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How to explain central sensitization to patients with ‘unexplained’ chronic musculoskeletal pain: Practice guidelines

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ABSTRACT

Central sensitization provides an evidence-based explanation for many cases of ‘unexplained’ chronic musculoskeletal pain. Prior to commencing rehabilitation in such cases, it is crucial to change maladaptive illness perceptions, to alter maladaptive pain cognitions and to reconceptualise pain. This can be accomplished by patient education about central sensitization and its role in chronic pain, a strategy known as pain physiology education. Pain physiology education is indicated when: 1) the clinical picture is characterized and dominated by central sensitization; and 2) maladaptive illness perceptions are present. Both are prerequisites for commencing pain physiology education. Face-to-face sessions of pain physiology education, in conjunction with written educational material, are effective for changing pain cognitions and improving health status in patients with various chronic musculoskeletal pain disorders. These include patients with chronic low back pain, chronic whiplash, fibromyalgia and chronic fatigue syndrome. After biopsychosocial assessment pain physiology education comprises of a first face-to-face session explaining basic pain physiology and contrasting acute nociception versus chronic pain (Session 1). Written information about pain physiology should be provided as homework in between session 1 and 2. The second session can be used to correct misunderstandings, and to facilitate the transition from knowledge to adaptive pain coping during daily life. Pain physiology education is a continuous process initiated during the educational sessions and continued within both the active treatment and during the longer term rehabilitation program.

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1. Introduction

Over the past decades, scientific understanding of ‘unexplained’ chronic pain disorders has increased substantially. It has become clear that the majority of cases of chronic musculoskeletal pain are characterized by alterations in central nervous system processing. More specifically, the responsiveness of central neurons to input from unimodal and polymodal receptors is augmented, resulting in a pathophysiological state corresponding to central sensitization, characterized by generalized or widespread hypersensitivity (Meyer et al., 1995). Central sensitization encompasses impaired functioning of brain-orchestrated descending anti-nociceptive

(inhibitory) mechanisms (Meeus et al., 2008), and (over)activation of descending and ascending pain facilitatory pathways (Meeus and Nijs, 2007; Staud et al., 2007). The net result is augmentation rather than inhibition of nociceptive transmission. In addition to the switch in balance between inhibitory and facilitatory pathways, central sensitization entails altered sensory processing in the brain (Staud et al., 2007). Indeed, a modulated ‘pain signature’ arises in the brain of patients with central sensitization. The altered pain neuromatrix comprises of a) increased activity in brain areas known to be involved in acute pain sensations e.g. the insula, anterior cingulate cortex and the prefrontal cortex, but not in the primary or secondary somatosensory cortex (Seifert and Maihöfner, 2009); and b) brain activity in regions generally not involved in acute pain sensations e.g. various brain stem nuclei, dorsolateral frontal cortex and parietal associated cortex (Seifert and Maihöfner, 2009). ‘Cognitive emotional sensitization’ (Brosschot, 2002) refers to the capacity of forebrain centres in exerting powerful influences

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on various nuclei of the brainstem, including the nuclei identified as the origin of the descending facilitatory pathways (Zusman, 2002). The activity in descending pathways is not constant but can be modulated, for example by the level of vigilance, attention and stress (Rygh et al., 2002).

From a musculoskeletal perspective, it is important to realize that distal/peripheral mechanisms take part in the pathophysiology of central sensitization as well. Many cases of chronic musculoskeletal pain evolve from traumatic or non-traumatic local nociceptive musculoskeletal problems characterized by a period of massive peripheral input in the (sub)acute to chronic stage (e.g. chronic whiplash associated disorders or patients reporting a history of several surgical procedures). In response the central nervous system modulates the sensitivity of the somatosensory system. In addition, once central sensitization is established in cases of chronic musculoskeletal pain, it remains highly plastic: any new peripheral injury may serve as a new source of bottom-up (peripheral) nociceptive input, which in turn sustains or aggravates the process of central sensitization (Affaitati et al., 2010). Without new peripheral input, central sensitization does not resolve quickly, but rather sustains the chronic nature of the condition.

From a clinical perspective, it remains challenging for clinicians to implement science into practice. Clinical guidelines for the recognition (Nijs et al., 2010) and treatment (Nijs and Van Houdenhove, 2009; Nijs et al., 2009) of central sensitization in patients with chronic musculoskeletal pain have been provided, yet many issues remain. For example, how should clinicians apply the science of central sensitization and chronic pain to a case of chronic whiplash where the patient is sceptical about the biopsychosocial model, and convinced that the initial neck trauma caused severe cervical damage that remains invisible to modern imaging methods? Or a patient with moderate hip osteoarthritis saying 'The cartilage of my hips is melting away due to erosion, which in turn is triggered by overuse of my lower limbs' and 'I will not participate in exercise therapy because it will worsen my hip pain and hence the erosion of my cartilage'. Likewise, a patient with fibromyalgia convinced that her pain and related symptoms are due to an undetectable or 'new' virus, is unlikely to adhere to conservative interventions.

It is clear that initiating a treatment like graded activity is unlikely to be successful in these patients. Prior to commencing treatment in such cases the gap between the perceptions of the patient and their health care professional about pain and its treatment should be narrowed. Therefore it is crucial to change the patient's maladaptive illness perceptions and maladaptive pain cognitions and to reconceptualise pain before initiating the treatment. This can be accomplished by patient education about central sensitization and its role in chronic pain, a strategy frequently referred to as 'pain (neuro)physiology education' or 'pain biology education'. Patients with 'unexplained' chronic musculoskeletal pain who are misinformed about pain, consider their pain as more threatening and demonstrate lower pain tolerance, more catastrophic thoughts and less adaptive coping strategies (Jackson et al., 2005). Treatment adherence for active treatments is often low in these patients. Therefore, education will increase motivation for rehabilitation in those with chronic musculoskeletal pain due to central sensitization. This requires a biopsychosocial assessment and an in-depth education of altered central nervous system processing of nociceptive and non-nociceptive input. This will be the focus of the present paper.

In what follows the reader is provided with a brief overview of the clinical evidence of pain physiology education in patients with chronic musculoskeletal pain. The largest part of the paper is dedicated to practice guidelines on how to apply pain physiology education in patients with chronic musculoskeletal pain.

2. Effectiveness of pain physiology education

Several groups have studied the clinical effects of pain physiology education in various chronic musculoskeletal pain populations such as chronic low back pain (Moseley, 2002, 2003b, 2004, 2005; Moseley et al., 2004; Ryan et al., 2010), fibromyalgia (Ittersum et al. submitted for publication; Ittersum et al., in press; Van Oosterwijck et al. submitted for publication), chronic whiplash associated disorders (Van Oosterwijck et al., 2011) and chronic fatigue syndrome with chronic widespread pain (Meeus et al., 2010a). In patients with chronic low back pain, pain physiology education alters pain perceptions and, in conjunction with physiotherapy, it improves functional and symptomatic outcomes (Moseley, 2002; Moseley, 2003b; Moseley et al., 2004; Moseley, 2005). A recent randomized controlled trial indicates that, in the short term, pain physiology education alone is more effective for pain relief and improving pain self-efficacy than a combination of pain physiology education and group exercise classes for patients with chronic low back pain (Ryan et al., 2010). Altered pain perceptions are directly associated with altered movement performance in those with chronic low back pain, even if there is no opportunity for the patients to be physically active during the treatment (Moseley, 2002, 2004). This implies that motor performance may be directly limited by pain perceptions. Indeed, a case series study of patients with chronic whiplash associated disorders showed improvements in illness perceptions, pain thresholds and movement performance (Van Oosterwijck et al., 2011).

In patients with chronic fatigue syndrome, pain physiology education alters pain perceptions such as catastrophizing, and pain behaviour (Meeus et al., 2010a). In another randomized controlled clinical trial, we showed that simply providing the detailed information booklet explaining pain physiology and central sensitization, did not change illness perceptions or health status in patients with fibromyalgia (Ittersum et al. submitted for publication). However, when the same written education about pain physiology was combined with two educational sessions (one face-to-face session and one by telephone) of individually-tailored pain physiology education, vitality, physical functioning, mental and general health of patients with fibromyalgia improved (Van Oosterwijck et al. submitted for publication). This indicates that physiotherapists or other health care professionals are required to provide tailored education to address individual needs rather than standardized, general written education. Written education about central sensitization and pain physiology alone is insufficient. Nevertheless, an educational booklet about pain physiology is highly appreciated by fibromyalgia patients (Ittersum et al., in press), indicating that it can be used in conjunction with face-to-face educational meetings.

From the available evidence it is concluded that face-to-face sessions of pain physiology education, in conjunction with written educational material, are effective for changing pain perceptions and health status in patients with various chronic musculoskeletal pain disorders, including those with chronic low back pain, chronic whiplash, fibromyalgia and chronic fatigue syndrome. Practice guidelines on how to apply pain physiology education in patients with chronic musculoskeletal pain are provided below (and are summarized in Fig. 1).

3. Practice guidelines for applying pain physiology education

3.1. Prior to initiating pain physiology education

Prior to commencing pain physiology education, it is important firstly to ascertain that pain physiology education is indicated in the chronic pain patient. Pain physiology education is indicated when:

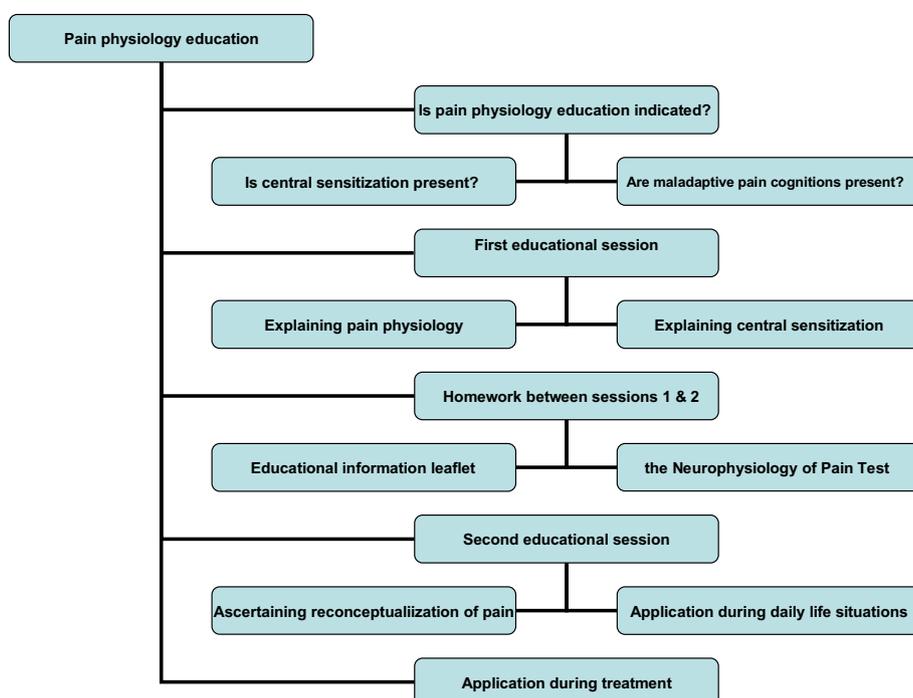


Fig. 1. Clinical guidelines for pain physiology education in patients with chronic musculoskeletal pain.

1) the clinical picture is characterized and dominated by central sensitization; and 2) maladaptive pain cognitions, illness perceptions or coping strategies are present. Both indications are prerequisites for commencing pain physiology education. Some (acute) musculoskeletal pain patients may not fulfil these requirements initially, but will do so later on during their course of treatment (e.g. a patient receiving physiotherapy for an acute muscle strain experiencing a whiplash trauma). To examine whether central sensitization is present, clinicians can use guidelines for the recognition of central sensitization in patients with chronic musculoskeletal pain (Nijs et al., 2010). In the assessment of illness perceptions patients must be asked about their perceptions about the cause of pain, the consequences, the treatment and the timeline of pain. Maladaptive pain cognitions include ruminating about pain, and hypervigilance to somatic signs, each of which can be easily assessed with short self-reported measures with excellent psychometric properties (e.g. the Pain Catastrophizing Scale¹, Pain Vigilance and Awareness Questionnaire², etc.) (Sullivan et al., 1995; Van Damme et al., 2002; Kraaijaat and Evers, 2003). Likewise, illness perception can be questioned or can be assessed by use of the brief Illness Perception Questionnaire³ (Broadbent et al., 2006). This information addressing pain perceptions and coping strategies should be used by the therapist to tailor the individual education sessions (remember that pain physiology education aims to reconceptualise pain).

3.2. First educational session

It is essential for clinicians to explain the treatment rationale and discuss the practical issues of the treatment with the patient. In

¹ <http://synergytherapiesofkc.com/forms/PCS-Pain%20Catastrophizing%20Scale.pdf>.

² The questionnaire can be obtained from the corresponding author or refer to the original publications addressing this measure.

³ <http://www.uib.no/ippq/>.

case of central sensitization and chronic musculoskeletal pain, explaining the treatment rationale is of prime importance. Basically, patients should understand the mechanism of central sensitization. Such education aims at altering patients' knowledge about their pain states and reconceptualising pain (Moseley, 2004). When solely cognitive and behavioural responses are encouraged, without reconceptualising pain, these responses may be counter-intuitive for chronic pain patients, because pain is still a sign of harm to them (Moseley, 2003b). Therefore education of the central sensitization model relies on deep learning, aimed at reconceptualising pain, based on the assumption that appropriate cognitive and behavioural responses will follow when pain is appraised as less dangerous (Moseley, 2003a). For example, remember the patient with chronic whiplash convinced that the initial neck trauma caused severe cervical damage that remains invisible to modern imaging methods. Simply providing education about the fear avoidance model to encourage a graded activity approach is unlikely to be beneficial. Detailed pain physiology education is required to reconceptualise pain, and to convince the patient that hypersensitivity of the central nervous system rather than local tissue damage is the cause of their presenting symptoms.

Educating patients with chronic musculoskeletal pain about central sensitization can be accomplished in one to two face-to-face educational sessions (approximately 30 min per session; depending on the change in cognitions). The aid of a booklet containing detailed written explanation and illustrations about pain physiology and central sensitization processes is recommended. The content of the education sessions can be based on the book "Explain Pain" (Butler and Moseley, 2003), covering the physiology of the nervous system in general and of the pain system in particular. Topics that should be addressed during the education sessions include the characteristics of acute versus chronic pain, the purpose of acute pain, how acute pain originates in the nervous system (nociceptors, ion gates, neurons, action potential, nociception, peripheral sensitization, synapses, synaptic gap, inhibitory/excitatory chemicals, spinal cord, descending/ascending pain pathways,

role of the brain, pain memory and pain perception), how pain becomes chronic (plasticity of the nervous system, modulation, modification, central sensitization, the pain neuromatrix theory) and potential sustaining factors of central sensitization like emotions, stress, illness perceptions, pain cognitions and pain behaviour. Acute nociceptive mechanisms are typically explained first and are then contrasted with central sensitization processes i.e. in the case of chronic pain. Illustrations (e.g. Figs. 2 and 3), examples, and metaphors are frequently used (van Wilgen and Keizer, *in press*). The education is presented verbally (explanation by the therapist) and visually (summaries, pictures and diagrams on computer and paper). During the sessions patients are encouraged to ask questions and their input should be used to individualise the information.

3.3. Homework between sessions 1 and 2

After the face-to-face education, patients receive an educational information booklet about the neurophysiology of pain and are asked to read it carefully at home. The written information does not provide new information, it reinforces the verbal information as it tells the same story using the same drawings. Patients with central sensitization often have neurocognitive impairments, including concentration difficulties and impairments in short-term memory (Nijs et al., 2010), which implies that they can forget a number of aspects of the verbal education. Therefore additional written information that can be read afterwards is a valuable and essential part of the intervention. Sections 1, 2 and 4 from the book “Explain Pain” (Butler and Moseley, 2003) can be provided as written education to native English speakers, while a Dutch educational booklet is included in a practical guide for applying pain physiology education (van Wilgen and Nijs, 2010).

To examine whether the patient understands pain physiology, the patient version of the Neurophysiology of Pain Test⁴ can be used (Moseley, 2003c; Meeus et al., 2010b). It is a valid and reliable measure for patients with chronic pain (Meeus et al., 2010b). At the end of session 1, the therapist asks the patient to fill out the Neurophysiology of Pain Test one day prior to returning to the clinic.

3.4. Second educational session

The outcome of the Neurophysiology of Pain Test can guide the clinician during the second educational session: it can identify those topics that require additional explanation. During the second session, the therapist answers and explains additional questions that arose after reading the information booklet. Based on the incorrect answers that were given on the ‘Neurophysiology of Pain Test’ the therapist explains these topics once again and if necessary in more detail. Hence, the clinician ascertains that the reconceptualization of pain has taken place and that illness perceptions have improved.

Next, the therapist discusses the existence of sensitization in this particular patient by giving the patient insight to somatic, psychosocial and behavioural factors associated with pain. This is followed by i.e. discussing with the patient how information provided can be applied during everyday situations. This is a crucial step in the overall treatment program, as it will set the way towards application of adaptive pain coping strategies, self-management programs and graded activity/graded exercise therapy. The therapist should start by asking the patient to explain his willingness to apply his

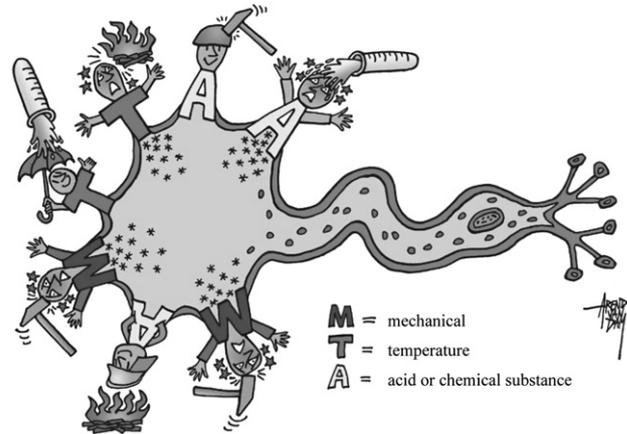


Fig. 2. Illustration used to explain basic principles of acute nociception (redrawn from reference (Butler and Moseley, 2003, p. 33) by Arend van Dam (van Wilgen and Nijs, 2010, p. 89); reproduced with permission from Bohn Stafleu van Loghum). This illustration presents a neuron, with on the left its ‘sensors’ which are capable of sensing temperature changes (indicated by the letter ‘T’), chemical substances (‘A’) and mechanical pressure (‘M’). Activation of such a sensor opens the corresponding ion channel in the cell membrane of the neuron. This enables an influx of sodium ions into the neuron (‘positive charges enter the cell’), possibly resulting in an action potential (‘the danger message’). It is important for the patient to realize that the presence of an action potential does not necessarily imply that pain is or will be experienced.

increased understanding of his medical problem in his life for instance by setting new goals. Typical examples are stopping rumination and worrying about the aetiology and nature of their pain disorder, reducing stress, increasing physical activity levels, decreasing hypervigilance, becoming more physically active, relaxation etc. These, and other adaptive strategies, can be discussed with the patient and should lead to a clear plan of action on ‘how to deal with the hypersensitive nervous system’. The transition from knowledge to adaptive pain coping can be enhanced by using the

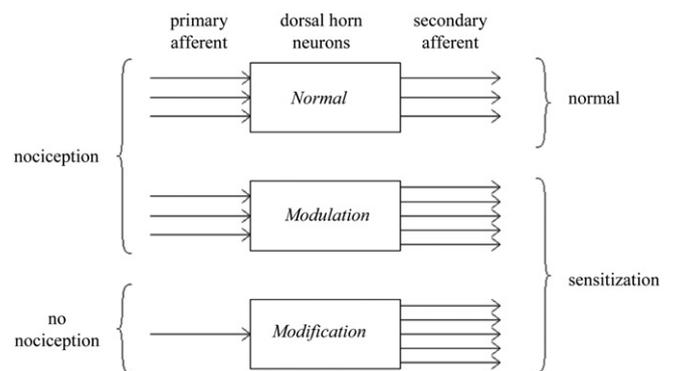


Fig. 3. Illustration used to explain the difference between acute nociception and central sensitization in chronic pain ((van Wilgen and Nijs, 2010, p. 102) reproduced with permission from Bohn Stafleu van Loghum). This illustration explains one of the essential features of central sensitization in chronic pain. The situation on top represents the normal situation, with primary afferents transporting 3 danger messages to the dorsal horn neurons, as is the case when you cut your finger. Next, the dorsal horn neurons activate the secondary afferents that transport the same 3 danger messages to the brain for processing. However, in many cases dorsal horn neurons modulate the incoming danger messages, as illustrated in the middle and below. The situation in the middle represents ‘real’ nociception, with 3 danger messages entering the spinal cord neurons, and 5 being sent to the brain. This implies that the incoming messages are amplified in the spinal cord prior to entering the brain. The situation below illustrates central sensitization in patients with chronic pain. Even in absence of nociception, messages from the periphery (e.g. touching the skin above the painful region or moving the affected limb) are amplified in a powerful way such that the dorsal horn neurons send several danger messages to the brain.

⁴ The Neurophysiology of Pain Test can be obtained from the corresponding author.

Pain Reaction Record (Sullivan, 2003), an easily applicable measure facilitating a cognitive approach to pain coping.

3.5. Application of pain physiology education during treatment

Pain physiology education is a continuous process initiated during the educational sessions prior to commencing active treatment (i.e. rehabilitation) and followed-up during the rehabilitation program. Indeed, pain physiology education is typically followed by various components of a biopsychosocial-oriented rehabilitation program, like stress management, graded activity and exercise therapy. It is important for clinicians to introduce these treatment components during the educational sessions, and to explain why and how the various treatment components are likely to contribute to decreasing the hypersensitivity of the central nervous system (as explained in Nijs and Van Houdenhove, 2009 and Nijs et al., 2009). Changing illness perceptions changes the patients motivation to undertake and comply with the rehabilitation program.

Likewise, long-term reconceptualization of pain, alterations in illness beliefs and adaptive pain cognitions are required at every stage of the rehabilitation program. This can be done easily by asking the patient to explain the treatment rationale of a specific treatment component. If during the treatment course any of the pain cognitions or illness beliefs have 'reset' towards maladaptive ones, then the therapist is advised to re-educate the patient. The latter can be accomplished by asking the patient to re-read the written information on pain physiology and to try to link that information with his/her current rehabilitation program. Long-term adaptive pain perceptions, and consequent adaptive pain coping strategies are required for long-term treatment compliance and continuous application of self-management strategies.

Finally, frequent side-effects and symptom fluctuations can be explained using the central sensitization model (van Wilgen and Keizer, *in press*). The latter should shift the patient's attention away from somatic signs towards adaptive coping strategies and reassurance. The patient's confidence in the treatment (outcome) should be a continuous treatment goal in those with chronic musculoskeletal pain.

4. Conclusion

There has been increased awareness that central sensitization provides an evidence-based explanation for many cases of 'unexplained' chronic musculoskeletal pain. Hence, rehabilitation of patients with chronic musculoskeletal pain should target, or at least take account of the process of central sensitization. Prior to commencing rehabilitation in such patients, it is crucial to change maladaptive illness beliefs, to alter maladaptive pain cognitions and to reconceptualise pain. This can be accomplished by patient education about central sensitization and its role in chronic pain, a strategy known as pain physiology education. Face-to-face sessions of pain physiology education, in conjunction with written educational material, are effective for changing pain cognitions and health status in patients with various chronic musculoskeletal pain disorders, including those with chronic low back pain, chronic whiplash, fibromyalgia and chronic fatigue syndrome. Pain physiology education comprises of a first face-to-face session explaining basic pain physiology and contrasting acute nociception versus chronic pain. Written information about pain physiology should be provided as homework in between session 1 and 2. The second session can be used to correct misunderstandings, and to facilitate the transition from knowledge to adaptive pain coping during daily life. Pain physiology education is a continuous process initiated during the two educational sessions prior to and continuing into active treatment and followed-up during the longer term rehabilitation program.

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References

- Affaitati G, Costantini R, Fabrizio A, Lapenna D, Tafuri E, Giamberardino MA. Effects of treatment of peripheral pain generators in fibromyalgia patients. *European Journal of Pain*; 2010. doi:10.1016/j.ejpain.2010.09.002.
- Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. *Journal of Psychosomatic Research* 2006;60:631–7.
- Brosschot JF. Cognitive-emotional sensitization and somatic health complaints. *Scandinavian Journal of Psychology* 2002;43:113–21.
- Butler D, Moseley GL. Explain pain. Adelaide: NOI Group Publishing; 2003.
- Ittersum van MW, Wilgen van CP, Schans van der CP, Lambrecht L, Groothof JW, Nijs J. Does pain physiology education change illness perceptions in patients with fibromyalgia? A multicentre randomized controlled trial with six months follow up. Submitted for publication.
- Ittersum van MW, Wilgen van CP, Groothof JW, Schans van der CP. Is appreciation of written education about pain neurophysiology related to changes in illness perceptions and health status in patients with fibromyalgia? Patient Education and Counselling, *in press*.
- Jackson T, Pope L, Nagasaka T, Fritch A, Iezzi T, Chen H. The impact of threatening information about pain on coping and pain tolerance. *British Journal of Health Psychology* 2005;10:441–51.
- Kraaimaat FW, Evers AWM. Pain-coping strategies in chronic pain patients: psychometric characteristics of the pain-coping inventory. *Journal of Behavioural Medicine* 2003;10(4):343–63.
- Moseley GL. Combined physiotherapy and education is efficacious for chronic low back pain. *Australian Journal of Physiotherapy* 2002;48:297–302.
- Moseley GL. Joining forces – combining cognition-targeted motor control training with group or individual pain physiology education: a successful treatment for chronic low back pain. *Journal of Manual and Manipulative Therapy* 2003a;11:88–94.
- Moseley GL. A pain neuromatrix approach to patients with chronic pain. *Manual Therapy* 2003b;8:130–40.
- Moseley GL. Unraveling the barriers to reconceptualization of the problem in chronic pain: the actual and perceived ability of patients and health professionals to understand the neurophysiology. *Journal of Pain* 2003c;4:184–9.
- Moseley GL. Evidence for a direct relationship between cognitive and physical change during an education intervention in people with chronic low back pain. *European Journal of Pain* 2004;8:39–45.
- Moseley GL, Nicholas MK, Hodges PW. A randomized controlled trial of intensive neurophysiology education in chronic low back pain. *Clinical Journal of Pain* 2004;20:324–30.
- Moseley GL. Widespread brain activity during an abdominal task markedly reduced after pain physiology education: fMRI evaluation of a single patient with chronic low back pain. *Australian Journal of Physiotherapy* 2005;51:49–52.
- Meeus M, Nijs J. Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome. *Clinical Rheumatology* 2007;26:465–73.
- Meeus M, Nijs J, Van de Wauwer N, Toeback L, Truijens S. Diffuse noxious inhibitory control is delayed in chronic fatigue syndrome: an experimental study. *Pain* 2008;139:439–48.
- Meeus M, Nijs J, Van Oosterwijck J, Van Alsenoy V, Truijens S, De Meirleir K. Pain physiology education improves pain beliefs in patients with chronic fatigue syndrome compared to pacing and self-management education: a double-blind randomized controlled trial. *Archives of Physical Medicine and Rehabilitation* 2010a;91:1153–9.
- Meeus M, Nijs J, Elsemans KS, Truijens S, De Meirleir K. Development and properties of the Dutch neurophysiology of pain test in patients with chronic fatigue syndrome. *Journal of Musculoskeletal Pain* 2010b;18(1):58–65.
- Meyer RA, Campbell JN, Raja SN. Peripheral neural mechanisms of nociception. In: Wall PD, Melzack R, editors. *Textbook of pain*. 3rd ed. Edinburgh: Churchill Livingstone; 1995. p. 13–44.
- Nijs J, Van Houdenhove B, Oostendorp RAB. Recognition of central sensitization in patients with musculoskeletal pain: application of pain neurophysiology in manual therapy practice. *Manual Therapy* 2010;15:135–41.
- Nijs J, Van Houdenhove B. From acute musculoskeletal pain to chronic widespread pain and fibromyalgia: application of pain neurophysiology in manual therapy practice. *Manual Therapy* 2009;14:3–12.
- Nijs J, Van Oosterwijck J, De Hertogh W. Rehabilitation of chronic whiplash: treatment of cervical dysfunctions or chronic pain syndrome? *Clinical Rheumatology* 2009;28:243–51.

- Ryan CG, Gray HG, Newton M, Granat MH. Pain biology education and exercise classes compared to pain biology education alone for individuals with chronic low back pain: a pilot randomised controlled trial. *Manual Therapy* 2010;15(4):382–7.
- Rygh LJ, Tjolsen A, Hole K, Svendsen F. Cellular memory in spinal nociceptive circuitry. *Scandinavian Journal of Psychology* 2002;43:153–9.
- Seifert F, Maihöfner C. Central mechanisms of experimental and chronic neuropathic pain: findings from functional imaging studies. *Cellular and molecular life sciences* 2009;66:375–90.
- Staud R, Craggs JG, Robinson ME, Perlstein WM, Price DD. Brain activity related to temporal summation of C-fiber evoked pain. *Pain* 2007;129:130–42.
- Sullivan MJL. 'Pain Reaction Record' in: Sullivan MJL. *Client Workbook Progressive Goal Attainment Program*. PDP Program Inc; 2003. p. 100.
- Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. *Psychological Assessment* 1995;7:524–32.
- Van Damme S, Crombez G, Bijttebier P, Goubert L, Van Houdenhove B. A confirmatory factor analysis of the Pain Catastrophizing Scale: invariant factor structure across clinical and non clinical populations. *Pain* 2002;96:319–24.
- Van Oosterwijck J, Nijs J, Meeus M, Truijen S, Craps J, Van den Keybus N, et al. Pain neurophysiology education improves cognitions, pain thresholds and movement performance in people with chronic whiplash: a pilot study. *Journal of Rehabilitation Research and Development* 2011;48(1):43–58.
- Van Oosterwijck J, Meeus M, Paul L, Lambrecht L, Nijs J. Does pain physiology education improve diffuse noxious inhibitory control in patients with fibromyalgia? A randomized clinical trial, submitted for publication.
- van Wilgen CP, Keizer D. The sensitization model to explain how chronic pain exists without tissue damage. *Pain Management Nursing*, in press.
- van Wilgen CP, Nijs J. *Pijneducatie: een praktische handleiding voor (para)medici*. [Pain education: a practical guide for (para)medics.]. The Netherlands: Bohn Stafleu van Loghum: Houten; 2010.
- Zusman M. Forebrain-mediated sensitization of central pain pathways: 'non-specific' pain and a new image for MT. *Manual Therapy* 2002;7:80–8.