



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



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ARTICLE INFO

Article history:

Received 20 January 2016

Received in revised form

17 August 2016

Accepted 22 August 2016

Available online 31 August 2016

Keywords:

Pain

Learning

Interruption

Interference

Identity

Pain-related fear

Attention

Avoidance

Conditioning

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 a modern learning perspective that incorporates cognitive, affective, behavioral and motivational aspects. We view 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 people 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 review 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 this review with a plea for the implementation of single-case experimental designs as a means to help customize and develop novel cognitive-behavioral treatments for individuals for chronic pain aimed at reducing the suffering of this large group of individuals.

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1. Introduction

Pain is a biologically relevant and vital signal of bodily threat, urging the individual to protect him/herself. Immediate protective responses to acute 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 11–15 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, psychological 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 a modern learning perspective in which attention, memory, behavior, and individual goals take a prominent place. We start from the idea that pain has an inherent interruptive function, and that the extent to

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which pain interrupts depends on the threat value as well as the environmental demands. Pain interrupts individuals to prepare for escape and avoidance of potentially harmful stimuli, which 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. The interruptive function of pain

Pain is a hardwired signal of bodily harm, and is designed to capture attention, and to 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 (Berryman et al., 2013; Moore, Keogh, & Eccleston, 2012). 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 intense, it 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). Individuals with chronic pain 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 (Crombez, Baeyens, & Eelen, 1994a, 1994b), 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).

2.1. 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 active 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, 1997).

2.2. 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 find 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, pp. 631–682). 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 be interrupted any time when more important demands such as threat and pain emerge. From this perspective, we hypothesize that distraction will work when pain is of low intensity, and when it is perceived as non-threatening. *Mutatis mutandi*, we expect that distraction will work less when pain is intense, or when pain is experienced as threatening. For the latter idea there is evidence. Several studies have shown that instructions to direct attention away from pain and to engage in another cognitive task reduce pain significantly less in participants who report high levels of catastrophic thinking about pain than in those who catastrophize less about pain (Heyneman, Fremouw, Gano, Kirkland, & Heiden, 1990). It may well be that those who catastrophize about pain become fearful and worry about the pain, possibly “biasing” their attention to pain-related information.

2.3. Attention for pain and competing goals

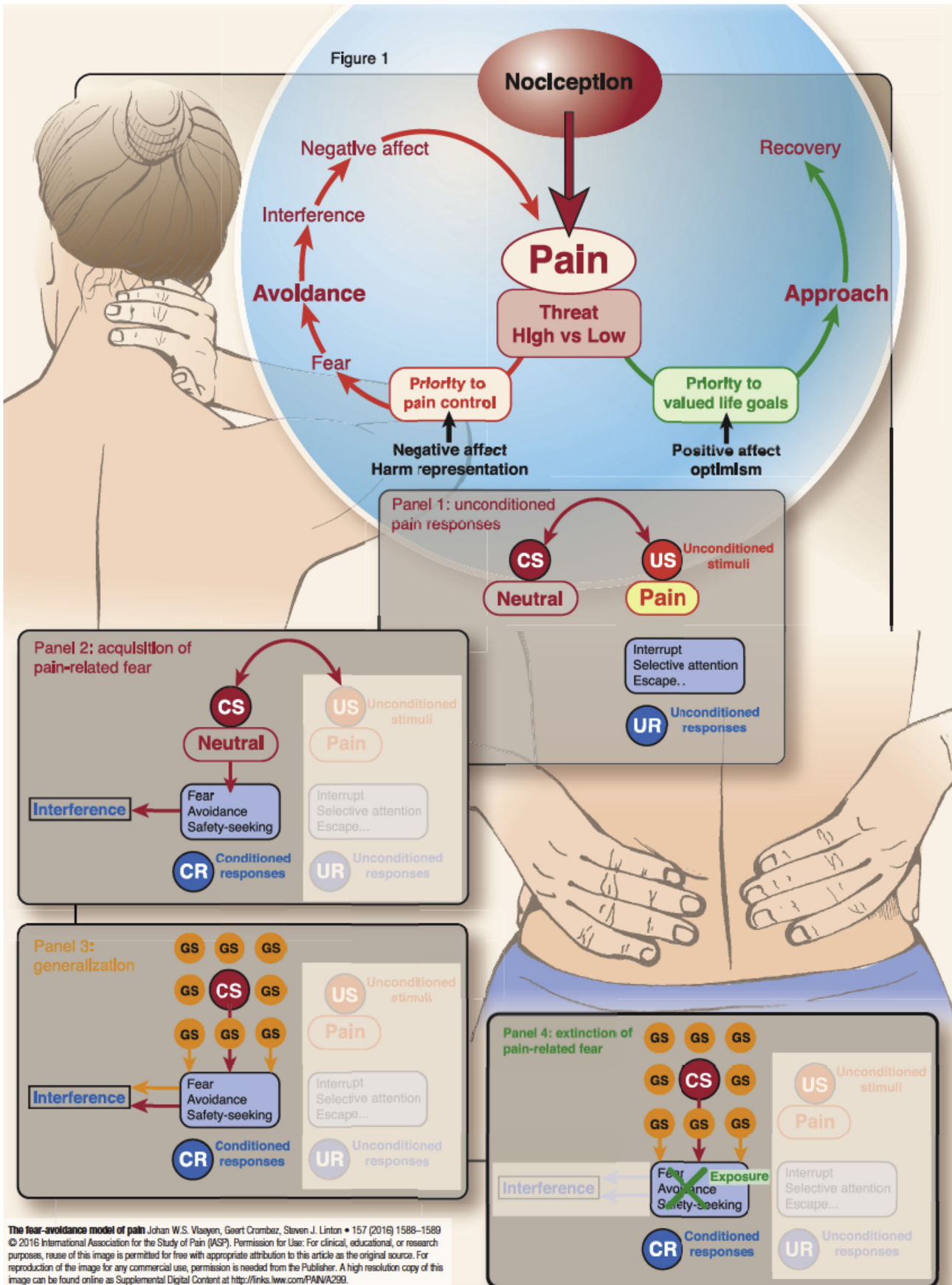
Recently, researchers have focused upon the role of “hot” cognitions in distraction, hence introducing the motivational and goal dynamics of human action back into the cognitive system (Anderson & Yantis, 2013; Munneke, Hoppenbrouwers, & Theeuwes, 2015). Individuals pursue goals because they consider these as personally relevant, or of value. Goal pursuit may lead to the delivery of positive outcomes, or, the avoidance of negative outcomes. We therefore expect that particular goal characteristics influence 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 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 (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; 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.

2.4. Pain and attentional bias

In the preceding paragraphs, we have gradually built a modern learning account of pain, which operates in a context with multiple demands incorporating affective and motivational aspects (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 a modern learning account of pain that incorporates cognitive, affective, behavioral and motivational aspects. 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 frustrating 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).

2.5. Conclusion

Pain is a hardwired signal of bodily harm, and has an inherent capacity to capture attention and the urge to 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 analog of the experienced interference of daily activities by pain.

3. The role of learning and memory in the maintenance of avoidance behavior

Pain not only has an interrupting function, it also is a potent motivator of avoidance learning (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 as 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 evoke 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; 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 (see Fig. 1).

3.1. Pain-related fear acquisition

A series of experimental studies has attempted to provide experimental evidence for the idea that anticipatory pain-related fear responses are the result of associative learning (Goubert, Crombez, & Peters, 2004; 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, we developed 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- movements (Meulders, Vansteenwegen, & Vlaeyen, 2011). We 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 (Meulders & Vlaeyen, 2013b). Comparable findings were also 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 (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 (Goubert, Vlaeyen, Crombez, & Craig, 2011; Helsen, Goubert, Peters, & Vlaeyen, 2011), or by virtue of symbolic representations of pain (Jepma & Wager, 2015), or the conceptual equivalence between stimuli, and their derived relationships with pain (Bennett, Meulders, Baeyens, & Vlaeyen, 2015).

In the previous paragraph, we described the acquisition of pain-related fear occurring in situations where there are cues that predict the onset of pain (cued pain-related fear). There are however situations in which pain is perceived as unpredictable. In those situations, individuals will consider more long-lasting contexts as valid predictors of pain (contextual pain-related fear) (Grillon, Baas, Cornwell, & Johnson, 2006). These contexts can concern the interpersonal, physical or bodily domain. Translated to the area of chronic pain, cued pain-related fear induced by predictable pain (i.e., pairings of movement and pain), may be typical for regional pain such as low back pain. In contrast, chronic contextual pain-related fear induced by unpredictable pain might be a model for widespread pain and fibromyalgia in which pain unpredictability is

Fig. 1. Figure depicts the reciprocal relations among pain and its effects, along with the role of conditioning. Depending on the interpretation of pain as threatening or not, priority will be given to pain control versus valued (non-pain) life goals. The left side of the picture represents the sequence of events that occur when pain is considered a sign of bodily harm that needs to be controlled. Such an interpretation is usually accompanied by fear and avoidance responses. Longstanding avoidance behavior interferes with daily life goals producing negative affect, which amplifies the experience of pain. The right side of the figure depicts the situation in which pain is not considered a sign of harm, and where priority is given to the pursuit and approach of valued life goals, leading to recovery. The panels illustrate the role of conditioning with the unconditioned pain response (panel 1), the acquisition (panel 2), generalization (panel 3) and extinction (panel 4) of pain-related fear (From Vlaeyen et al., 2016, reprinted with permission of Kluwer-Wolters and IASP).

reported to be characteristic (e.g. Johnson, Zautra, & Davis, 2006; Meulders & Vlaeyen, 2013a).

3.2. 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 lowers the risk of missing positive alarms, but may increase responses 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 in then last decade probably due to its explanatory power. As space limitations do not allow us to elaborate this further, we mention a couple studies relevant to pain-related fear. Using the joystick movement paradigm mentioned earlier, we could establish 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 (Meulders & Vlaeyen, 2013a; Meulders, Vandebroek, Vervliet, & Vlaeyen, 2013). We also demonstrated non-perceptual generalization of pain-related fear from conditioned nonsense words (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). In patients with fibromyalgia, a striking 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 (Meulders, Jans, & Vlaeyen, 2015; Meulders et al., 2014). 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. In sum, by virtue of the process of generalization, novel bodily, interpersonal and ecological stimuli that somehow share features with the conditioned stimuli may play a key role in the maintenance of pain-related fear and avoidance.

3.3. Pain, fear and avoidance behavior

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 e.g. Arntz, Rauner, & van den Hout, 1995), due to lack of actual exposure, avoidance limits learning about the alleged threat. As a result, the memory representations may become subject to various distortions, and the characteristics of the feared pain may become dissociated from the actual experience.

One of the impediments 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 may provide a suitable 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 however 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 (Meulders, Franssen, Fonteyne, & Vlaeyen, 2016). The same paradigm might be used to test the generalization of such pain-related avoidance behavior, and the hypothesis that stimuli that share features with the discriminative stimulus (the presence of a person or location) also evoke similar avoidance behaviors.

3.4. 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, for example operationalized as obtaining a monetary reward (Claes, Karos, Meulders, Crombez, & Vlaeyen, 2014). Using the 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 pain only. The results showed in 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).

3.5. 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, Vansteenwegen, Lysens & Eelen, 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 (Vlaeyen, Morley, Linton, Boersma, & De Jong, 2012) and irritable bowel syndrome (Boersma et al., 2016; Craske et al., 2011). 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 (Den Hollander et al., in press; 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, daily functioning, quality of life, and return to work (de Jong, Vlaeyen, Onghena, Cuyper, et al., 2005; de Jong, Vlaeyen, Onghena, Goossens, et al., 2005; de Jong, Vlaeyen, van Eijsden, 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 do not seem to favor the adoption of safety-seeking behavior during exposure-based interventions (Meulders, Van Daele, Volders, & Vlaeyen, 2016). 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.

3.6. 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, 2016), 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 (Crombez et al., 1994a, 1994b), and insights from placebo/nocebo research might be conducive here (e.g. Buchel, Geuter, Sprenger, & Eippert, 2014). For example, a recent study was able to show changes in pain threshold as a result of a simultaneous conditioning procedure. Non-noxious (vibrotactile) stimuli at a certain body location that had been associated with painful nociception later influenced the perception of ambiguous nociceptive stimuli in the presence of the conditioned non-noxious stimulus (Madden et al., 2016). 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. Fourth, the main focus of this section was on Pavlovian associative learning, or learning to predict the occurrence of potentially harmful stimuli in that environment. However, learning about consequences of verbal and non-verbal expressions of pain through operant learning is relevant as well (Fordyce, 1976; Gatzounis, Schrooten, Crombez, & Vlaeyen, 2012; Main, Keefe, Jensen, Vlaeyen, & Vowles, 2014). 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. The effects of chronic pain on the sense of self, individual goals 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., (Karoly & Ruhlman, 1996, 2007). Daily process studies further reveal the relationships between pain and individual goal pursuit and goal attainment. For example, Affleck et al. (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 can pursue their valued goals despite pain. Another study corroborated these findings and revealed more optimistic individuals were less likely to perceive pain-related goal barriers and less likely to reduce their goal-directed effort (Affleck et al., 2001). Indeed, optimism is considered a resilience factor receiving increased attention in the pain research field e.g. (Hanssen, Peters, Vlaeyen, Meevisse, & Vancleef, 2013).

The repeated interference by pain with daily activities can have a significant effect on one's "sense of self" as well (Charmaz, 1983, 1999). The inability to complete a task or to perform it to an acceptable standard or to one's expectations of what others might require is deeply frustrating, and leads to a steady degradation in one's behavioral 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). 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.

4.1. Pain-related self-discrepancies

Morley and colleagues have also investigated the relationships between aspects of self, pain and affect by drawing on the self-discrepancy theory (SDT) and self-regulation theory (Carver, 2004, pp. 13–39; Carver & Scheier, 1998; Higgins, 1997). Higgins identifies the *magnitude* of the discrepancy between self-aspects as the determinant of the consequent affect and behavioral 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 behavioral response. 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, which is the extent to which elicitation of the "self" schema primes the "pain" schema and vice versa (Pincus & Morley, 2001). As expected, the predictions of SDT were confirmed. The extent to which persons regarded themselves as enmeshed with pain impacted the level of depression. 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 which also indicated 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 Gavrín (1999) noted: "*The development of painful arthritis in the fingers would have a minor impact for most middle-aged people, but could be devastating for a professional concert musician because it affects what he or she is and can hope to be in the*

future" (p. 2234).

4.2. Conclusion

This section has only briefly touched on the relationship between the repeated experience of pain, the sense of self, individual goals and identity. 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.

Putting it all together, there is good evidence for a modern learning perspective for the transition from an acute pain episode to a chronic pain syndrome, which incorporates cognitive, affective, behavioral and motivational aspects. A naturally occurring pain sensation may grab special attention when it is perceived as intense, novel or unpredicted. Given the increased salience, cues may help the individual anticipating subsequent occurrences of such painful stimuli and prepare engaging in protective actions. Learning occurs quickly, and these cues can become conditioned stimuli that are likely to be avoided, if possible. Initially, such avoidance behaviors may be strategic, but they may quickly become habits that are evoked by a wider range of stimuli that share features with the original cues. Sustained as well as generalized avoidance behavior may lead to various degrees of interference in daily life, finally affecting the sense of self. Negative affect that is associated with the non-accomplishment of individual life goals as well as with conflicts between competing goals holds the risk to maintain the threat value of pain and its cues.

Inhibitory responses can be learned when avoidance behavior is omitted, and the individual is exposed to those stimuli and situations that align with valued life goals, but were previously avoided because of (anticipated) pain. In such exposure treatments, new non-threat associations with the CSs are formed, and subsequently may generalize across time and contexts. In contrast to its acquisition, the extinction of pain-related fear is fragile, context-dependent, and it does not easily generalize to novel situations.

5. Novel chronic pain management strategies

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, and there is ample room for improvement.

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 novel study designs, such as the *replicated single case methodology* are indicated as viable strategies for improving treatment effectiveness. In addition, they hold a key to bridging the well-known scientist-practitioner gap.

5.1. Novel study 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, p. 57). Single-case experiments were introduced more than 40 years ago (Barlow & Hersen, 1973), are ideally suited to assess treatments that are tailored to individual patient characteristics, but are yet to be widely adopted by pain researchers. SCEDs are particularly forceful 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, and finally also by pain intensity reports, but at a slower pace (de Jong, Vlaeyen, Onghena, Cuyper, et al., 2005; de Jong, Vlaeyen, Onghena, Goossens, et al., 2005). 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 held 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 statistical (randomization) tests available that require no assumptions about data distribution, which facilitate reliable analysis. Fourth, SCEDs allow for immediate feedback on the outcome of a given treatment to both patient and health care provider, and present empirical evidence that can be used to guide subsequent decision-making. As such, SCED is a promising bridge narrowing the scientist-practitioner gap. Fifth, statistical outcome parameters of replications of SCEDs can be combined in a single meta-analysis, with each additional and successful replication supporting the external validity of a particular treatment. 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. Seventh, 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.

Last but not least, SCEDs can also be used to assess the effects of compensatory strategies used by patients in chronic pain. For example, SCEDs have also been applied in the manipulation of attention (Sohlberg, & Mateer, 1987), and Flink, Nicholas, Boersma, and Linton (2009) used SCEDs to test the effects of a form of interoceptive exposure as well as a relaxation/distraction breathing-based technique in patients with chronic back pain. The same design can also be used to test whether a Self-Systems Therapy (SST; Strauman et al., 2006; Waters et al., 2016) improves the “sense of self”, and reduces distress in patients with chronic pain. SST is a brief structured therapy designed for individuals who are experiencing difficulties pursuing their valued life goals, and it would be worthwhile to test whether a compound SST-exposure treatment would be more effective in depressed patients with chronic pain as compared to exposure alone, for example using a cross-over ABC/ACB SCED, with A = baseline, B = exposure or SST and C = SST or exposure. A similar design has been used earlier to disentangle the differential effects of graded activity and exposure (Vlaeyen, de Jong, Geilen, Heuts, & van Breukelen, 2001), and education and EXP (De Jong et al., 2005) in patients with chronic low back pain. In addition to SCEDs, there are other novel study designs that may enable pain psychologists to increase the potency of their behavioral interventions. One is the Multiphase Optimization Strategy (MOST; Collins, Murphy, Nair, & Strecher, 2005). Another novel approach is the Sequential Multiple Assignment Randomized Trial (SMART; Murphy, 2005) characterized by an iterative process with a repeated update of the initial treatment chosen, and random assignment to one of two alternative treatments if the outcome is unsatisfactory. SMART designs do not randomize participants but rather use decision rules to guide treatment, and fit well with a stepped-care approach starting with the least intensive approach, moving on with more elaborate treatments. Both MOST and SMART designs allow for the development of adaptive interventions that use patient characteristics to tailor treatment.

6. General conclusion

The main underlying theme in this review is the competitive-conflictual nature of pain, and the individual's adaptation to it, 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 modern learning approach, incorporating cognitive, affective, behavioral and motivational aspects 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.

Acknowledgements

We are grateful to two anonymous reviewers for helpful suggestions. Johan W.S. Vlaeyen is supported by the Asthenes research program “From acute aversive sensations to chronic bodily symptoms”, a long term structural Methusalem funding (METH/15/011) by the Flemish government, Belgium.

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