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The experimental analysis of the interruptive, interfering, and identity-distorting effects of chronic pain

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Abstract

Pain is an unpleasant sensory and emotional experience urging the individual to take action to restore the integrity of the body. The transition from a common episode of acute pain to a state of intermittent or chronic pain has been a constant preoccupation of researchers and clinicians alike. In this review, we approach chronic pain from an affective-motivational perspective, viewing pain as a biologically hard-wired signal of bodily harm that competes with other demands in the person's environment. The basic tenet is that pain urges to interrupt ongoing activity, elicits protective responses that paradoxically increase interference with daily activities, and compromises the sense of self. Here we briefly summarize existing evidence showing how pain captures attention, and how attention for pain can be controlled. We also consider pain as a strong motivator for learning, and review the recent evidence on the acquisition and generalization of pain-related fear and avoidance behavior, which are likely to interfere with daily life activities. We highlight the paradoxical effects of pain avoidance behavior, and treatment effects of exposure in vivo. A generally neglected area of research is the detrimental consequences of repeated interference by pain with daily activities on one's sense of "self". We end the review with a plea for the implementation of single-case experimental designs as a means to help customize cognitive-behavioral treatments for individuals with chronic pain aimed at reducing the suffering of this large group of individuals.

1. Introduction

Pain is a biologically relevant and vital signal of bodily threat, urging the individual to protect him/herself. Immediate protective responses to pain include increased arousal, orientation to the sources of threat, and various safety-seeking behaviors including escape and avoidance. Acute pain usually disappears within days or weeks, but in some individuals, pain persists despite the alleged healing of the initial injury. The transition from a common episode of acute pain to a state of intermittent or chronic pain has been a constant preoccupation of researchers and clinicians alike. Despite the difficulty to provide precise estimates of prevalence and incidence, the burden of chronic pain is unquestionably large, both in youth as in adults. For example, a survey in 400,000 children and adolescents aged 11 to 15 years reported the 1-month prevalence of low back pain to be no less than 37.0% (Swain et al., 2014). In adults, the median prevalence of chronic low back pain, which is back pain that lasts for at least 12 weeks lies between 5.6 and 18.1% (Henschke, Kamper, & Maher, 2015). Pain problems have been viewed as complex, multidimensional developmental processes where various biological, psychosocial and social factors are considered of utmost importance (Gatchel, Peng, Peters, Fuchs, & Turk, 2007). However, it has been difficult to specifically spell-out the mechanisms by which pain acute problems become chronic. In this invited review, we will approach this question from an affective-motivational perspective in which attention, learning, memory and individual goals take a prominent place. We start from the idea that pain has an inherent interruptive function, and that the extent to which pain interrupts depends on the threat value as well as the environmental demands. Pain interrupts to prepare for escape and avoidance of potentially harmful stimuli, and is adaptive. However, the general tenet of our approach is that prolonged protective and recuperative behavior that usually is adaptive in the short term, may in the long term paradoxically maintain the problem through the adverse effects of avoidance and the spreading of these behaviors to an increasing set of situation that share perceptual features with the initial event during the original pain episode. The longer the problem persists, the greater the discrepancy between the actual situation and the valued goals of the individual thereby compromising the sense of “self”. In this paper we will review the recent research on the interruptive function of pain, the role of learning and memory in the maintenance of avoidance behavior, and the effects of chronic pain on individual goals and identity.

2. Pain interrupts and captures attention

Pain is a hardwired signal of bodily harm, and is designed to capture attention, and interrupt ongoing activities (Eccleston & Crombez, 1999; Gatzounis, Schrooten, Crombez, & Vlaeyen, 2014). There is a wealth of experimental studies that demonstrate this automatic function of pain (Moore, Keogh, & Eccleston, 2012) (Berryman et al., 2013). In an example of the primary task paradigm, participants perform as quickly as possible an auditory discrimination task in the presence or absence

of painful stimuli (Crombez, Eccleston, Baeyens, & Eelen, 1996). Despite the fact that the processing of pain is task irrelevant and not instrumental for immediate escape and avoidance, clear interruptive effects of pain on task performance were found. When a painful stimulus was present, participants were slower in the auditory discrimination task than when pain was absent. Several pain-related variables have been identified that contribute to the interruptive capacity of pain. Evidently, the intensity of pain is a key variable. When pain is more intense, pain interferes more with the performance on a cognitive task in healthy participants (Van Ryckeghem, Crombez, Eccleston, Legrain, & Van Damme, 2013) and chronic pain patients (Eccleston, 1994). Chronic pain patients who report pain of high intensity at the moment of testing, show substantial decrements of performance on a cognitively demanding task in comparison with patients who report pain of low intensity. Research has further indicated that attention is more easily captured when pain is novel (Crombez, Eccleston, Baeyens, & Eelen, 1997; Legrain, Bruyer, Guerit, & Plaghki, 2005), when pain is unpredictable (G. Crombez, F. Baeyens, & P. Eelen, 1994), and when pain is experienced as highly threatening (Crombez, Eccleston, Baeyens, & Eelen, 1998a). All in all, this line of research reveals that pain has a profound capacity to capture attention and to interrupt ongoing activities in order to facilitate escape and avoidance. This interruptive function is not easily relinquished, even when pain proves to be a false alarm, or when pain has become chronic. It may then be no surprise that one of the prominent complaints of patients with chronic pain concerns difficulties concentrating and remembering things (Turk et al., 2008).

Individual differences

Although the capture of attention by pain is unintentional, the effect is variable and not unconditional. Indeed, experimental studies reveal averaged causal effects, which do not imply that each individual will display the same effect. Furthermore, the careful manipulation of one variable while others are kept constant, does not imply that these other variables are unimportant, and should be ignored. This also is the case with the capture of attention by pain. First, not all participants show the interruptive effect of pain. As yet, we do not fully understand which individual characteristics contribute to the variability of the effect within a particular study. A usual suspect is trait anxiety or neuroticism, which is defined as the predisposition to experience anxiety and distress across situations. Although evidence in the anxiety literature indicates that participants scoring high on trait anxiety are more easily distracted by irrelevant events (Moser, Becker, & Moran, 2012), its role in the capture of attention by pain is largely unsubstantiated. The role of individual differences in catastrophic thinking about pain is better documented (Crombez, Eccleston, Baeyens, & Eelen, 1998b). When threatening information about an impending pain stimulus is provided, those who report catastrophic thoughts about pain, show a pronounced attentional capture by pain. This effect remains even after controlling for the effect of trait anxiety (Crombez, Eccleston, Van den Broeck, Van Houdenhove, & Goubert, 2002). Second, the attentional capture by pain is conditional upon the presence of other, contextual

variables. These non-pain related variables may profoundly affect the interruptive function of pain. Well-known is the example provided by Henry Beecher, a surgeon during the World War II, who observed that soldiers leaving the battlefield, did not report pain despite the presence of severe wounds. Later studies, most often using non-human animals, revealed that stress may activate brain mechanisms that dampen or even inhibit pain (Bodnar, Kelly, Brutus, & Glusman, 1980), hence overruling the capacity of pain to capture attention. More mundane -at least for an experimental psychologist-, is the following unpublished observation. Whilst piloting and developing the primary task paradigm, we quickly found out that instructions did matter. When participants were informed that we were interested in the study of the interruptive effect of pain, the effect was masked. It turned out that participants were compensating an expected task decrement by increasing their effort to overcome the decrement. It may well be that such compensatory strategy has also downsized the interruptive effects of pain on task performance in our published studies. In line with this argument, participants reported to have put substantial effort to perform the task in the presence of pain, and to be eager not to be distracted by pain (Crombez et al., 1996; Crombez et al., 1997).

Controlling attention for pain

An interesting question is then how and when the capacity of pain to capture attention can be controlled. Answers to this question may inform us about which tasks or techniques are to be learned by patients to better live with chronic pain. These questions have mainly been addressed in distraction research, which investigates how and when directing attention away from pain affects pain. This research has a long pedigree, but results are not consistent in healthy volunteers as well as in patients with chronic pain (Snijders, Ramsey, Koerselman, & van Gijn, 2010). Based upon the disappointing results of an earlier study (McCaul, Monson, & Maki, 1992), Leventhal provocatively stated in an accompanying editorial “I know distraction works even though it doesn’t!” (p 209) (Leventhal, 1992). We do not want to go as far in our conclusion as Leventhal does. There is abundant evidence that directing attention away from pain is effective (Legrain, Crombez, Plaghki, & Mouraux, 2013). What is puzzling is the difficulty to found out why, when and for whom distraction from pain works. Research has often manipulated “cold”, cognitive characteristics of the task, such as task difficulty and complexity (McCaul et al., 1992). The basic idea is that when individuals use their processing capacity for the performance of an ongoing task, there is no processing capacity left for processing pain. This idea may be overly simplistic, and relying too much on the metaphor that humans process information just as a computer does. We concur with Alan Allport that attention is a mechanism of selection of information to protect the coherence of action (Allport, 1989). Attention thus is a selection mechanism for action. According to him, an efficient attentional system has to serve two apparently contradictory functions. First, attention protects the pursuit of current goals, by amplifying or “biasing” the processing of goal-congruent information and by inhibiting the processing of goal-irrelevant information. Second, in an unpredictable and potentially dangerous environment, it is necessary that

ongoing behavior can be interrupted at any time when more important demands such as threat and pain emerge. From this perspective, we may hypothesize that distraction will work when pain is of low intensity, and when it is perceived as non-threatening. *Mutatis mutandi*, we may expect that distraction will work less when pain is very intense, or when pain is experienced as threatening. For the latter idea there is evidence. Several studies has shown that instructions to direct attention away from pain and to engage in another cognitive task reduce pain less in participants who report high levels of catastrophic thinking about pain than in participants who report low levels of catastrophic thinking (Heyneman, Fremouw, Gano, Kirkland, & Heiden, 1990). It may well be that those how catastrophize about pain become fearful and worry about the pain, possibly “biasing” their attention to pain-related information.

Attention for pain and competing goals

Recently, researchers has focused upon the role of “hot” cognitions in distraction, hence introducing the motivational and goal dynamics of human action back into the cognitive system (Anderson & Yantis, 2013; Munneke, Hoppenbrouwers, & Theeuwes, 2015). Individuals pursue goals because they consider these as personally relevant, or of value: Goal pursuit may lead to the delivery of positive outcomes, or, the avoidance of negative outcomes. We may then expect that particular goal characteristics affect the efficacy of distraction. In an attempt to experimentally investigate this idea we manipulated the motivational value of the distraction task (Verhoeven et al., 2010). Healthy volunteers were undergoing a painful cold pressor task while either performing no extra cognitive task (control group), a tone discrimination task without reward (distraction group), or a tone discrimination task with financial reward (rewarded distraction group). Participants were also categorized based on their level of catastrophic thinking about pain. The pattern of results was remarkable. Participants with a low level of catastrophic thinking showed that performing the cognitive task (with or without reward) reduced the pain experience in comparison with the control group. For participants with a high level of catastrophic thinking about pain, distraction was not effective when no reward was present. However, in these participants directing attention away from pain became efficacious when the distraction task was of value. We posit that goal pursuit will more effectively lead to a reduction of irrelevant events (such as pain) when goals are motivationally relevant. Applying this idea in the clinical context requires an identification of activities that patients (still) value. It may well be that training patients to direct their attention away from pain is far less useful than (re)engaging patients in these valued activities, which may then more naturally compete with pain.

Our analysis also points at the possible devastating effects, in particular when individuals pursue goals related to pain. Indeed, when individuals attempt to control pain, they may become more “biased” to pain-related information (Durnez & Van Damme, 2015; Notebaert et al., 2011). Probably, it is sufficient to have thoughts about pain on your mind, in order to facilitate the attentional capture by pain (Van Ryckeghem, Crombez, et al., 2013). Definitely, chronic pain is a fertile ground in which

worry and frustrative attempts to control pain flourish and persevere (Eccleston & Crombez, 2007). It is then no surprise that these patients report being (hyper)-vigilant for their pain (L. Goubert, Crombez, & Van Damme, 2004). Paradoxically, giving up attempts to control pain, and accepting pain may prove advantageous, and reduce the capacity of pain to capture attention (McCracken, 2007; H. Moore, Stewart, Barnes-Holmes, Barnes-Holmes, & McGuire, 2015). We do not contend that pain will entirely lose its capacity to interrupt. Pain is designed to interrupt, and as argued earlier, does not easily relinquish this capacity. However, we may bring the interruptive effects of pain back to its basics.

Pain and attentional bias

In the preceding paragraphs, we have gradually built an affective-motivational account of pain, which operates in a context with multiple demands (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012). Attention serves to protect the coherence of ongoing action, but leaves open the eventuality of interruption when demands of higher priority are met (Van Damme, Legrain, Vogt, & Crombez, 2010). In doing so, we stress that the processes underlying the attentional effects of pain are normal, generic, and applicable to various experiences (Andersson, Juris, Classon, Fredrikson, & Furmark, 2006; Lewis et al., 2011). One may contend that this view is common sense and already well-embedded in research and clinical practice. According to us, this is not the case. We may further clarify our position by contrasting our view with a psychopathology perspective on attention, and in particular attentional bias. An attentional bias to threatening information has been proposed as a causal factor contributing to the development and maintenance of anxiety and fear in various models of psychopathology (Van Bockstaele et al., 2014). Attentional bias to threatening information, most often words and pictures representing that particular threat, is also well documented in the anxiety and fear literature (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van, 2007). In a summary of the research on attentional bias for pain-related information, Crombez et al. were able to show that patients with chronic pain display an attentional bias towards words that represent the sensory characteristics of their pain, albeit that the effect size was small (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013). Definitely, there is room for improvement, but space limitations do not allow us to elaborate this further. Following the rationale on the causal role of attentional bias in anxiety and fear (Hakamata et al., 2010), pain researchers have formulated a similar role for attentional bias in the development and maintenance of chronic pain (Todd et al., 2015). They also argued to directly modify the attentional bias towards pain-related information by teaching patients to direct their attention away from pain-related information (Sharpe et al., 2012). Left aside that there is still controversy whether attentional bias modification training is effective (Cristea, Kok, & Cuijpers, 2015), we argue that such attentional repair technique ignores the dynamics of an affective-motivational account of pain. It also narrows the problem focus and the available arsenal of cognitive-behavioral techniques (Crombez, Heathcote, & Fox, 2015). Indeed, throughout our excursion we have

argued for the role of various factors that contribute to the attentional capture by pain, such as the threat value of pain, catastrophic thinking about pain and frustrative attempts to control pain. Clinicians have various tools to directly target these contributing factors. Also experimental evidence points at other ways to target attentional bias. Signals of impending threat may lose their capacity to capture attention, when these signals turn out to be not valid anymore (Van Damme, Crombez, Hermans, Koster, & Eccleston, 2006). Furthermore, learning to direct attention away from threatening information may run the risk that individuals become less sensitive to what actually happens in the environment (Van Bockstaele, Verschuere, De Houwer, & Crombez, 2010).

Conclusion

Pain is hardwired signal of bodily harm, and has an inherent capacity to capture attention and the urge escape. Nevertheless, we have argued that the interruptive effect of pain is conditional, can be controlled to some extent, and is best understood within a broad motivational context of human action. There may be situations in which other motivational demands prevail over pain, and the interruptive effect of pain is reduced. Future research may reveal when and how exactly this is accomplished, but we plea for a systematic exploration of the role of goal characteristics in this endeavor (Austin & Vancouver, 1996). If attention to pain is best conceived within a system of selection for action, research may benefit from adopting a goal and self-regulation perspective, which is geared towards action in natural environments. We may then realize that the experimental study of the capacity of pain to capture attention is an experimental analogue of the experienced interference of daily activities by pain.

3. When chronic pain interferes with daily activities: the key role of conditioning and avoidance

Pain not only has an interrupting function, it also is a potent motivator of learning (J. W. Vlaeyen, 2015). In addition to the negative detrimental influence of repeated interruptions on daily activity performance, learned anticipatory avoidance responses to pain cues interfere with daily life activities. Here, we briefly review the acquisition, generalization and extinction of pain-related fear. Given its biological relevance, pain can be considered an unconditioned stimulus eliciting protective responses such psychophysiological arousal (increased muscle tone, skin conductance, startle), and escape (including withdrawal reflexes). These unconditioned responses may vary across individuals, depending on the threat value of pain, and the extent to which pain represents bodily harm. Learning occurs quickly, and neutral exteroceptive (tactile, visual, auditory), interoceptive (visceral, olfactory) and kinesthetic/ proprioceptive (change of position) stimuli that somehow are functionally related to the pain can act as conditioned stimuli and hence elicit pain-related fear avoidance responses in the anticipation of pain and bodily harm.

There is accumulating evidence that pain-related fear predicts the level of disability in patients with chronic pain, which may in turn reinforce further pain experiences and negative thoughts, completing a downward spiral. This evidence stems from cross-sectional studies with chronic pain patients (Crombez, Vlaeyen, Heuts, & Lysens, 1999; Lethem, Slade, Troup, & Bentley, 1983; J. W. Vlaeyen & Linton, 2000), prospective studies in acute pain (Jensen, Karpatschhof, Labriola, & Albertsen, 2010; Swinkels-Meewisse, Roelofs, Verbeek, Oostendorp, & Vlaeyen, 2003), studies using structural equation modeling (Gheldof et al., 2010) (Simons & Kaczynski, 2012), and meta-analyses (Zale, Lange, Fields, & Ditre, 2013), although there are exceptions as well (e.g. (Wideman, Adams, & Sullivan, 2009)). Collectively, these findings underscore the role of pain-related fear in the development of disability. A relevant question, however, is how pain-related fear occurs in the first place.

Pain-related fear acquisition

A series of experimental studies has attempted to provide experimental evidence for the idea the anticipatory pain-related fear responses are the result of associative learning (L. Goubert, Crombez, & Peters, 2004; J. W. Vlaeyen, 2015), and the overall result is that pain-related fear can be acquired through the pairing of neutral cues with a painful stimulus. For example, in an attempt to model fear of pain in musculoskeletal pain patients, Meulders et al. used a voluntary joystick movement paradigm with proprioceptive stimuli as CSs of which the direction predicted painful electrocutaneous stimulus to the hand as the US (e.g., moving upward as CS+ and moving downward as CS-). As compared with a condition in which both movements were explicitly unpaired with the pain-US, the CS+ movement elicited increased fear of movement-related pain, larger eye-blink startle amplitudes, and slower movement latency responses than the CS- (A. Meulders, Vansteenwegen, & Vlaeyen, 2011). The authors were also able to show that the mere intention to perform a painful movement, preceding the actual performance of the movement, also elicited similar responses (A. Meulders & Vlaeyen, 2013b). Similar findings were found in patients with complex regional pain syndrome who showed increased pain and swelling of the affected limb when instructed to think about the painful movement (Moseley et al., 2008). These findings support the idea that imagining the painful feared movement activates the memory representation of the movement-pain association, and in turn may trigger conditioned responses (A. Meulders & Vlaeyen, 2013b) It is therefore not surprising that pain-related fear can also be acquired indirectly, without having actually experienced the cue-pain association, for example through observation of others in pain (Helsen, Goubert, Peters, & Vlaeyen, 2011) (L. Goubert, Vlaeyen, Crombez, & Craig, 2011), or by virtue of the conceptual equivalence between stimuli, and their derived relationships (Bennett, Meulders, Baeyens, & Vlaeyen, 2015).

Pain-related fear generalization

There is increasing evidence that not just conditioned pain-related fear responses themselves, but the generalization of these responses to novel stimuli may be more disabling. Indeed, a particular feature of Pavlovian conditioning is that stimuli sharing characteristics with the original fear-provoking CS (so-called generalizing stimuli; GS) may become capable of eliciting similar conditioned responses, following a gradient dependent on the perceptual or functional proximity between CS and GS. Generalization reduces the risk of missing positive alarms, but has the drawback of responding to false alarms (Lissek et al., 2010). Generalization can occur based on perceptual or non-perceptual similarities between stimuli (Dymond, Dunsmoor, Vervliet, Roche, & Hermans, 2015). While perceptual generalization concerns the physical similarity of stimuli, humans may learn from past experiences based on regularities that are based on non-physical, conceptual or symbolic equivalences. Although generalization of electrodermal responses has been studied early on e.g. (Bass & Hull, 1934), there has been a renewed interest in generalization given its explanatory power. As space limitations do not allow us to elaborate this further, we mention a couple relevant studies. Using the joystick movement paradigm in healthy subjects, we recently demonstrated a typical generalization gradient in pain expectancy ratings and eye-blink startle reflexes for novel movements that varied in proprioceptive similarity with the painful CS+ movement (A. Meulders, Vandebroek, Vervliet, & Vlaeyen, 2013; A. Meulders & Vlaeyen, 2013a). We also demonstrated non-perceptual generalization of pain-related fear from conditioned nonsense word (CS) to joystick arm movements, from within the same stimulus equivalence category. Although movements themselves were never paired with pain-US, movements from the pain-relevant stimulus equivalence category spontaneously prompted higher pain-US expectancy ratings, fear of pain ratings, and unpleasantness ratings as compared to those from the pain-irrelevant stimulus equivalence category (Bennett et al., 2015). Interestingly, in patients with fibromyalgia, non-differential generalization was observed. That is, regardless of their resemblance to the original CS+ or CS-, all novel movements appeared to elicit strong conditioned fear responses (A. Meulders et al., 2014; A. Meulders, Jans, & Vlaeyen, 2015). As a result, these patients might experience a sustained lack of safety, possibly increasing their negative affect, which in turn may fuel pain-related fear (Elsenbruch & Wolf, 2015). More experimental and longitudinal studies in individuals with chronic pain are needed to draw conclusions about the causal status these learning deficits.

Pain, fear and avoidance

Avoidance is defined as overt behavior preventing the occurrence of an aversive (painful) stimulus, and is likely to be reinforced by the relief that the anticipated US did not occur (Volders, Boddez, De Peuter, Meulders, & Vlaeyen, 2015). Avoidance behavior is also related to the willingness to take risks (Carleton, Fetzner, Hackl, & McEvoy, 2013). Prolonged avoidance is assumed to be critical for the development of chronic pain and for several reasons. First, avoidance behaviors are

often incompatible with the pursuit of valued life goals. For example, fear and avoidance of lifting movements might interfere with household and work activities that require lifting. Second, avoidance of CSs may generalize to novel stimuli that were never followed by pain, but that are considered part of the same stimulus category. The result is that in the course of time an increasing number of stimuli will be avoided, with increasingly more interference with daily life as a result. Third, avoidance behavior, although initially protective, may paradoxically increase the threat value of the pain-US. Not only is there the possible ex-consequencia reasoning “*I avoid, there must be danger*” (see (Arntz, Rauner, & van den Hout, 1995)), due to lack of actual exposure, it limits learning about the alleged threat and the representation in memory may become subject to various distortions, and the characteristics of the feared pain may become dissociated from the actual experience.

One of the drawbacks of the conditioning studies mentioned earlier is that they provide limited information about conditioned avoidance responses. In most studies, increased joystick movement latencies, or choice behavior is taken as an index of avoidance behavior. Therefore, a novel avoidance paradigm based on instrumental learning using a 3 degrees-of-freedom robotic arm provides an index of avoidance behavior. The idea is that avoidance behavior is the result of a trade-off between more pain and less effort vs. less pain and more effort. In a reaching task, participants moved their arm to a target location using the robot arm via one of three possible trajectories. The shortest/easiest trajectory was always associated with a painful stimulus. If they deviated from this trajectory, the painful stimulus could be partly or totally prevented (T2=50% reinforcement; T3=0% reinforcement), but more effort was needed for T2, and even more effort for T3. The participants of the Yoked Group received the same reinforcement schedule irrespective of their own choice of trajectory. The results clearly showed that trajectory T3 was more often chosen in the experimental group as compared to the yoked control group, and the deviation from T1 was significantly correlated with the level of pain-related fear in the experimental group (A. Meulders, Franssen, Fonteyne, & Vlaeyen, 2016).

Pain avoidance and competing goals

Pain-related fear often occurs in a context of multiple, competing goals, and there is preliminary evidence showing that avoidance behavior can be attenuated when individuals are faced with another valued but competing goal, operationalized as obtaining a monetary reward (Claes, Karos, Meulders, Crombez, & Vlaeyen, 2014). Using a joystick paradigm, a movement to one target (CS+) conditioned was followed by a painful and a rewarding stimulus on 50% of the trials, thus installing competing avoidance and approach tendencies. Another movement (CS-) was unreinforced. In the control condition, the CS+ movement was followed by pain only. The results showed that in both conditions the CS+ elicited pain-related fear, but that participants in the experimental condition showed a different avoidance response: they initiated the CS+ movement as quickly as the CS- movement, while control participants hesitated more when initiating the CS+ movement. Also, in choice trials, participants performed the CS+ movement more frequently in the experimental than in

the control condition. These results suggest that the presence of a valued competing goal can attenuate avoidance behavior, and are reminiscent of one of the pioneering behaviorists Wilbert Fordyce's sayings "*Pain patients would suffer less if they have something better to do*" (Fordyce, 1988).

Extinction of pain-related fear

When the pain-US, or the catastrophic (mis)representation of pain ceases to follow the CS, when approached, the latter loses its predictive value, and consequently the conditioned avoidance response extinguishes e.g. (den Hollander et al., 2010). Extinction is a fragile process, as the original CS-US propositional knowledge remains stored in memory after gathering disconfirmatory evidence. Extinction is also context-dependent, and CRs may return when the individual encounters a novel CS that is slightly different from the extinguished CS (Crombez, Eccleston, Vlaeyen, et al., 2002). An unexpected flair-up of pain-US (reinstatement) or a non-pain stressor US (cross-reinstatement) can easily reinstate pain-related fear e.g. (Gramsch et al., 2014). Reinstatement is particularly relevant for patients with chronic pain, as these patients will –per definition- be regularly exposed to pain exacerbations even after successful treatment.

Exposure in vivo is the clinical analog of such an extinction procedure, and has successfully been applied in patients with chronic musculoskeletal pain (J.W. Vlaeyen, Morley, Linton, Boersma, & De Jong, 2012). When individuals confront rather than avoid painful movement, expectancies will likely to be violated, and predictions about the learned associations between movements and increased pain or harm be corrected. Exposure treatments are effective in reducing pain-related fear and the perceived harmfulness of physical activity (Leeuw et al., 2008; Linton et al., 2008; Woods & Asmundson, 2008), and trials with replicated single-case experimental designs also showed reduced pain reports and successful resumptions of personal goals (de Jong et al., 2005; de Jong, Vlaeyen, van Eijnsden, Loo, & Onghena, 2012).

There has been a longstanding debate amongst theorists whether the judicial allowance of safety-seeking behaviors facilitates or on the contrary hampers the extinction of (pain-related) fear during cognitive-behavioral treatment. This is relevant as there is evidence showing that safety-seeking behavior is correlated with the level of health anxiety (Tang et al., 2007). A recent meta-analysis concluded that based on the existing literature, the jury is still out, and that the findings not seem to favor the adoption of safety-seeking behavior during exposure-based interventions (A Meulders, Van Daele, Volders, & Vlaeyen, Under review). Using the Voluntary Joystick movement paradigm, we tested whether engaging in safety behavior, conceptualized as an avoidance response, hampers the extinction of fear of movement-related pain (Volders, Meulders, De Peuter, Vervliet, & Vlaeyen, 2012). In the safety group, participants received the opportunity to avoid the pain-US by pressing a safety button during the extinction phase, whereas in the control group, this option was not included. When in a subsequent test phase, this safety button was no longer available, return of fear of pain occurred in the safety group, but not in the control group. In a subsequent study the same

researchers tested the hypothesis that fear reduction is only disrupted by behavior that serves a pain-avoidance goal (safety seeking), but not when it is serving an achievement goal (attain a reward), using the same paradigm (Volders, Meulders, De Peuter, & Vlaeyen, 2015). Fear of movement-related pain ratings showed a gradual fear reduction in the Control Group, but a return of fear when the button is pressed to avoid the pain-US (Safety group). However, when the same button is used to attain a reward (Reward group), subsequent return of fear is attenuated. These results support the relevance of the motivational context in understanding the role of safety-seeking behavior in exposure-based therapies.

Conclusion

Here we have reviewed how conditioned pain-related fear responses, and avoidance in particular may interfere with daily life performance. However, a number of intriguing questions remain, and we mention some here. First, pain-related fear and psychophysiological correlates of pain can be conditioned, but how about pain responses that were not elicited by nociceptive input? This would mean that pain be regarded as a response rather than a stimulus (Moseley & Vlaeyen, 2015). Despite a number of efforts to classically condition pain, and despite widespread beliefs amongst clinicians (Madden & Moseley, in press), the results almost always reveal the amplification of pain in the presence of the CS at best, but not the occurrence of pain. The conditions in which a neutral stimulus elicits a painful experience by virtue of previous associations still need to be uncovered, if at all possible (G. Crombez, F. Baeyens, & P Eelen, 1994), and insights from placebo/nocebo research might be helpful here (Buchel, Geuter, Sprenger, & Eippert, 2014). Second, learning, prediction, and perception are closely tied. Perception currently is seen an inferential process in which prior information is used to interpret sensory information, often resulting in minimization of sensory prediction errors. Evidence outside the pain domain reveals that aversive learning increases perceptual discrimination thresholds (Resnik, Sobel, & Paz, 2011), and an intriguing question is how such perceptual biases in turn influence subsequent associative learning (Zaman, Vlaeyen, Van Oudenhove, Wiech, & Van Diest, 2015). Third, although avoidance behavior is considered pivotal in the development of chronic pain, it seems a largely neglected research topic. Not only do we need reliable and valid assessment tools, the basic assumption that avoidance behavior paradoxically maintains pain-related fear and hampers its extinction remains largely untested. Finally, as is the case with the interruption function of pain, the pursuit of valued goals may inhibit the avoidance responses e.g. (Claes et al., 2014).

4. Chronic pain influences the sense of self – pain and identity

The previous sections have considered the impact of pain over relatively short-term time scale and the common feature is the competitive and conflictual nature of pain: the presence of pain nearly always entails conflict with on-going motivation. Cross-sectional surveys consistently show a

relationship between pain-severity and life-task interference although it is important to note that psychological variables such as pain catastrophizing, pain-related fear and beliefs about pain control contribute to task interference e.g., (P. Karoly & Ruehlman, 1996, 2007). Daily process studies further reveal the relationships between pain and individual goal pursuit and goal attainment. For example, Affleck and colleagues (1998) found that increasing pain over the day reduced the attainment of health-fitness and social interpersonal goals. Participants who did make progress towards their goals showed improved mood regardless of any changes in pain or fatigue on that day, suggesting that some individuals pursue their valued goals despite pain. In another study (Affleck et al., 2001) observed that on days with greater pain barriers to goal completion were perceived as greater, participants made less effort and there was less progress towards the goal. Again there were individual differences so that more optimistic individuals were less likely to perceive pain-related goal barriers and less likely to reduce their goal-directed effort. Indeed, optimism is considered a resilience factor receiving increased attention in the pain research field e.g. (Hanssen, Peters, Vlaeyen, Meevissen, & Vancleef, 2013).

These and other studies e.g., (Paul Karoly, Okun, Enders, & Tennen, 2014), establish the relationship between pain and interference on a daily basis, but the repeated interference by pain with daily activities can have a significant effect on one's sense of self as well (Kathy Charmaz, 1983; K. Charmaz, 1999). The inability to complete a task or to perform it to a standard acceptable to oneself or one's expectations of what others might require is deeply frustrating and leads to a steady degradation in one's behavioural repertoire, loss of role with a corresponding challenge to the sense of who you are and perhaps more importantly who you might become (Harris, Morley, & Barton, 2003). There are many descriptive, qualitative studies of this distorted identity. A meta-synthesis of the data relevant to chronic musculoskeletal pain identified several pertinent themes including 'a struggle to affirm the self and construct the self over time' and 'being valued and believed' (Toye et al., 2013). In living successfully with pain, patients reported the need renegotiate their place in the community, 'letting go' of their previous sense of self, and redefining new elements of the self. An important insight for many is the realisation that they must relinquish a search for cure and accommodate to the continuing presence of pain.

Pain enmeshment

Qualitative studies are necessarily descriptive, and this is understandably so given the protracted time course and complexity of chronic pain. In the two previous sections it has been possible to abstract aspects of pain sufficiently and to test the hypothesised relationships experimentally. Thus far, isolating experimentally testable hypotheses relevant to self and identity in chronic pain has not been a significant part of the research agenda, and is a considerable challenge. In reviewing the extant literature on cognitive biases in pain processing, Pincus and Morley (2001) hypothesised that the results could be accounted for by the so-called "enmeshment" hypothesis. This hypothesis proposed that schema representing aspects of the self and of chronic pain became

enmeshed, so that elicitation of one schema primed the other. This was an essentially post hoc hypothesis and evidence for an overlap in self and pain was indirect. Additional evidence was found in a study using an Implicit Association Test comparing health controls with chronic pain patients. In line with the enmeshment model, self- and pain-schema were more strongly associated in the chronic pain group and associated with greater pain severity, suffering, anxiety and depression (Van Ryckeghem, De Houwer, et al., 2013).

Pain-related self-discrepancies

Morley and colleagues have also investigated the relationships between self, pain and affect by drawing on theories and methods from social psychology. Self-discrepancy (SDT) and control theories of the self provide affective-motivational accounts of the relationship between aspects of the self (Charles S. Carver, 2004; C.S. Carver & Scheier, 1998; Higgins, 1997) but there is a subtle distinction between the two main accounts. Higgins identifies the *magnitude* of the discrepancy between self-aspects as the determinant of the consequent affect and behavioural output. Specifically the perceived difference between the actual-self and the ideal-self will be proportional to experience of dejection related emotions whereas actual-self and ought-self discrepancies will be related to emotions of agitation. In contrast, Carver and Scheier's control theory hypothesises that it is not the magnitude of the discrepancy *per se* but the perceived rate at which the discrepancy can be resolved that drives the affective and behavioural response. In the first study Morley, Davies and Barton (2005) had chronic pain patients generate self-descriptions, as single words or short phrases, for their current (actual) self and their hoped-for self (analogous to the ideal self). In addition, participants were asked to make a judgment on whether they thought each aspect of the hoped-for self could be achieved even with the continued presence of pain. The proportion of these conditional statements was defined as a measure of enmeshment. As expected the predictions of SDT were confirmed when depression was the dependent variable. The enmeshment model, a test of control theory, provided additional predictive power, suggesting that the extent to which persons regarded themselves as enmeshed with pain impacted their adjustment. The reverse relationship was found when a measure of acceptance was the dependent variable. Thus participants who perceived their future self as not dependent on the absence of pain were better adjusted. These results were essentially replicated in a second study (Sutherland & Morley, 2008). In this which participants generated measures of their hoped-for self from their own perspective and that of another person. A measure of trait sociotropy and autonomy was also taken. The perspective of the other person captured the participants view of how they think others regard them and it was predicted that those with high trait sociotropy would be particularly sensitive to enmeshment of the 'other' rated self, whereas the reverse would be true for those with high trait autonomy. The same measure of conditionality of each self-aspect on the continuing presence of pain was used. In addition to replicating the previous finding the main analysis confirmed a predicted interaction between trait sociotropy and trait autonomy and the degree of enmeshment in different

self-aspects. Highly enmeshed subjects were more anxious for both self-aspects but those with low levels of sociotropy or autonomy were only vulnerable when the relevant self-aspect was enmeshed. The study suggests that it is not merely the fact that pain captures some aspect of the self but that the meaning and value of what is captured is critical. As Chapman and Gavrin noted (1999) mild pain and disability of the fingers is an inconvenience for most but highly threatening to a concert pianist. None of the previous studies can test the causal relationship of enmeshment and adjustment. To date there is no laboratory manipulation available for chronic pain patients. However, Vangronsveld et al (2011) provided some evidence that a reduction in pain was associated with reduced enmeshment whereas the magnitude of self-discrepancies remained the same.

Conclusion

This section has only briefly touched on the relationship between the repeated experience of pain and the sense of self. As noted, the abundance of qualitative studies attest to the potentially deleterious consequences of pain on one's sense of self. One of the biggest challenges facing researchers in this field is to develop suitable explanatory models, quantitative and experimental methods that will facilitate the analysis of the self in pain and consequently the implications for improving treatment.

5. Novel assessment of chronic pain management

There are many RCTs of psychological treatments, predominantly CBT, for chronic pain and these have been the focus of several meta-analytic reviews (Morley, Eccleston, & Williams, 1999). While there is good evidence that treatment is effective the magnitude of the effect is relatively small with typical meta-analytic effect sizes (Cohen's *d*) in the range of around 0.2 for the difference between active treatment and waitlist control or treatment as usual. A benchmarking study using the trials from a recent meta-analysis showed that the pre-post effect size for control groups was limited (Fenton & Morley, 2013). Furthermore there is little evidence that the magnitude of current treatment effects is improving. Thus while current treatments are effective, the magnitude is small. A recent review argued that '*as more trials of psychological treatments are published, clarity becomes more, not less, elusive.*' (Morley, Williams, & Eccleston, 2013)(p. 1930). These authors argued for a paradigm shift that would develop precise testable models linking specific treatment procedures to specific psychological changes with detailed experimental work. This is not likely to be achieved with further RCTs along the lines of the current ones, and replicated single case methodology is indicated as a viable strategy for improving treatment effectiveness.

Single-case experimental designs

Group studies are designed to transfer sample-wise knowledge towards the whole population, which might be of value for epidemiologists and policy makers, but not so much for clinicians. Means

and variances obtained from the group loosely correspond with the data of any single participant in the group, let alone an individual outside that group. Fortunately, behavioral science has moved on, and a sophisticated methodology is now available for single-case experimental designs (SCEDs). A single case experiment is “*an experiment in which one unit is observed repeatedly during a certain period of time under different levels of at least one manipulated variable*” (Onghena & Edgington, 2005). Single-case experiments are ideally suited to assess treatments that are tailored to individual patient characteristics. SCEDs are particularly persuasive when the intervention is under clear experimental control, when there is a behavioral outcome variable that is both robust against repeated measurement and sensitive enough to change, and when these changes can be evaluated against a relatively stable baseline.

There are several advantages of SCEDs over the more traditional group designs. *First*, they accommodate the large inter-individual variability and heterogeneity, which is typical for the chronic pain population. *Second*, because of repeated measurement, the data provide rich information about the sequence of changes during the treatment. For example, during an exposure treatment in a patient with in complex regional pain syndrome type I (CRPS-I) reporting increased pain-related fear, fear of movement was the variable that responded relatively fast to the treatment, followed by the achievement of individual life goals (de Jong et al., 2005). Intriguingly, pain intensity reports also diminished significantly, but at a slower pace. These data are remarkable as they suggest that pain reduction is not a prerequisite per se for the reduction of disability, an assumption that is often hold by many health care providers. Similar results were reported in a replicated SCED study examining the effect of exposure in vivo in patients with chronic work-related upper extremity pain (de Jong et al., 2012). *Third*, there currently are randomization tests available that require no assumptions about data distribution thus facilitating reliable analysis. *Fourth*, SCEDs allow for immediate feedback on the outcome of a current treatment to both patient and health care provider, and provide empirical evidence to guide subsequent care if necessary. As such, they may help to bridge the scientist-practitioner gap. *Fifth*, statistical outcome parameters of replications of SCEDs can be combined in a meta-analysis, supporting the external validity of a particular treatment. In fact, data of every subsequent trial contributes to the generality of the treatment under study. This approach places replication rather than between-subject (RCT) randomization and the heart of the scientific enterprise (Schork, 2015). *Sixth*, new insights into the effectiveness of treatments can be accumulated at a faster pace as compared to the traditional group design methodology, for which large samples are needed. *Last but not least*, data from SCEDs can also be used for educational purposes, e.g. in the training of health care professionals where data of patient progress can be used as an additional tool to monitor progress of the health care providers’ treatment skills and competences. Despite these advantages, their practical application in the area of chronic pain has lagged behind the theoretical and methodological advances. Clinicians are often unaware of the SCED possibilities, and often have no

easy access to (diary) data of repeated measures generated by their patients, and to the statistical methods to analyze these data in an appropriate fashion.

6. General Conclusion

The main underlying theme in this review is the competitive-conflictual nature of pain, whether we look at the momentary interruptive effect, its interfering effects on the pursuit of daily life goals, or at the macro level of the sense of “self”. Clinically, this experimental affective-motivational approach has made a contribution to advance our understanding of the development and reduction of persistent disability, but considerable challenges remain in order to harvest the full benefit of the knowledge gained. Future efforts should focus on developing more specific assessment procedures that could direct clinicians to the best treatment options and optimize tailoring. Although exposure techniques are clearly helpful, there is promise in developing them further incorporating our knowledge on generalization, inhibition and goal pursuit. These new avenues are likely to strengthen our treatment arsenal for individuals suffering chronic pain and disability.

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