden de bevindingen dat het anticiperen van lichamelijke dreiging leidt tot een prioritering van informatie ter hoogte van de bedreigde locatie bij gezonde vrijwilligers. Dit dreigingsgerelateerd prioriteringseffect is niet gelimiteerd tot de exacte pijnlocatie, bovendien ook geldig voor andere sensorische modaliteiten en niet meer uitgesproken bij individuen die de neiging hebben om lichamelijke sensaties als bedreigend te ervaren. Verder onderzoek dient uitsluitsel te brengen omtrent de dominantie van de twee referentiekaders met betrekking tot dit prioriteringseffect. Ondanks het gebruik van een somatosensorisch aandachtsparadigma vonden we geen evidentie voor somatosensorische hypervigilantie op de pijnlijke locatie bij personen met (sub)acute en chronische pijn.

De robuuste bevindingen omtrent het prioriteren van informatie op een bedreigde lichaamslocatie bij gezonde vrijwilligers bieden een sterk theoretische meerwaarde met betrekking tot modellen die het idee van de aandachtsset in kaart brengen (Legrain et al., 2009). Onze resultaten laten toe het model uit te breiden door te stellen dat ook niet-pijnlijke somatosensorische sensaties en zelfs informatie uit andere modaliteiten, zoals visuele stimuli, geprioriteerd worden op de lichaamslocatie waar pijn verwacht wordt. Voorts kan er aan het model toegevoegd worden dat de spatiale kenmerken van lichamelijke dreiging in de

aandachtsset niet gecodeerd worden in termen van de exacte locatie van pijn, hoewel alternatieve verklaringen voor deze laatste bevinding eerst dienen uitgeklaard te worden in toekomstig onderzoek. Onze bevindingen in de klinische studies wijzen op het belang van toekomstig onderzoek om hypervigilantie te onderzoeken in meer ecologisch valide situaties.

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Dankwoord

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leerde me dat alles relatief is, ook een doctoraat. Vanaf nu heeft tante weer tijd om mee te gaan zwemmen!

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Eindigen doe je in schoonheid. Bij deze word je dan ook vermeld als laatste. Dat ik je lief heb, hoef ik eigenlijk niet nogmaals te herhalen, na meer dan 11 jaar weten we ondertussen wel beter. Onze wetenschappelijke werelden liggen dan wel mijlenver uit elkaar (hoewel ik nu eindelijk begrijp wat kojibiose is, of misschien ook niet?), we vormen het perfecte team. *"It's always better, when we are together"*. De laatste periode was niet de meest boeiende ooit. Doctoraten afwerken en de zoektocht naar een nieuwe thuis was bij nader inzien niet bepaald de meest ideale combinatie. Bedankt voor je luisterend oor tijdens 'het zaag- en klaagkwartiertje' (of uurtje), je bewonderingswaardige pogingen om alles te relativieren, je überdroge humor, je geduld, de nodige ontspanning in stresserende tijden, om 'je ziet er stralend uit' te zeggen op uiterst mottige dagen,

je kook-en strijkprestaties (misschien wel beter dan mams), maar vooral om me te laten zijn wie ik ben!

Het is mooi geweest... Tijd om uit te vliegen en nieuwe horizonten te verkennen...

Charlotte Vanden Bulcke

april 2015

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- file(s) that describe the content of the stored files and how this content should be interpreted. Specify:

- other files. Specify: raw data file:

-RAW_DATA_EXPERIMENT5.xlsx
-RAW_DATA_EXPERIMENT5A.xlsx
-GENERAL_INFO_EXPERIMENT5.xlsx
-GENERAL_INFO_EXPERIMENT5A.xlsx

* On which platform are these other files stored?

- individual PC
- research group file server
- other: responsible ZAP PC

.

* Who has direct access to these other files (i.e., without intervention of another person)?

- main researcher
- responsible ZAP
- all members of the research group
- all members of UGent
- other (specify): ...

4. Reproduction

=====

* Have the results been reproduced?: YES / NO

* If yes, by whom (add if multiple):

- name
- address
- affiliation
- e-mail

Data storage fact sheet (01/04/2015)

% Data Storage Fact Sheet (versie 1 april 2015)
 % Data Storage Fact Sheet <Phd Charlotte Vanden Bulcke, Chapter 5, Experiment 1>
 % Author: Charlotte Vanden Bulcke
 % Date: 01/04/2015

1. Contact

1a. Main researcher

- name: Charlotte Vanden Bulcke
 - address: Henri Dunantlaan 2, 9000 Gent
 - e-mail: Charlotte.VandenBulcke@UGent.be

1b. Responsible ZAP (if different from the main researcher)

- name: Stefaan Van Damme
 - address: Henri Dunantlaan 2, 9000 Gent
 - e-mail: Stefaan.VanDamme@UGent.be

If a response is not received when using the above contact details, please send an email to data-ppw@ugent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium.

2. Information about the datasets to which this sheet applies

* Reference of the publication in which the datasets are reported:
 - Vanden Bulcke, C. (2015). Hypervigilance and pain: the role of bodily threat. PhD dissertation, Chapter 5, Experiment 1.

* Which datasets in that publication does this sheet apply to?:
 All datasets reported in PhD dissertation chapter.

3. Information about the files that have been stored

3a. Raw data

* Have the raw data been stored by the main researcher? [] YES / [] NO

If NO, please justify:

* On which platform are the raw data stored?

researcher PC
 research group file server
 research group file server via DICT
 responsible ZAP PC

* Who has direct access to the raw data (i.e., without intervention of another person)?

main researcher
 responsible ZAP
 all members of the research group
 all members of UGent
 other (specify): ...

3b. Other files

* Which other files have been stored?

- file(s) describing the transition from raw data to reported results. Specify:

 Excelfile: - ANALYSES_EXPERIMENT_KNEE_PATIENT.xlsx

- file(s) containing processed data. Specify:

 - DATA_FILE_EXPERIMENT_KNEE_PATIENTS.sav

- file(s) containing analyses. Specify:

 - OUTPUT_EXPERIMENT_KNEE_PATIENTS.spv

 - SYNTAX_PSS_EXPERIMENT_KNEE_PATIENTS.sps

- files(s) containing information about informed consent. Specify: ...

- a file specifying legal and ethical provisions. Specify: ...

- file(s) that describe the content of the stored files and how this content should be interpreted. Specify:

- other files. Specify: raw data file:

 - RAW_DATA_EXPERIMENT_KNEE_PATIENTS.xlsx

 - GENERAL_INFO_EXPERIMENT_KNEE_PATIENTS.xlsx

 - CORRELATIONS_FINAL.xlsx

* On which platform are these other files stored?

- individual PC

- research group file server

- other: responsible ZAP PC

* Who has direct access to these other files (i.e., without intervention of another person)?

- main researcher

- responsible ZAP

- all members of the research group

- all members of UGent

- other (specify): ...

4. Reproduction

* Have the results been reproduced?: YES / NO

* If yes, by whom (add if multiple):

- name

- address

- affiliation

- e-mail

Data storage fact sheet (01/04/2015)

% Data Storage Fact Sheet (versie 1 april 2015)
 % Data Storage Fact Sheet <Phd Charlotte Vanden Bulcke, Chapter 6, Experiment 1/2/3>
 % Author: Charlotte Vanden Bulcke
 % Date: 01/04/2015

1. Contact

1a. Main researcher

- name: Charlotte Vanden Bulcke
 - address: Henri Dunantlaan 2, 9000 Gent
 - e-mail: Charlotte.VandenBulcke@UGent.be

1b. Responsible ZAP (if different from the main researcher)

- name: Stefaan Van Damme
 - address: Henri Dunantlaan 2, 9000 Gent
 - e-mail: Stefaan.VanDamme@UGent.be

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2. Information about the datasets to which this sheet applies

* Reference of the publication in which the datasets are reported:
 - Vanden Bulcke, C. (2015). Hypervigilance and pain: the role of bodily threat. PhD dissertation, Chapter 6, Experiment 1/2/3.

* Which datasets in that publication does this sheet apply to?:
 All datasets reported in PhD dissertation chapter.

3. Information about the files that have been stored

3a. Raw data

* Have the raw data been stored by the main researcher? YES / NO

If NO, please justify:

* On which platform are the raw data stored?

researcher PC
 research group file server
 research group file server via DICT
 responsible ZAP PC

* Who has direct access to the raw data (i.e., without intervention of another person)?

main researcher
 responsible ZAP
 all members of the research group
 all members of UGent
 other (specify): ...

3b. Other files

* Which other files have been stored?

- file(s) describing the transition from raw data to reported results. Specify:

Excelfile: - ANALYSES_EXPERIMENT_TMD_STUDENTS.xlsx
- ANALYSES_EXPERIMENT_TMD_HEALTHY.xlsx
- ANALYSES_EXPERIMENT_TMD_CONTROLS.xlsx
- ANALYSES_EXPERIMENT_TMD_PATIENTS.xlsx
- FINAL_EXPERIMENT_TMD_STUDENTS.xlsx
- FINAL_EXPERIMENT_TMD_HEALTHY.xlsx
- FINAL_PATIENT_CONTROLS.xlsx

- file(s) containing processed data. Specify:

- DATA_FILE_EXPERIMENT_TMD_STUDENTS.sav
- DATA_FILE_EXPERIMENT_TMD_HEALTHY.sav
- DATA_FILE_EXPERIMENT_TMD_CONTROLS.sav
- DATA_FILE_EXPERIMENT_TMD_PATIENTS.sav

- file(s) containing analyses. Specify:

- OUTPUT_EXPERIMENT_TMD_STUDENTS.spv
- OUTPUT_EXPERIMENT_TMD_HEALTHY.spv
- OUTPUT_EXPERIMENT_TMD_CONTROLS.spv
- OUTPUT_EXPERIMENT_TMD_PATIENTS.spv
- SYNTAX_PSS_EXPERIMENT_TMD_STUDENTS.sps
- SYNTAX_PSS_EXPERIMENT_TMD_HEALTHY.sps
- SYNTAX_PSS_EXPERIMENT_TMD_CONTROLS.sps
- SYNTAX_PSS_EXPERIMENT_TMD_PATIENTS.sps

- files(s) containing information about informed consent. Specify: ...

- a file specifying legal and ethical provisions. Specify: ...

- file(s) that describe the content of the stored files and how this content should be interpreted. Specify:

- other files. Specify: raw data file:

-RAW_DATA_EXPERIMENT_TMD_STUDENTS.xlsx
-RAW_DATA_EXPERIMENT_TMD_HEALTHY.xlsx
-RAW_DATA_EXPERIMENT_TMD_CONTROLS.xlsx
-RAW_DATA_EXPERIMENT_TMD_PATIENTS.xlsx
- GENERAL_INFO_EXPERIMENT_TMD_STUDENTS.xlsx
- GENERAL_INFO_EXPERIMENT_TMD_HEALTHY.xlsx
- GENERAL_INFO_EXPERIMENT_TMD_CONTROLS.xlsx
- GENERAL_INFO_EXPERIMENT_TMD_PATIENTS.xlsx

* On which platform are these other files stored?

- individual PC

- research group file server

- other: responsible ZAP PC

* Who has direct access to these other files (i.e., without intervention of another person)?

- main researcher

- responsible ZAP

- all members of the research group

-
- all members of UGent
 - other (specify): ...

4. Reproduction

=====

- * Have the results been reproduced?: YES / NO
- * If yes, by whom (add if multiple):
- name
- address
- affiliation
- e-mail

Data storage fact sheet (01/04/2015)

% Data Storage Fact Sheet (versie 1 april 2015)
% Data Storage Fact Sheet <Phd Charlotte Vanden Bulcke, Chapter 7, Experiment 1>
% Author: Charlotte Vanden Bulcke
% Date: 01/04/2015

1. Contact

1a. Main researcher

- name: Charlotte Vanden Bulcke
- address: Henri Dunantlaan 2, 9000 Gent
- e-mail: Charlotte.VandenBulcke@UGent.be

1b. Responsible ZAP (if different from the main researcher)

- name: Stefaan Van Damme
- address: Henri Dunantlaan 2, 9000 Gent
- e-mail: Stefaan.VanDamme@UGent.be

If a response is not received when using the above contact details, please send an email to data-ppw@ugent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium.

2. Information about the datasets to which this sheet applies

* Reference of the publication in which the datasets are reported:
- Vanden Bulcke, C. (2015). Hypervigilance and pain: the role of bodily threat. PhD dissertation, Chapter 7, Experiment 1.

* Which datasets in that publication does this sheet apply to?:
All datasets reported in PhD dissertation chapter.

3. Information about the files that have been stored

3a. Raw data

* Have the raw data been stored by the main researcher? YES / NO

If NO, please justify:

* On which platform are the raw data stored?

- researcher PC
- research group file server
- research group file server via DICT
- responsible ZAP PC

* Who has direct access to the raw data (i.e., without intervention of another person)?

- main researcher
- responsible ZAP
- all members of the research group
- all members of UGent
- other (specify): ...

3b. Other files

* Which other files have been stored?

- file(s) describing the transition from raw data to reported results. Specify:

 Excelfile: - ANALYSES_EXPERIMENT_IND_DIF.xlsx

- file(s) containing processed data. Specify:

 - ANALYSIS_EXPERIMENT_IND_DIF.sav

- file(s) containing analyses. Specify:

 - OUTPUT_EXPERIMENT_IND_DIF.spv

- files(s) containing information about informed consent. Specify: ...

- a file specifying legal and ethical provisions. Specify: ...

- file(s) that describe the content of the stored files and how this content should be interpreted. Specify:

- other files. Specify: raw data file:

* On which platform are these other files stored?

- individual PC

- research group file server

- other: responsible ZAP PC

* Who has direct access to these other files (i.e., without intervention of another person)?

- main researcher

- responsible ZAP

- all members of the research group

- all members of UGent

- other (specify): ...

4. Reproduction

=====

* Have the results been reproduced?: YES / NO

* If yes, by whom (add if multiple):

- name

- address

- affiliation

- e-mail