Attentional bias to pain-relevant body locations: new methods, new challenges

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Abstract

In a recent issue of Consciousness and Cognition, Filbrich, Torta, Vanderclausen, Azanon, and Legrain (2016) commented on a paper in which we used a tactile Temporal Order Judgment (TOJ) task to show that expecting pain on a specific body location biased attention to that location (Vanden Bulcke, Crombez, Durnez, & Van Damme, 2015). Their main criticism is that the effects are likely to reflect response bias rather than genuine attentional bias. We agree that the TOJ task used may be susceptible to response bias, and welcome the authors' methodological suggestions to control for such bias. However, we feel that certain aspects of our work are misrepresented in their paper. Most importantly, we contest their argument that our instructions made the threat location task-relevant, thereby increasing risk of response bias. Further, we reply to other methodological and theoretical issues raised by these authors.

Key words (max. 10): attention; Temporal Order Judgment; experimental pain; bodily threat;

In a recent commentary on the use of Temporal Order Judgment (TOJ) tasks to investigate pain-related attentional bias, Filbrich et al. (2016) discussed a study we have published in this domain (Vanden Bulcke et al., 2015). We agree with some of the issues raised, and welcome critical appraisal and constructive debate, which eventually will advance the field. Nevertheless, we wish to reply to some of their comments, which we feel, misrepresent aspects of our work. Before focusing on these comments, we will first briefly discuss the theoretical background and aims of the conducted studies.

Biases in processing of pain-related information, such as excessive focus of attention on somatosensory signals, have been proposed as predisposing and/or maintaining factors in pain-related disability and distress in several models of pain suffering (Crombez, Van Damme, & Eccleston, 2005; Legrain, Van Damme, Eccleston, Davis, Seminowicz, & Crombez, 2009; Pincus & Morley, 2001; Todd, Sharpe, Johnson, Perry, Colagiuri, & Dear, 2015; Van Damme, Legrain, Vogt, & Crombez, 2010; Vlaeyen & Linton, 2012). While this idea has attracted significant research effort, it is worth noting that the study of pain-related attentional bias has long been dominated by experimental paradigms using visual stimulus material (i.e., pain-related words or pictures). For instance, in a typical study using the dot-probe paradigm, pain-related stimuli (words or pictures) and neutral stimuli are simultaneously presented at different locations of a display, after which one of the stimuli is being replaced by a dot. The reaction time to respond to the location of the dot is measured. Pain-related attentional bias typically results in faster responses when the dot is presented at the "pain location". Recent meta-analyses of such studies showed that attentional bias was overall smaller in magnitude than would have been expected, and that its manifestation was dependent upon specific procedural aspects, such as type of stimuli and presentation time of stimuli (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013; Schoth, Nunes, & Liossi, 2012). One potential explanation for these underwhelming results is that visual representations of pain may not sufficiently capture bodily threat, and that the adaptive value of bias to (the location of) such stimuli is very limited (Crombez et al., 2013; Van Damme et al., 2010). Consequently, it was recommended to develop new research paradigms implementing actual bodily threats, for example by experimentally inducing pain, and to measure responses to actual somatosensory inputs, to assess pain-related attentional bias.

There have been several attempts to develop somatosensory attention paradigms. For instance, Peters and colleagues (Peters, Vlaeyen, & Kunnen, 2002; Peters, Vlaeyen, & van Drunen, 2000) investigated biases attention in chronic pain patients by looking at the detection of electrical stimuli of increasing intensity in combination with a second attention-demanding task. They hypothesized that patients, compared with healthy controls, would display facilitated detection of these somatosensory stimuli. This hypothesis was not confirmed. However, a potential problem with these studies is that participants were explicitly instructed to detect the pain stimuli, which was likely to induce a strong focus on the target locations, thereby possibly wiping out individual differences in somatosensory attention. A possible solution is to design paradigms in which pain stimuli are task-irrelevant, and in which the effect of threat of pain on attention is examined. Indeed, it is likely that attention is specifically biased to body locations that are pain-relevant or threatened. This seems to be confirmed in a study by Crombez and colleagues (Crombez, Eccleston, Baeyens, & Eelen, 1998). They presented mildly painful stimuli on the left and right arm during performance of an auditory task in healthy volunteers, and led participants to falsely believe that stimulation on one of the arms (either left or right) would occasionally be increased to a pain stimulus of high intensity. Especially participants scoring high on catastrophic thinking about pain rated the pain stimuli at the threatened arm as more intense and unpleasant. Of particular interest, in these participants, auditory task performance was most strongly disrupted on trials in which the pain stimulus was administered on the threatened arm, possibly indicating threat-induced attentional bias. Demonstrating pain-related attentional bias in chronic pain patients in this way may, however, be challenging. Although the use of reaction times may be useful in homogenous samples of undergraduate students, it may be less suitable in more heterogeneous clinical samples. Chronic pain populations are often characterized by cognitive dysfunction resulting in overall slowing of and high variability in reaction times (Moriarty, McGuire, & Finn, 2011), which may obscure the typically short-lived and subtle effects of attention (Van Damme, Crombez, & Eccleston, 2002; Van Hulle, Durnez, Crombez, & Van Damme, 2015).

In order to avoid this problem, we went out to develop new approaches to assess attentional bias for pain-related body locations. In one such approach, we adopted a TOJ task, which has been previously used to assess bodily threat-related shifts in attention (Moseley, Gallace, & Spence, 2009; Van Damme, Gallace, Spence, Crombez, & Moseley, 2009; Zampini, Bird, Bentley, Watson, Barrett, Jones, & Spence, 2007). The TOJ methodology is based upon Titchener's law of prior entry, stating that attended stimuli come to consciousness more quickly than unattended stimuli (Spence & Parise, 2010). We adapted this methodology to examine if threat of pain at a certain body location biased attention to that location (Vanden Bulcke, Van Damme, Durnez, & Crombez, 2013). Specifically, we asked participants 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 measures on such task, especially the point of subjective similarity (PSS; virtual SOA at which both stimuli are perceived as occurring simultaneously), may provide information about which hand is attended to (Shore, Gray, Spry, & Spence, 2005). Crucial in this study, participants were informed that the color of the cue preceding each TOJ trial would either signal the possible delivery (threat trials) or absence (neutral trials) of painful electrical stimulus on one hand. Analysis of PSS values indicated that in trials during which pain was expected, there was a shift of attention to the threatened hand (Vanden Bulcke et al., 2013). Follow-up studies replicated this effect, and additionally showed that pain-related bias was not limited to the exact pain location but even generalized to other body parts of the same body half (Vanden Bulcke, Crombez, Spence, & Van Damme, 2014), and that similar effects could be found when using visual instead of tactile TOJ suggesting that prioritization is not limited to somatosensory information (Vanden Bulcke et al., 2015).

While our approach, which generated consistent findings over studies, is relatively straightforward, and was maximally aimed at potential application in clinical samples, this may have a drawback in terms of experimental control. A possible criticism of the TOJ task is its susceptibility to response bias. Participants are typically required to make a choice between a "left-first" or "right-first" response, with no possibility to report that they did not perceive a temporal difference. However, especially in trials with very short SOAs, perceptually undecided participants could be inclined to respond with the location that was most salient in the experiment, namely the location in which they expected pain. A shift in PSS values could then reflect a bias in the decision process, rather than a genuinely perceptual effect of pain anticipation (for a more extensive discussion of response bias in TOJ tasks, see García-Pérez & Alcalá-Quintana, 2012; Spence & Parise, 2010). Filbrich et al. (2016) argued that it is likely that the instructions used in our studies (Vanden Bulcke et al., 2013, 2014, 2015) have strongly induced such response bias. Specifically, they state that "participants were explicitly instructed to attend one side of space", that "participants reported more often the side of space they had been instructed to attend, that is, the side of the threat", and that "participants simply resolved temporal uncertainty by choosing the side of space they expected to be the most task-relevant" (page 136). We object to these statements, and argue that their suggestion that the pain location in our studies was task-relevant is misleading. In fact, the pain stimulus was *task-irrelevant*. In none of our studies we have provided *any* explicit instruction that participants were required to attend to the threatened hand or the side of the threat. We only provided information about which hand could receive pain just *before* the start of each block. This message was not repeated *during* performance of the block, and the visual cue preceding each TOJ trial was presented centrally on a display and was spatially uninformative for the task (i.e., indicating which hand was stimulated first).

It may be premature to conclude that effects of cueing a body location by means of threat of pain are non-perceptual. In fact, two lines of research using paradigms in which response bias was unlikely, suggest that such effect could be genuinely perceptual. First, recent studies examining the effect of visual cues presented near the left or right hand on a TOJ using nociceptive electrical stimuli, showed that attention was biased to the cued location (De Paepe, Crombez, & Legrain, 2015; De Paepe, Crombez, Spence, & Legrain, 2014). In these studies each TOJ trial was preceded by a lateral cue, making it very likely that participants, in case of uncertainty, would select the cued location. However, to prevent such response bias, the authors included blocks in which participants were asked to indicate "which is second" instead of "which is first". This had no impact at all upon the results, suggesting that the effect was perceptual in nature. Although the design of this study is not identical to the design in our studies, the results at least indicate that cueing a location does not necessarily result in response bias to the cued location. Second, recent studies demonstrated spatial prioritization of a threatened location by means of a tactile change detection (TCD) paradigm (Durnez & Van Damme, 2015; Van Hulle, et al., 2015). Participants were requested to judge whether or not they perceived a change between two consequently presented spatial patterns of 3 tactile stimuli on 8 possible body locations. In half of the trials, a painful electrical stimulus could be administered on one of these locations, and this was announced by a cue (threat trials). In the other half of the trials, no threat was induced (neutral trials). Changes in tactile patterns either did or did not involve the threatened body location. Results of both studies showed that, in trials during which pain was expected, change detection was better when it involved the threatened location. It is evident that the response format in this study design (“change” or “no change”) was orthogonal to the spatial dimension (threat location involved or not), and that results thus cannot be accounted for by response bias. Of course, the results of this study cannot be automatically generalized to the TOJ methodology, but at least they indicate that the effect of expecting pain at a certain body location on responses to stimuli presented at that location could be perceptual in nature.

Nevertheless, as is the case in many TOJ studies in different research areas, we cannot exclude that response bias may have contributed to the effects reported in our studies to some extent. We therefore welcome the strategies suggested by Filbrich et al. (2016) to control for this by (a) using a response organization that is orthogonal to the spatial dimension of the stimuli (which should prevent bias in selecting the response option that is equivalent with the experimental manipulation), (b) including blocks in which participants are asked to indicate "which is second" instead of "which is first" (which should - in case of response bias - result in reversed effects), and (c) using simultaneity judgments or allowing a third response "both stimuli came at the same time" (which should prevent participants to guess in case they did not perceive a difference in timing between stimuli). We also welcome studies that demonstrate that our results are owing to reponse bias. Indeed, as yet it remains a hypothesis, which still needs to be confirmed. The studies by Vanden Bulcke and colleagues represent the first steps in developing a new approach to assess pain-related attentional bias that may be suitable for application in clinical pain populations. One obvious advantage over previous studies is that our approach does not depend on reaction times, which could be problematic in detecting biases in chronic pain patients due to overall slowing and variability. Another potential advantage in the context of research in clinical populations and settings is that the straigtforward setup allows collecting data in one relatively short test session. Admittedly, our studies are not perfect, and methodological refinement requires time and involve progressive insight.

There are three further comments on our work by Filbrich et al. (2016) that we would like to reply to. *First*, referring to the TOJ study of Vanden Bulcke et al. (2015), they challenge our conclusion in terms of a multisensory effect. In that study, it was found that induction of pain biased PSS values not differently when using tactile versus visual TOJ, suggesting that effects of pain anticipation may not be specific for somatosensory processing. The message we intended to convey was that anticipation of pain might also prioritize processing of non-somatosensory stimuli when these are presented at the threatened location. While we discussed that multisensory integration may be in line with such finding, this is not necessarily the same as saying that there was actual cross-modal *integration* between *pain* and *visual* stimuli in this specific study. Indeed, the experiment was never designed to examine such cross-modal integration, but rather as a test of an attentional theory (Legrain et al., 2009; Van Damme et al., 2010). Specifically, we wanted to examine the idea that anticipation of pain may result in activation of ‘attentional control settings’, biasing attention to certain stimulus features that are relevant for adequate reaction to threat. The location where one expects pain to occur is likely to be an important feature, as a result of which all sensory input, irrespective of its modality, may be prioritized when experiencing threat. We agree, though, that our framing in terms of a "multisensory effect" may be confusing, and that this is best avoided. Note that Filbrich et al. (2016) also questioned our multisensory effect from a statistical perspective. They argued that the effect of threat on the PSS was mainly driven by the tactile TOJ condition, because in the visual TOJ condition the values "were smaller and not significantly different from 0". This is, however, an invalid interpretation. Two separate tests of which one is significant (tactile TOJ) and the other is non-significant (visual TOJ), do not allow one to conclude that the effects are different, especially when the crucial interaction involving modality is not significant (for an elaborate discussion of this error, see Gelman & Stern, 2006).

Second, Filbrich and colleagues suggest that we have incorrectly concluded that our effects are pain-specific. We can only express strong disagreement with their interpretation. In fact, we have consistently and explicitly warned against conclusions in terms of pain-specificity (Van Damme et al., 2002; Vanden Bulcke et al., 2013). Even more, we have been amongst the first to systematically argue that a search for what is unique to pain, has led to an unduly focus on the sensory characteristics of the experience, distracting from the central role of its affective-motivational (Eccleston & Crombez, 1999). We may not confuse two levels of explanation. The first explanation is on a descriptive and operational level: there is no doubt that the delivery of a pain stimulus brings along particular effects. The second explanation is on a mechanistic or mediating level. Here, we hypothesize that the arousal dimensions is critical. In that respect, we believe that if a stimulus is equally arousing (or salient) as a pain stimulus, we will observe equal effects. Indeed, it has been demonstrated that attentional bias to certain stimuli depends on the level of arousal they evoke, irrespective of whether they have a negative or positive valence (Vogt, De Houwer, Crombez, Koster, & Van Damme, 2013). From this perspective, it is not helpful to search for attentional bias effects that are unique to pain.

Third, they argue that similar TOJ tasks have been used in patients with complex regional pain syndrome (CRPS). Moseley et al. (2009) found indications for an attentional bias away from the painful body part. The reasoning of Filbrich and colleagues that this finding contradicts our results and questions our hypothesis of increased attention to threatened body parts in chronic pain patients is invalid. On the one hand, the study of Moseley et al. (2009) investigated the effect of the *presence* of *persistent* pain in a limb on tactile TOJ in CRPS patients, whereas our studies went out to examine the effects of *anticipated phasic* pain stimulation in healthy volunteers. The substantial differences in research question, study design, type of participants, and type of pain, render any direct comparison between the results of our study and the study of Moseley et al. (2009) meaningless. Also note that the sample in the study of Moseley et al. (2009) was small (10 patients), and that their interpretation awaits further corroboration. On the other hand, it is well known that CRPS patients are an atypical population that may not be representative for the broader chronic pain population. Specifically, we should be very cautious in generalizing the neglect-like avoidance of the space in which the painful limb usually resides in CRPS patients (Legrain, Bultitude, De Paepe, & Rossetti, 2012) to other chronic pain populations, and to question theoretical assumptions on over-attentiveness that are present in several pain models based upon these CRPS studies.

In sum, our work presents a promising, but inevitably imperfect, first step into a new generation of paradigms assessing pain-related attentional bias. Although we regret that certain aspects of our work were misrepresented in the paper by Filbrich and colleagues, we welcome critical discussion, and appreciate some of their methodological recommendations to exclude alternative explanations. Ultimately, we hope that this discussion will result in further methodological progress, and that it will invite new studies advancing the field.

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