J Rat-Emo Cognitive-Behav Ther (2010) 28:4–24
DOI 10.1007/s10942-010-0109-x

ORIGINAL ARTICLE

Maladaptive Cognitions and Chronic Pain: Epidemiology, Neurobiology, and Treatment

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Published online: 22 January 2010

Abstract Maladaptive cognitions are widespread and play a significant role in the development of chronic pain. (1) Catastrophizing seems to increase the risk of chronicity. In the laboratory it amplifies temporal summation of pain with repeated stimulation and delays the disengagement of attention from pain. In neuroimaging it is associated with increased activation in regions of the cortex involved in attention, the aversiveness of pain, and possibly pain intensity. (2) Fearful anticipation of pain seems to pre-activate brain regions involved in both the sensory and emotional intensity of pain and primes a stronger initial pain response. It may lead to abnormal patterns of muscle recruitment that, speculatively, may predispose to injury. (3) Belief that normal activity should be avoided seems to promote unnecessary long-term disability in nonspecific low back pain. Extreme guarding may intensify pain through loss of inhibition from motor cortex. (4) Educational programs targeting maladaptive beliefs have shown benefit in the primary prevention of chronic back pain in both pain-free and acute pain populations. In established chronic pain, cognitive-behavioral therapy has shown efficacy in improving pain intensity, coping and pain behaviors when compared with usual treatment. (5) Possible future research directions and clinical implications are discussed.

Keywords Catastrophizing · Fearful anticipation · Pain · Maladaptive cognitions · Neurobiology

Introduction

The impact of belief on pain is illustrated by a recent study: The pain produced by an electric shock delivered to the ankle was measured in healthy volunteers via

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self-report, via somatosensory evoked potential EEG, and via leg withdrawal reflex (Goffaux et al. 2007). At short durations, leg withdrawal can be due to startle, and at long durations, of course, it can be a conscious decision, but between 85 and 120 ms, too slow for startle and too quick for the round trip to the brain, it is a reflex, indicating the sensitivity of the spinal gray matter to pain (Kiernan et al. 1995).

Now, on some trials, subjects also immersed their left arms in ice water and, as was expected, this second pain inhibited the first pain on all three measures. Colloquially we think of a second pain as "taking our mind off" the first, but pain-on-pain inhibition ("diffuse noxious inhibitory controls"), unlike distraction, mostly reduces pains of moderate intensity. Pains that are either mild or severe are less affected (Plaghki et al. 1994). Moreover, animal research has demonstrated that diffuse noxious inhibitory controls can be traced to a brainstem reflex: The second pain activates the dorsal reticular nucleus in the medulla, which reduces the first pain via the endorphin system (Willer et al. 1999).

What makes this a study of belief is that half the subjects were told that the ice water was expected to induce a whole-body hyperalgesic state, magnifying the intensity of all other pains. Of course, hyperalgesia was not expected, nor did it occur. However, the misinformation was enough to completely abrogate the analgesic effect of the ice water—at the level of self-report, at the level of evoked potential, and at the level of spinal reflex. A false belief that took less than a minute to inculcate proved to be stronger than a well-validated brainstem reflex. The authors ask: What then is the effect of maladaptive beliefs that develop over years?

Belief and the Risk of Chronic Pain

The study by Goffaux et al. is an example of the nocebo effect (from the Latin, "I will harm," Wall 1999), an inverse placebo in which belief or expectation produces rather than relieves symptoms (Kennedy 1961). Other maladaptive cognitions studied in relation to pain are catastrophic appraisals, the fearful regard of pain, and the belief that physical activity can intensify injury and should be avoided.

Corresponding to these variables, psychometric instruments have been developed with acceptable internal consistency and support for their validity. Thus, catastrophizing is generally measured with either the catastrophization subscale of the Coping Strategies Questionnaire (Rosenstiel and Keefe 1983) or the Pain Catastrophizing Scale (Sullivan et al. 1995). Fear of pain is generally measured with the Fear of Pain Questionnaire (McNeil and Rainwater 1998) or the Pain Anxiety Symptoms Scale (McCracken et al. 1992). The belief that physical activity is harmful in pain is generally operationalized with the Fear Avoidance Beliefs Questionnaire (FABQ; Waddell et al. 1993), the Tampa Scale for Kinesiophobia (Kori et al. 1990; French et al. 2007), or with the Pain and Impairment Rating Scale for patients (PAIRS; Riley et al. 1988) or for healthcare providers (HC-PAIRS; Houben et al. 2004; Rainville et al. 1995).

Studies with these instruments have shown, among other things, that the propensity to think about pain catastrophically is relatively stable over intervals of

at least 6 months—it has a trait-like quality (e.g., Keefe et al. 1989)—and that although it correlates to a degree with anxiety, depression, and the tendency to negative affect, it contributes uniquely to acute and chronic pain (Sullivan et al. 2001). Moreover, catastrophizing and fear-avoidance beliefs are relatively uncorrelated, despite good reliability of the individual scales (e.g., Linton et al. 2000).

Catastrophizing

The term "catastrophizing" was introduced by Albert Ellis, who illustrated it by noting that "even physical pain is experienced and reacted to not only in relation to the intensity of the painful stimulus but largely in relation to the subjective, individual, attitudinal prejudices of the person who is stimulated" (Ellis 1962, p. 71). Current definitions of pain catastrophizing include feeling overwhelmed and helpless, ruminating on the pain, and having an exaggerated sense of the likely negative consequences of the pain (Sullivan et al. 1995).

Catastrophizing has emerged as a strong predictor of future pain level. Thus, Picavet et al. (2002) in a population based study, found that among individuals free of low back pain at baseline, those scoring in the top third of the distribution on the Pain Catastrophizing Scale were 2.1 times more likely to have low back pain that was chronic, 2.2 times more likely to have low back pain that was severe, and 3.1 times more likely to have low back pain that was disabling at 6 month follow-up, than people scoring in the lowest third.

In Picavet et al.'s study, catastrophizing at baseline was not a risk factor for the onset of back pain, only for its persistence, severity, and tendency to disable. Similarly, Linton et al. in prospective study of 415 individuals initially without back pain, sampled randomly from the general population of Sweden ages 35–45, found no predictive relationship between catastrophizing at baseline and incidence of back or neck pain over the next year (Linton et al. 2000).

In a prospective study of people who already had acute or subacute low back pain, catastrophizing accounted for 47% of the variance in the development of chronic pain (Burton et al. 1995). Among people with chronic pain from rheumatoid arthritis, the level of catastrophizing at baseline predicted further deterioration in the level of pain, mood, and functioning over the next 6 months, after controlling for potential confounds (Keefe et al. 1989). Very similar results for pain intensity have been reported from an 8-week prospective trial in post-herpetic neuralgia (Haythornthwaite et al. 2003). Note that in these three diagnostic categories, two distinct types of pain generator are represented: nerve damage (neuropathic pain) in post-herpetic neuralgia, and tissue damage (nociceptive pain) in rheumatoid arthritis. Thus, the effects of catastrophizing seem robust.

(The situation is not as clear for a third type of pain, deafferentative, in which the key process is a loss of sensory input—phantom limb pain being the prototypical exemplar. Jensen et al. (2002) found no influence of catastrophization at 1-month post-amputation on phantom limb pain at 6 months. However, deafferentative pain is unusual in that it may arise on a purely cortical level (Flor et al. 1995; Harris 1999). Moreover, 6 months post-amputation is a bit early for the development of

phantom limb pain (Wall 2000) and, indeed, there was no overall increase in pain over the 5 months of Jensen et al.'s study.)

In cross-sectional studies, catastrophizing seems related to pain intensity primarily during the first 3 years of the condition (Boersma and Linton 2005; Citero et al. 2007). Although we cannot infer causality from this data, there is the hint that catastrophizing may exert its malignant effects on pain primarily from the acute phase to the consolidation of chronicity (Citero et al.).

In contrast, cross-sectional data suggests that physical functioning, influenced only by pain level early on, comes increasingly under the control of catastrophizing (Sullivan et al. 2002) and fear-avoidance beliefs/kinesiophobia (Boersma and Linton 2005) during the first few years after onset. Thus, while catastrophizing is exerting progressively less influence on pain intensity, catastrophizing and fear of reinjury seem to exert progressively greater influence on functioning over time.

Fear-Avoidance Beliefs

The distinction between catastrophizing and fear-avoidance beliefs, suggested by the low correlations between their respective psychometrics, raises the possibility that they have different effects on pain. Perhaps fear of pain contributes to new-onset back or neck pain while, as we have seen, catastrophizing seems to relate only to the course of pain once it begins. (We will encounter a theory of how fear of pain can predispose to back injury in the next section.) Thus, Linton et al. (2000) found that in a random sample of 415 individuals initially free of spinal pain, an above-median score on the Fear-Avoidance Beliefs Questionnaire conferred a 2.0-fold greater risk for incident pain, and a 1.7-fold increased risk for physical impairment due to pain, 1 year later. Van Nieuwenhuyse et al. (2006) report a 1.8-fold increase in risk of onset of low back pain in pain fearful subjects. This finding has not always replicated, however: Picavet et al. report no predictive value for kinesiophobia in the onset of low back pain over 6 months. Among those who already had back pain, however, the fear-avoidance belief increased the probability that the pain would be present (odds ratio = 1.6), chronic (odds ratio = 1.6) and severe (odds ratio = 3.0), 6 months later (Picavet et al. 2002).

Not surprisingly, the belief that physical activity will worsen pain seems to be strongly related to disability 1 year later (Waddell et al. 1993). In the study of Picavet et al., noted above, a score in the top third of the distribution on the Tampa Scale for Kinesiophobia conferred a 3.4-fold increased risk for disabling low back pain 6 months later, compared with people scoring in the bottom third. This was for people who were initially pain-free. For those who already had back pain at baseline, the risk of disability was increased by a factor of 4.4.

The prognostic value of pain-related fear and avoidance in the acute stage for later disability has been noted by others as well. For example, Fritz and George (2002) found that the work subscale of the Fear-Avoidance Beliefs Questionnaire predicted the persistence of work restrictions after 4 weeks of physical therapy (odds ratio = 1.2). Indeed, Crombez et al. found that while the Fear-Avoidance Beliefs Questionnaire and the Tampa Scale for Kinesiophobia predicted self-reported disability and performance on a computerized exercise machine, pain

intensity did not correlate with either disability or performance. Only on a lifting task did pain intensity predict as well as the fear of activity measures (Crombez et al. 1999).

Now, for fear-avoidance measures, the situation may not be as clear as for catastrophizing—the strength and consistency of association of fear-avoidance with outcome for acute pain has been questioned. Using a conservative, random-effects meta-analysis model, Pincus et al. (2006) computed a pooled effect size for prospective cohort studies of 0.17, rather small by conventional criteria (Cohen 1988). The authors point out that avoidance can result from depression and from affectively neutral beliefs about the proper way to manage back pain, and that these may be more important early in the course of an injury. Other reviews have been more favorable (e.g., Leeuw et al. 2007), with the difference seeming to trace to the inclusion criteria for studies. We will return to some of the complexities of the field at the end of this article, and encounter additional support from intervention studies based on the fear-avoidance model.

Nonetheless, maladaptive cognitions clearly play a role in chronic pain. And they have two other properties that impel us to study them: They are common and they can be changed. But before we examine these facets in detail, let us consider how it is that these psychological variables could have an effect on physical pain.

Towards the Mechanism: Psychophysics, Cognition, and Neuroimaging

By what mechanisms do maladaptive beliefs influence pain? We will look for explanations on the cognitive, the psychophysical, and the biological planes.

Note that the neural structures involved in pain processing have at least three characteristics that allow psychological factors to affect pain:

(1) Pain is encoded by a distributed network of central nervous system structures. It is in the coordinated firing of brain regions encoding the sensory and affective components of pain, body schema, physical threat, cognitive evaluation, emotional reaction, and alertness, orienting and arousal that pain is encoded (Apkarian et al. 2005). Therefore, psychological states encoded by overlapping regions can partially prime the pain network. Thus, depression seems to activate the same region as the affective quality of pain, and a region encoding body schema (and presumably physical threat) is activated in posttraumatic stress disorder as it is in pain (Geuze et al. 2007; Tucker et al. 2003).

(2) Descending pathways inhibit and facilitate transmission along the bottom-up pain pathways. The most well-known pain inhibitory system uses endorphins as its neurotransmitter, but the descending network is likely complex and varied (Bandler et al. 2000; Fields 2000). These systems allow the brain to modulate—inhibit or facilitate—activity in the spinal gray matter.

(3) Synapses in pain pathways can strengthen as a result of repeated activation (Sandkühler 2000; Woolf and Salter 2000). This central sensitization of pain pathways has been studied primarily in the spinal gray matter, and may be a

key component in the transition from acute to chronic pain. Because top–down processes influence firing rates in the pain pathways, it is possible that these processes also influence whether central sensitization to pain takes place (Gjerstad et al. 2001).

Catastrophizing

In psychophysical studies, catastrophizing does not seem to influence the initial pain caused by an experimental stimulus (e.g., George et al. 2007; Gracely et al. 2004). Rather, it predicts a steeper slope of pain increase when stimulation is repeated at short intervals—i.e., a faster "windup" or acceleration of pain ratings (Edwards et al. 2006; George et al. 2007; Granot et al. 2006).

Windup is thought to be an early step in the development of central sensitization of pain processing regions (Woolf 1996). Thus, the faster windup seen in catastrophization could be a core process leading to long-term worsening of pain. This seems to dovetail with evidence that after an acute pain has subsided, pain thresholds may remain lower in high catastrophizing individuals (Edwards et al. 2004).

Animal studies trace windup to the superficial dorsal horn, the portion of the spinal gray matter most involved in pain processing (e.g., Woolf and Salter 2000). A natural hypothesis, then, is that catastrophization involves decreased activity in descending pain-control pathways such as the endorphin system, or an increase in descending pain facilitation. This would permit higher firing rates in the dorsal horn, resulting in faster windup, the development of central sensitization and, ultimately, the transition to chronic pain seen in clinical populations.

Further adding to the appeal is that certain types of placebo response, particularly placebo responding generated by expectation of relief (as opposed to, for example, classical conditioning with non-opioid drugs), involve an increase in endorphinergic tone (Amanzio and Benedetti 1999; Bingel et al. 2006). Further, self-efficacy in pain coping seems to produce an increase in endorphinergic tone (Bandura et al. 1987). As the overwhelmed, helpless aspect of catastrophizing is in some senses the inverse of self-efficacy or a placebo effect, it seems natural to presume a reduction in descending pain inhibition.

All this assumes, however, that the increased windup can indeed be traced, not just in animals but in people, to the dorsal horn. We can measure the sensitivity of the dorsal horn somewhat directly using the limb withdrawal reflex. As it turns out, whether this reflex is measured in healthy populations (who, however, show a broad range of catastrophizing scores; Sullivan et al. 1995) or in people with osteoarthritis, and whether catastrophizing is measured as a trait prior to the pain or as a state following the pain, and whether the Pain Catastropizing Scale, the Coping Strategies Questionnaire, or a rating scale is used, no correlation with catastrophizing emerges (France et al. 2002, 2004; Rhudy et al. 2007). Moreover, while cognitive coping skills training can reduce the withdrawal reflex significantly, this effect does not seem to depend on scores on the Pain Catastrophizing Scale (Emery et al. 2006). Proponents of the endorphin theory point out that activity in one particular brain

region—the dorsolateral prefrontal cortex—does correlate negatively with catastrophization during pain (Seminowicz and Davis 2006), and that this region of cortex has been linked to the endorphin system (Lorenz et al. 2003). However, with no change in spinal reflexes, it appears that the influence of catastrophization exists purely within the brain.

What, then, is happening in the brain? In cognitive studies, the combination of catastrophizing and the anticipation of a high pain level seems to increase the amount of attention sequestered by pain (Crombez et al. 1998). More exactly, the combination seems to delay the disengagement from pain and from signals that pain is impending (Van Damme et al. 2004).

Using functional MRI, Gracely et al. report that when a noxious level of pressure is applied, fibromyalgia patients who score high in catastrophizing have increased activation in brain regions associated with selective attention (rostral anterior cingulate cortex, medial frontal cortex), the sensory intensity of pain (secondary somatosensory cortex), and motor responses (e.g., cerebellum, premotor cortex; Gracely et al. 2004). Thus, the imaging results seem to fit with the idea that catastrophization engages attention to the pain, increasing brain activation associated with pain intensity and with preparing for escape/avoidance behavior.

Similarly, studying healthy volunteers, Seminowicz and Davis (2006) found positive correlations with catastrophizing for regions involved in selective attention (rostral anterior cingulate cortex) and emotional pain intensity (insula). These same two regions seem to be deactvitated in at least certain forms of placebo analgesia (Wager et al. 2004). Moreover, for more intense pain stimuli, Seminowicz and Davis found that activation of dorsolateral prefrontal cortex—possibly involved in pain control—was correlated negatively with catastrophizing score.

Thus, it appears that catastrophization, by focusing attention on pain, intensifies brain activity associated with the experience of pain, may decrease activity associated with pain control, and in people with fibromyalgia, also increases activity associated with motor (presumably escape/avoidance) behavior. In both the laboratory and neuroimaging, catastrophization seems to intensify the degree to which pain captures attention. Presumably, this process leads to sensitization of pain processing structures in the brain, without affecting descending pain modulation at the spine.

Fear-Avoidance Beliefs

How does fear increase pain? Path analytic studies have supported two links: by way of increased vigilance to pain (Goubert et al. 2004) and by way of depression and disability (Cook et al. 2006). In theory, disability can increase pain by limiting involvement in competing activities. Depression may increase pain through priming, if depressing thoughts are connected to pain (Rainville et al. 2005), through direct activation of brain regions associated with pain aversiveness (Tucker et al. 2003), through induction of inflammatory processes (Kim et al. 2007), and possibly by changing how pain is processed at the spinal level (Müller and Schwarz 2007). To delve into the mechanisms connecting fear and pain, however, we will

first divide fear-avoidance beliefs into (1) fearful anticipation of future pain, (2) fearful experience of current pain, and (3) avoidance of activity.

Anticipation

We would expect fear of pain to entail scanning the environment for threat-related stimuli, and then selectively attending to these stimuli (Eysenck 1992). There is indeed a little evidence that pain-related fear includes vigilance to bodily sensations, at the expense of attentiveness to other sensory modalities (Peters et al. 2002). However, the direct attention-sequestering effects of fear-avoidance beliefs have not been studied as extensively as for catastrophizing. Rather, it is in psychophysics that the effects of anticipation seem most apparent.

For unlike catastrophizing, fear of pain seems to be associated with a greater initial pain response, as if the fear had primed the pain system (George et al. 2007). Not surprisingly, then, it appears that fearful anticipation of pain activates some of the same brain structures as are involved in the perception of pain. This is especially true at the insula (Ploghaus et al. 1999), a region of the cortex that may encode body schema and thus be involved with the physical threat associated with pain. However, activation at somatosensory cortex and the anterior cingulate cortex, encoding sensory and affective intensity of the pain, respectively, has also been reported (Porro et al. 2002). Fear seems to be central to the priming. When subjects are familiar with the pain stimulus from repeated presentation, such that it is presumably no longer a source of anxiety, anterior cingulate cortex is instead deactivated during anticipation (Hsieh et al. 1999).

That a pain-relevant brain region would be deactivated in anticipation of pain may be a coping response. Similarly, using fMRI, Fairhurst et al. found that anticipation of pain activated some of the structures involved in pain perception, including the insula, anterior cingulate cortex, the thalamus, and premotor cortex. They also found anticipatory activation in a number of brainstem nuclei involved in pain processing (periaqueductal gray, entorhinal cortex) but here the interpretation is equivocal. Because activation of these brainstem regions during anticipation correlated with subsequent activation of pain-sensitive structures during the painful stimulus, Fairhurst et al. suggest that the brainstem structures were intensifying the pain signal. However, these regions are also part of the endorphin system, and could reflect an attempt to modulate the pain in advance. The neuroimaging results to date allow for anticipatory modulation in either direction (Fairhurst et al. 2007).

Current Pain

These possible dual aspects—a heightened pain response and efforts to reduce the pain—are clearer during ongoing pain. In healthy volunteers, Ochsner et al. found that the fear was associated with increased activation in anterior and posterior cingulate cortex, presumably reflecting attentiveness to the aversive and threatening aspects of pain. However, there was also activation of right lateral orbital frontal cortex (Ochsner et al. 2006). This region seems to be involved in inhibiting a habitual response. It is notably hypoactive in substance abuse (see, e.g., Fumal et al.

2006). Conversely, its activation increases when a person uses cognitive reappraisal to reduce a negative emotion (Ochsner et al. 2004) and when pain is reduced by absorption in a competing task (Petrovic et al. 2000). Thus, during exposure to pain, fear seems to elicit both awareness of threat and compensatory efforts to manage the aversiveness.

The effects of fear of pain on windup seem to have been little studied, but the research to date does not suggest an influence (George et al. 2007). This is in contrast to state and trait anxiety, which do seem to increase the rate of temporal summation (Granot et al. 2006; Robinson et al. 2004). If fear of pain indeed lacks this effect, it might be further evidence of recruitment of descending pain control. Of note, however, the spinal nociceptive limb withdrawal reflex does not seem to have been studied in relation to fear of pain specifically, and thus, whether fear of pain has effects on the spinal level has not yet been determined.

Avoidance Behavior

All this pertains to fear, but what about avoidance? Traditionally, fear-avoidance beliefs were thought to intensify pain over time through disuse and deconditioning: By avoiding activity, patients would progressively lose muscle tone, flexibility, and aerobic capacity, thus making subsequent activity progressively more uncomfortable. However, despite its intuitive appeal, the theory has received little support from cross-sectional (Smeets et al. 2006) and longitudinal (Bousema et al. 2007) studies.

Perhaps, then, avoidance beliefs pertain more to long-term disability than to pain sensation. Yet we must not discount a role in pain too quickly. Consider: Activation of motor cortex, whether by electrodes on the overlying dura mater (Nuti et al. 2005), or by magnetic stimulation from outside the skull (Leo and Latif 2007), or simply by preparing to move the affected body part (Le Pera et al. 2007), reduces pain. There are neurons in motor cortex that project directly, without intervening synapses, to the dorsal horn, the pain-processing region of the spine (Fields 2000; Millan 2002), where they presumably have an inhibitory function. Moreover, electrical activation of motor cortex—and thus presumably movement itself—seems to release endorphins in cortical and subcortical structures (Maarrawi et al. 2007), change the firing in cortical regions involved in pain perception (Kishima et al. 2007), and, at least in animals, inhibit the spinal dorsal horn's responsiveness to painful stimuli (Senapati et al. 2005).

If movement lowers pain, can guarding from movement, encouraged by fear-avoidance beliefs, contribute to pain by reducing these inhibitory processes? The question has been little studied. But in reflex sympathetic dystrophy, a condition in which the guarding is so profound it induces a subtle sensory neglect of the extremity (Moseley 2004a), imaginal desensitization to movement partially reverses the disorder (Moseley 2004b, 2006).

Other mechanisms have been proposed for low back pain specifically. Thus, Moseley et al. have shown that low back pain, both acute and chronic, leads to a shift in how postural stabilization is achieved. The deep muscles of the low back are partially deactivated, and postural control is implemented by a sharp increase in

contraction of superficial back muscles (Moseley et al. 2004). This stiffens and stabilizes the spine, and is likely to be protective in the short-term (van Dieën et al. 2003). However, activation of the superficial muscles also exerts a mild compressive, downward force on the spine (Gardner-Morse and Stokes 1998). Further, the relative deactivation of deeper muscles means that shearing forces between adjacent vertebrae are not dampened as effectively (Hodges et al. 2001). Compression and shear can cause pain by stimulating receptors in the discs and facet joints of the spine and, in theory, may be a risk factor for damage to these structures in the long term (Moseley et al.). We should note that such long-term damage has not yet been demonstrated. However, in healthy, pain-free people, reduced recruitment of deep muscles in the low back is associated with a sixfold increased risk for developing low back pain over the next 2 years (Moseley 2004c).

What makes this relevant is that not only back pain, but fear of impending pain in a person who is, at the moment, pain-free, is sufficient to deactivate the deep muscles of the low back (Moseley et al. 2004). Thus, fear of pain may lead to continuous use of a muscular protective strategy. Designed for acute pain, the overuse of this strategy, in theory, may be a risk factor for eventual sensitization and degenerative changes in the spine.

Epidemiology

Thus, it appears that certain maladaptive cognitions have a deleterious effect on the course of pain, and there is preliminary evidence on how these effects take place. These cognitive variables take on added significance when we consider that maladaptive cognitions about pain are not at all rare.

Studies in this area tend to focus on low back pain specifically, because of its frequency (in Western countries, a lifetime prevalence of 65–85%; Anderson 1999; Lawrence et al. 1998; Manchikanti 2000) and costliness (c. 2% of the US workforce receives compensation for a back injury in any given year; Anderson 1999). Moreover, low back pain is a somewhat clear cut area because there is evidence from randomized, controlled trials that in the absence of sciatica (leg pain in a distribution suggesting nerve root impingement) remaining active ultimately leads to mildly improved pain (Hagen et al. 2004; Waddell et al. 1997). Further, because 90% of patients with acute low back pain recover within 12 weeks, with recovery slow and uncertain thereafter (Anderson 1999; Pengel et al. 2003), there is a natural incentive to identify people at risk for chronicity.

As we have seen, Picavet et al. found increased probability of chronic low back pain for people in the top tertile of catastrophizing, effectively placing one-third of the population at risk. Alternatively, Buer and Linton (2002) administered a version of the Fear-Avoidance Beliefs Questionnaire (FABQ) Physical Activity Scale, slightly modified so as not to require current pain to answer, to a representative sample in Sweden, ages 35–45. The original Physical Activity Scale correlated highly with the modified version ($r = .97$). Assuming that the original cutoff still applies and estimating from the histograms, it appears that 14% of the pain-free respondents were above threshold for a high score.

In a large population-based sample in Belgium, Goubert et al. found that 77% of their respondents (approximately three-quarters of whom had no back pain at the time of the survey) believed that when one has back pain a wrong move can cause serious problems. Moreover, 70% of respondents agreed that "the worst thing about back pain is that in time you can do increasingly less." Certainly this does not seem to bode well for long-term recovery. Yet if such beliefs are widespread they also seem complex, as 68% endorsed remaining active as "the best remedy against back pain" and only 15% felt that "back pain means one should refrain from physical activity" (Goubert et al. 2004). Thus, it seems possible that an individual may hold a range of beliefs about back pain. Some of these beliefs may consolidate into a strongly held schema some time after the onset of pain.

It is not only the beliefs of patients that are at issue. Coudeyre et al. (2006) found that in a representative national sample, 16% of general practitioners in France scored above threshold on the FABQ Physical Activities scale. The physicians' demographic characteristics, education about back pain and their own personal experience with back pain were unrelated to their scores. However, high scoring physicians reported being more likely to recommend bed rest, long-term sick leave, and job accommodations, and less likely to recommend activity, than their low scoring counterparts. Similar results have been noted by others: Linton et al. (2002) found that in Sweden, physical therapists and general practitioners scoring high in fear-avoidance beliefs reported being more likely to endorse sick leave. Houben et al. (2005) found that advanced physical therapy students scoring high on a measure of biomedical orientation (which correlated strongly, $r = .79$, with the Tampa Scale for Kinesiophobia) were more likely to recommend reducing or discontinuing exercise in the face of pain.

All this fits with reports from a large population based survey in Belgium: Of 679 people who had experienced low back pain in the preceding 6 months, 23% noted having received advice from their general practitioner to rest in bed; only 14% were told to stay active (On the other hand, 30% were referred to physical therapy or to a "back school" providing self-care and ergonomic advice; Goubert et al. 2004a, b).

It seems a small step to connect all these results with older, prospective research suggesting that physicians' recommendations for bed rest and as-needed analgesics tend to promote disability in their patients (Von Korff et al. 1994).

Still, a direct effect of physicians' fear-avoidance beliefs on patient outcomes has not yet been demonstrated. For example, in a representative sample of 266 rheumatologists who were treating 440 patients with subacute (4–12 weeks' duration) low back pain, 10% of the physicians (and 68% of the patients) scored above threshold on the Fear Avoidance Beliefs Questionnaire. As with general practitioners, fear-avoidant rheumatologists tended not to recommend activity to their patients. However, while patients' fear-avoidance beliefs provided a small unique prediction that the pain would persist 3 months later, the rheumatologists' beliefs did not (Poiraudeau et al. 2006).

Thus, at this point, misconceptions about back pain seem to be widespread in the general population, are represented to a degree among health care providers as well, and seem to guide provider practice. However, some of the misconceptions seem contradictory and it is not clear with what conviction they are held. The beliefs that

precede the pain may matter only insofar as they persist and crystallize into a dysfunctional schema after the onset of pain (Goubert et al. 2004a, b). It is not clear whether provider beliefs play a role in this process.

Outcome Literature

Thus, the tendency to think about nonspecific low back pain in biomedical terms seems to be widespread in the general population, presumably with an associated risk of developing entrenched fear-avoidance beliefs. This suggests that providing an alternative view of back pain when it is still in the acute stage will be helpful preventively. There is indeed evidence for this.

On the simplest level, Burton et al. compared a standard educational booklet describing the various pain-sensitive structures in the spine, medical interventions, and rest, to a novel booklet emphasizing the need to actively restore the spine to "normal function and fitness," in acute low back pain. A greater proportion of those receiving the new booklet had reductions in fear-avoidance beliefs beginning at 2 weeks, followed by improvements in daily activities at 3 months (Burton et al. 1999). This same booklet has been shown to reduce disability at 3 months compared to physical therapy alone for patients with subacute low back pain (Coudeyre et al. 2006). Similarly, Symonds et al. note reduced risk of long-term disability (Symonds et al. 1995) and Roland and Dixon (1989) report lower health care utilization over 1 year, with booklets teaching active coping.

By design, these were interventions in acute low back pain before psychosocial factors could become entrenched. Thus, in the study by Burton et al. people with a psychiatric condition or signs of nerve root impingement (sciatica) were excluded. Moreover, the back difficulties seem to have been rather mild in this cohort, as total lost work time over 1 year was 3 days in the control group, 2 days in the experimental group (not significantly different).

There may be additional benefit from psychoeducational groups in acute low back pain. Thus, in a randomized, controlled study, Linton and Andersson (2000) compared usual care plus written information (on ergonomics, encouragement to remain active) with a 6-session group. The group participants were guided in rationally evaluating the risks associated with various activities, in problem solving, in developing a self-management plan, and in scheduling activities to ensure mobilization. Although the written information was sound, the risk of disability in the cognitive-behavioral group was 90% lower at 1-year follow-up. Moreover, at 5 years post-intervention, broad improvements were noted, including lower "usual" and "worst" pain, lower anxiety and depression scores, and higher activity level and quality of life. Further, participants in the treatment group were 2.9 times less likely to be on long-term disability for any reason 5 years after the group (Linton and Nordin 2006).

Efforts at prevention have been more ambitious still. That is, because maladaptive cognitions about pain seem to be widespread and to precede injury, there is a rationale for intervening on a population level. Such an intervention was undertaken in the Australian state of Victoria, where the expense of workers' compensations claims provided a motivation. Thus, from 1997 to 1999, a public health campaign was

mounted to change beliefs about the management of uncomplicated low back pain. Television commercials discouraged bed rest and showed celebrities who had successfully managed their back pain. The educational booklet used by Burton et al. was made widely available, and evidence-based guidelines were sent to all physicians in the state. The aims of the campaign were achieved: Large-scale random surveys of physicians and of the general population of Victoria showed a shift in beliefs to a more active and hopeful form of management. No such change occurred in the neighboring state of New South Wales, where no campaign had occurred. Moreover, the number of worker's compensation claims for low back pain decreased by 15% during the campaign, and the claims that did occur were shorter and less costly (Buchbinder et al. 2001). Further, the change in beliefs was largely maintained 3 years after the campaign had ended. For example, at the follow-up, 40% of respondents in Victoria, but only 24% in the "control" state of New South Wales, agreed that back pain did not necessarily require rest (Buchbinder and Jolley 2004).

For pain that has already become chronic, cognitive-behavioral treatment has shown favorable outcome (Morley et al. 1999). The cognitive component generally includes education about psychological influences on pain, training in skills for reducing pain such as applied relaxation and absorption in non-pain activities, and skills in problem-solving and in accurately evaluating the risks with various activities. In programs based on operant principles, the behavioral component focuses on a gradually progressive exercise program in which rest is contingent on goal attainment rather than pain. Outside reinforcement for expressions of pain is eliminated if possible, and increased functioning is systematically rewarded (Fordyce 1976). In programs based on the fear-avoidance model, the behavioral component consists of a series of progressively more challenging real life experiments in which the patient tests their beliefs by directly taking on feared activities (Vlaeyen et al. 2004).

In a meta-analysis, cognitive-behavioral and behavioral treatment was superior to waiting list control on a wide range of outcomes including pain intensity, pain behaviors, coping, depression, and functioning in daily life. For pain intensity, pain behaviors, and coping, the outcome was also superior when compared to usual treatment (Morley et al. 1999).

Process studies suggest that education is effective to a degree in reducing fear, but that functional gains require the behavioral component (Leeuw et al. 2007; Kole-Snijders et al. 1999). In vivo exposure seems to cause significant reductions in catastrophizing, fear-avoidance beliefs, emotional distress, and, of note, pain intensity, in comparison with a waiting list control (Woods and Asmundson 2008). Preliminary evidence suggests that the cognitive components may be particularly important when affective distress and poor coping, rather than catastrophization and physical impairment, predominates (Thieme et al. 2007).

Future Directions

The work in this field is far from done. We have seen that catastrophization and fearful anticipation seem to involve different central nervous system responses. It

would be useful to know, for example, if depression also has unique physical overlap with the pain system. Depression resembles physical illness in lowering thresholds for pain from within the body while raising thresholds for pain at the skin (Bär et al. 2005). Moreover, in clinical depression, blood levels of interleukin-6 and other proinflammatory cytokines are elevated (Kim et al. 2007). This in turn might slow reuptake of glutamate—a key excitatory neurotransmitter for pain—in the dorsal horn (Müller and Schwarz 2007), and cause a slower decay of pain after the conclusion of stimulation. Information of this type would allow psychological treatment to be coordinated with specific problems in a patient's pain processing, identified on psychophysical testing. This could add to both the specificity and the convincingness of treatment.

The role of fear-avoidance in the sequence of how chronic pain develops leads to further questions. For example, laboratory data suggests overactivity can promote sensitization by stimulating the pain pathways, and that resting (negative reinforcement) once the pain has become intolerable can cause further sensitization through operant effects on the dorsal horn (Hölzl et al. 2005). That is, the dorsal horn may "learn" sensitization when a high pain level is followed by the negative reinforcement of rest. It is possible that fear of pain is learned over time as a byproduct of poor activity pacing. In vivo exposure might be effective in part by addressing this cycle: Exposure treatment generally involves preset exercise quotas and scheduled rest periods, so that overactivity is prevented and the contingency between pain and rest is reduced (Fordyce 1976).

Maladaptive beliefs are generally treated as main effects in predicting chronicity and disability, but their interaction with medical diagnosis seems important to explore as well. There is some evidence that early mobilization is effective for uncomplicated low back pain, but confers no advantages when sciatica is also present (Hagen et al. 2004). More generally, pain conditions in which flare-ups can be triggered by sympathetic activity (e.g., complex regional pain syndrome type I, episodic migraine, possibly myofascial pain syndrome; Borkum 2007; Drummond et al. 2001; McNulty et al. 1994) may be particularly prone to a vicious cycle with anxiety. More generally, fear-avoidance has been studied primarily in patients with low back pain. Thus, examining fear of pain in relation to pathophysiology will involve broadening the research to other diagnostic groups. This will likely be most feasible in relation to fear of pain specifically, rather than fear of activity, but analogies to kinesiophobia may emerge (e.g., fear of mental strain in chronic headaches; Todd et al. 1998, cited in Martelli et al. 1999).

This process will likely stimulate further development of the fear-avoidance construct, which has been questioned as too broad (fearful beliefs about one's usual work activities may be more relevant) and as too narrow (disability can be intensified by depression, other psychological disorder, or affectively neutral beliefs about the proper way to manage back pain; Pincus et al. 2006). As we have seen, fearful anticipation of pain, fear of current pain, and avoidance, may operate through different mechanisms.

The late effects of anxiety also deserve further study. We have encountered the theory that fear of pain leads to overuse of muscle patterns in the low back that are appropriate for splinting in acute pain, but that may predispose to back injury and

degenerative changes when maintained long-term. But there may be more at stake. Several pain conditions, including musculoskeletal and neuropathic back pain (Apkarian et al. 2004), chronic tension-type headache (Schmidt-Wilcke et al. 2005), and fibromyalgia (Kuchinad et al. 2007) have been associated with loss of gray matter in regions associated with the perception and the endorphinergic control of pain. Because the amount of loss seems to depend on the length of time since diagnosis, it can be thought of as a kind of accelerated aging of pain-relevant brain structures (Kuchinad et al.). Presumably, the loss of gray matter is due to glutamate toxicity—cell death from overstimulation of the receiving neurons (Berg-Johnsen et al. 1998). It is possible, although so far unproven, that loss of volume in regions associated with the endorphin system becomes, over time, a structural reason that pain becomes chronic.

Moreover, at least in back pain, it seems to be the affective components specifically—the unpleasantness or aversiveness of the pain—that correlate with gray matter loss (Apkarian et al. 2004; Schmidt-Wilcke et al. 2006). Thus, because fearful anticipation of pain is sufficient to activate pain networks, and because catastrophizing adds to pain unpleasantness, future research should examine whether how one copes with pain has implications for the long-term integrity of the central nervous system.

Implications

We have seen that the process by which catastrophizing, inactivity and fear can intensify pain is becoming clearer, on a sensory, cognitive, and neuroanatomical level. This allows a degree of synthesis between psychological and biomedical models, in which the variables most relevant to a given patient can be assessed, explained in biological terms, and treated. For patients, the leap of faith involved in beginning cognitive-behavioral treatment can become much shorter.

For clinicians, the translation from the literature to practice seems straightforward. For catastrophizing, fear of pain, and fear of activity, psychometrics and approximate thresholds based on normative data are available. Their incorporation into clinical assessment in subacute and chronic pain seems reasonable. For the Pain Catastrophizing Scale and the Tampa Scale for Kinesiophobia it appears that even moderate elevations are associated with increased risk of chronicity, suggesting that more extreme elevations should be treated aggressively.

For the low back, the probability of pain becoming chronic rises sharply over the first 12 weeks (Anderson 1999). Pain sensitization processes would suggest a qualitatively similar curve for other conditions. Thus, more intensive intervention is warranted for patients whose pain has persisted for at least 4 weeks.

The intensity of treatment can vary with the degree of fear and the conviction with which maladaptive beliefs are held. For simple misconceptions, presumably most common in the first few weeks after pain onset, education appears sufficient. For entrenched avoidance beliefs, more probable in chronic pain, individual cognitive-behavioral treatment will likely be needed.

In practice, there are people whose disability or experience of pain seems well described by the constructs of catastrophizing, fear of pain, and fearful avoidance of activity. The current literature seems sufficient to allow some degree of treatment matching. Other psychological variables, too, seem to be reasonably strong predictors of chronicity, including depression and clinical levels of anxiety. In the clinic, of course, we would treat any significant factor that was impeding recovery.

But the largest implication is simply the central relevance of cognitive-behavioral variables, and of the types of maladaptive cognitions first noted by Ellis nearly a half-century ago. For we have seen that such cognitions pertain not merely to quality of life, or to adjustment, or to how a patient copes with pain. Rather, in psychophysical studies, in the development of sensitization, in the transition from acute to chronic states, and in the patterns of brain activation that are the correlates of subjectivity, belief, for ill or for healing, is intrinsic to the nature of pain.

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