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Exercise therapy for chronic musculoskeletal pain: Innovation by altering pain memories

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ABSTRACT

Even though nociceptive pathology has often long subsided, the brain of patients with chronic musculoskeletal pain has typically acquired a protective (movement-related) pain memory. Exercise therapy for patients with chronic musculoskeletal pain is often hampered by such pain memories. Here the authors explain how musculoskeletal therapists can alter pain memories in patients with chronic musculoskeletal pain, by integrating pain neuroscience education with exercise interventions. The latter includes applying graded exposure in vivo principles during exercise therapy, for targeting the brain circuitries orchestrated by the amygdala (the memory of fear centre in the brain).

Before initiating exercise therapy, a preparatory phase of intensive pain neuroscience education is required. Next, exercise therapy can address movement-related pain memories by applying the 'exposure without danger' principle. By addressing patients' perceptions about exercises, therapists should try to decrease the anticipated danger (threat level) of the exercises by challenging the nature of, and reasoning behind their fears, assuring the safety of the exercises, and increasing confidence in a successful accomplishment of the exercise. This way, exercise therapy accounts for the current understanding of pain neuroscience, including the mechanisms of central sensitization.

1. Introduction

In acute musculoskeletal pain, the main focus for treatment is to reduce the nociceptive trigger. Such a focus on peripheral pain generators is often effective for treatment of (sub)acute musculoskeletal pain (Surenkok et al., 2009; Grunnesjo et al., 2011; Brantingham et al., 2013; Struyf et al., 2013). In patients with chronic musculoskeletal pain, ongoing nociception rarely dominates the clinical picture. Chronic musculoskeletal pain conditions including osteoarthritis (Lluch Girbes et al., 2013), rheumatoid arthritis (Meeus et al., 2012), whiplash (Curatolo et al., 2001; Banic et al., 2004; Sterling, 2010), fibromyalgia (Staud, 2002; Meeus and Nijs, 2007), low back pain (Roussel et al., 2013), pelvic pain (Kaya et al., 2013) and lateral epicondylitis (Fernandez-Carnero et al., 2009), are often characterized by brain plasticity that leads to hyperexcitability of the central nervous system (central sensitization). Growing evidence supports the clinical importance of central sensitization in patients with chronic musculoskeletal pain (Sterling et al., 2003; Jull et al., 2007; Coombes et al., 2012; Smart et al., 2012).

In such cases, musculoskeletal therapists need to think and treat beyond muscles and joints (Nijs et al., 2013). Within the context of the management of chronic pain, it is crucial to consider the concept of central pain mechanisms including central sensitization (Gifford and Butler, 1997). Modern pain neuroscience calls for treatment strategies aimed at decreasing the sensitivity of the central nervous system (i.e. desensitizing therapies).

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Treatments capable of desensitizing the central nervous system in patients with chronic pain have been proposed, including exercise prescription (Mease et al., 2011; Woolf, 2011; Nijs et al., 2011a; Lluch Girbes, Nijs, 2013), but up to now exercise therapy as a potential desensitizing treatment (Nijs et al., 2012) for chronic musculoskeletal pain has not been adequately addressed. Here it is explained how musculoskeletal therapists can integrate pain neuroscience education (Butler and Moseley, 2003; Nijs et al., 2011b) with exercise interventions, and how they can apply graded exposure in vivo principles (Vlaeyen et al., 2012) during exercise therapy for patients with chronic musculoskeletal pain. Together, the treatment proposed here aims at altering pain memories in patients with chronic musculoskeletal pain.

2. Step 1: Preparations to provide cognition-targeted exercise therapy

2.1. Prerequisites for the therapist to provide cognition-targeted exercise therapy

The therapist should have certain prerequisites for providing cognition-targeted exercise therapy. First, therapists require an in-depth understanding of pain mechanisms (Butler and Moseley, 2003) and the dysfunctional central nociceptive processing in those with chronic musculoskeletal pain (Woolf and Salter, 2000; Woolf, 2011). This includes a thorough understanding of the role of fear (of movement) in the development and sustainment of chronic pain (Vlaeyen and Crombez, 1999). Second, therapists require the skills to explain to their patients the mechanism of central sensitization as an evidence-based explanation for their chronic musculoskeletal pain (Nijs et al., 2011a; Puentedura and Louw, 2012). Third, specific communication skills are required. For instance, a Socratic-style dialogue of education (Siemonsma et al., 2008) is preferred over 'lecturing' to the patient. Fourth, therapists should be familiar (and preferentially experienced) with current evidence-based biopsychosocially-driven pain management strategies including graded activity (Macedo et al., 2010), graded exposure in vivo (de Jong et al., 2005), and acceptance-based interventions (e.g. acceptance and commitment therapy) (Wicksell et al., 2008, 2010). Finally, therapists should have the skills to apply a variety of exercise interventions, including neuromuscular training (Richardson and Jull, 1995; Jull and Richardson, 2000; Jull et al., 2008).

2.2. Preparing patients for cognition-targeted exercise therapy using therapeutic pain neuroscience education

Before implementing cognition-targeted exercise therapy, a preparatory phase implying deep learning and reconceptualization of pain, is proposed. It can be accomplished by providing intensive pain neuroscience education, which should mostly rely on evidence from modern pain neuroscience rather than from psychology (Nijs et al., 2011b). If not, patients often misunderstand the neuroscience education message and believe that they are being told "the pain is all in your head", which is a common pitfall of this approach. In addition, the crucial point in all kind of cognition-targeted therapy is that it starts from the patient's perspective (including pain cognitions and beliefs (Nicholls et al., 2013)) and expectations for care (Macfarlane et al., 1997). Guidelines for enabling clinicians to apply pain neuroscience education in clinical practice are available (Nijs et al., 2011b; van Wilgen and Keizer, 2012), and imply the use of an information leaflet or an explanatory handbook (e.g. Explain Pain (Butler and Moseley, 2003)). This approach assumes that the patient will be intelligent enough to understand the information provided. Before considering step 2, it is first necessary to have a closer look at the role of movement-related fear in the pain neuromatrix.

3. The role of fear (of movement) in the pain neuromatrix

In those with central sensitization pain, the pain neuromatrix is likely to be overactive: increased activity is present in the insula, anterior cingulate cortex, prefrontal cortex, various brain stem nuclei, dorsolateral frontal cortex and the parietal associated cortex (Seifert and Maihofner, 2009). Long-term potentiation of neuronal synapses (Zhuo, 2007), as well as decreased gamma-aminobutyric acid-neurotransmission (Suarez-Roca et al., 2008) represent two mechanisms contributing to the overactive pain neuromatrix.

One key brain area involved in the pain (neuro)matrix is the amygdala, often referred to as the fear-memory centre of the brain. The amygdala has a key role in negative emotions and pain-related memories (Li et al., 2013). In addition to the amygdala, the anterior cingulate cortex takes part of the central fear network in the brain (Kattoor et al., 2013). Recent research supports the cardinal role of the amygdala as a facilitator of chronic pain development, including sensitization of central nervous system pain pathways (Simons et al., 2012; Hadjikhani et al., 2013; Kattoor, Gizewski, 2013; Kim et al., 2013; Li, et al., 2013; Schwedt et al., 2013). In line with this is the finding that the amygdala, as well as the somatosensory cortex and insula, shows less activity during pain delivery in case of positive treatment expectations (Schmid et al., 2013).

Of major relevance for providing exercise therapy to patients with chronic musculoskeletal pain is the amygdala's role in pain memories, and more precisely in memories of painful movements. Therefore the amygdala closely collaborates with the hippocampus and the anterior cingulate cortex. Even though nociceptive pathology has often long subsided, the brain of patients with chronic musculoskeletal pain has typically acquired a protective pain memory (Zusman, 2004). For movements that once provoked pain, this implies protective behaviours (e.g. antalgic postures, antalgic movement patterns including altered motor control, or even avoidance of such movements).

Kinesiophobia or fear of movement is seldom applicable to all kinds of physical activity, but rather applies to certain movements (e.g. neck extension in patients post-whiplash, overhead smashes in patients with shoulder impingement syndrome, or forward bending in patients with low back pain). Even though these movements provoked pain in the (sub)acute phase, or even initiated the musculoskeletal pain disorder (e.g. the pain initiated following an overhead smash), they are often perfectly safe to perform in a chronic stage. The problem is that the brain has acquired a long-term pain memory, associating such movements with danger/threat. Even preparing for such 'dangerous' movements is enough for the brain to activate its fear-memory centre and hence to produce pain (without nociception), and employ an altered (protective) motor control strategy (Tucker et al., 2012). Exercise therapy can address this by applying the 'exposure without danger' principle (Zusman, 2004), which is detailed below.

4. Step 2: Cognition-targeted exercise therapy for chronic musculoskeletal pain

Following pain neuroscience education, as soon as the patient with chronic pain understands that all pain is produced in the brain and has adopted less threatening perceptions about pain, one can proceed to the next level: cognition-targeted exercise therapy (Nijs et al., 2014). Here it is explained how therapists can use cognition-targeted exercise therapy for altering pain memories in patients with chronic musculoskeletal pain and central sensitization. Such exercise therapy can include various types of exercise interventions

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(e.g. motor control training, aerobic training or muscle strengthening), and theoretically can be applied in a variety of chronic musculoskeletal pain disorders when central sensitization is present.

Cognition – targeted = time – contingent exercises using goal setting

'Cognition-targeted' stands for several principles to be applied during exercise therapy for patients with chronic musculoskeletal pain (Table 1) (Nijs, et al., 2014). 'Cognition-targeted' implies a time-contingent rather than symptom-contingent approach to exercise interventions. It accounts for the individual (pain) cognitions that should have been addressed during the individually-tailored pain neuroscience education. The concept of time-contingent performance of exercises and activities should be introduced and discussed during the pain neuroscience education. Importantly, the cognition-targeted exercise therapy will apply the reconceptualization of pain to exercises (and in a later stage to daily physical activities, e.g. gardening and lifting heavy objects). Hence, goal setting should be a central part of the exercise program.

Goal setting involves establishing treatment goals using the SMART (Specific, Measurable, Achievable, Realistic and Time-targeted) principle. For example the patient is asked to define personal treatment goals that are specific, measurable, achievable, realistic and time-targeted. Patients should be encouraged to (re) define functional goals (e.g. getting back to work). The goals can be used to design the content of the exercises, to motivate the patient, and to increase performance and patient's expectations for treatment outcome.

Cognition – targeted = addressing patients' perceptions about exercises

Thorough questioning and discussion of the patient's perceptions about the exercise (before, during and following the exercise) is required. This includes discussion of the anticipated consequences of the exercises. The following questions can guide clinicians in initiating such discussion: "*Is this particular exercise threatening for your back?*"; "*Are you confident in successfully executing the exercise/movement/activity?*"; "*Do you feel that the exercise is useful for your recovery?*". Proceeding this way is likely to reveal the patient's perceptions about the exercise, and will certainly reveal (irrational) fear for performing it. In the latter case, more information is required to understand why the patient feels that the exercise is dangerous or threatening, for instance by asking the patient: "*Why do you thing this exercise is dangerous for you? And what do you think will happen when you perform the exercise?*".

Table 1
Principles for providing cognition-targeted exercise therapy for chronic musculoskeletal pain.

	Principles	Explanation
1.	Time-contingent exercises	Do net let pain determine the number of repetitions or exercise duration.
2.	Goal-setting	Let the patient define the treatment goals. Use the predefined goals to design the exercise program. Use the goals for motivating patients.
3.	Address perceptions about exercises	Question and if required discuss thoroughly the patient's perceptions about the exercises.
4.	Motor imagery	When progressing to a next level of (more difficult) exercises, a preparatory phase of motor imagery can be useful.
5.	Address feared movements	Retrain pain memories especially for feared movements. Discuss the fears thoroughly, and challenge the perceptions about negative consequences of performing the movement(s). Apply graded exposure in vivo principles.
6.	Make use of stress	Progress towards exercising under cognitively and psychosocially stressful conditions.

An example of a therapist addressing the patient's perceptions about exercises, including challenging the patient's cognitions in relation to the exercises, can be found online[2] (available in different languages including English, Dutch and Italian). The example illustrates how communication before commencing the exercises can be as important as performing the exercises itself. The pre-exercise communication facilitates the application of the principles learned during the preparatory phase of pain neuroscience education during exercise interventions. At the same time it increases the therapeutic alliance, defined as the relationship between patients and health care providers (Ferreira et al., 2013).

Therapists should try to decrease the anticipated danger (threat level) of the exercises by challenging the nature of, and reasoning behind their fears, assuring the safety of the exercises, and increasing confidence in a successful accomplishment of the exercise. In case irrational fear towards certain physical activities or exercises become apparent, graded exposure in vivo experiments (Leeuw et al., 2008) can be applied.

Clinicians should be cautious of not using 'inappropriate safety behaviour' (e.g. cocontraction of stabilization muscles – segmental stabilization exercises) to convince the patients of their ability to successfully perform the exercise or physical activity. Such inappropriate safety behaviour is likely to enhance the biomedical perceptions of the patient, and hence increases the threat value of performing the exercise/activity without such safety measures. On the other hand, one should not get a patient to rotate and extend the head in cases where this closes down a compromised foramen resulting in the patient experiencing more symptoms. This approach is intended for patients having central sensitization pain rather than nociceptive or neuropathic pain.

After performing the exercise(s) for the first time, the therapist discusses the patient's experience with the exercises, including their threatening nature. Generally, the threat value of the exercise(s) decreases after performance. This is due to the experienced difference between the anticipated (pre-exercise) pain increase and the actual experience. Even if the pain increase following exercise is similar to what was anticipated, the threat value of the exercise is typically decreased by the patient's enthusiasm about his/her ability to perform it. An example illustrating how clinicians can discuss the patient's experience with the exercises at follow-up can be found online at http://www.paininmotion.be/EN/sem-tools.html (available in different languages including English, Dutch and Italian). Associative learning, defined as the product of discrepancy between actual and expected outcomes, is required in such exercise interventions, so that learning only occurs for events, or sensory inputs, that the brain did not expect ('error of prediction') (McNally et al., 2005). Exposure of chronic pain patients to exercises or daily activities without danger to convince the brain of its error (Zusman, 2004, 2008) is crucial when applying cognition-targeted exercise therapy.

Cognition – targeted = tackling the feared movements & activities

Progression of exercises is targeted and developed towards those movements and/or activities for which the patient is fearful

[2] http://www.paininmotion.be/EN/sem-tools.html.

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(e.g. forward bending in case of low back pain) (Moseley, 2003). Indeed, especially those movements and/or activities which are fearful should be exercised, meaning that the exercise programme should be individually-tailored. The Photograph Series of Daily Activities (PHODA) Scale (Leeuw et al., 2007) and the Pictorial Fear of Activities Scale-Cervical (Turk et al., 2008; Pedler and Sterling, 2011) can be used to obtain a hierarchy in fearful movements/activities, at least for patients with low back and neck pain, respectively. Final progression should include exercising during physically demanding tasks, but also exposure to the feared movements or activities, and exercising under cognitively and psychosocially stressful conditions (Moseley, 2003). This includes performing simple exercises: e.g. rotation together with extension of the neck (coupled three-dimensional movements), not only while sitting comfortably on a kitchen chair, but also while walking and during cycling or cleaning. As always, the patients should be instructed to perform a daily set of home exercises.

During the exercise program, the therapist should remind the patient of the principles learned during the pain neuroscience education, as it is known that chronic musculoskeletal pain patients who are fear avoidant show larger correlations between pain expectancies for movements depicted in the PHODA and their ratings of predicted and experienced pain during exercises (Trost et al., 2009). Again, this is illustrated in the online material.

4.1. *Using stress for altering movement-related pain memories*

In practice, exercises in the cognition-targeted exercise therapy are allowed to be stressful, as stress, through the availability of cortisol and adrenaline in the brain, facilitates long-term potentiation of brain synapses especially of excitatory synapses (Timmermans et al., 2013). This is often the case when feared exercises are practised, often after a long time of avoiding these movements/activities. For example a patient with chronic shoulder impingement syndrome who was injured playing tennis, with the tennis serve being the 'provoking' movement avoided above-shoulder height movements for months, and now starts practicing the tennis serve again. This will definitely trigger a stress response in the early phases of exercising the tennis serve. Even more stress-provoking is returning to driving the car following a whiplash trauma, especially in cases with post-traumatic stress symptoms. However, increasing stress can also increase central sensitization (Suarez-Roca, Leal, 2008; Quintero et al., 2011). It is a balance between enough stress to cause memory consolidation but not enough to increase central sensitization.

5. Conclusion

The goal of cognition-targeted exercise therapy is systematic desensitization, or graded, repeated exposure to generate a new memory of safety in the brain, replacing or bypassing the old and maladaptive movement-related pain memories. Hence, such an approach directly targets the brain circuitries orchestrated by the amygdala (the memory of fear centre in the brain).

Central sensitization or hyperexcitability of the central nervous system implies increased synaptic efficiency and development of more excitatory synapses. Such brain mechanisms are identical to those seen in learning and memory, for instance in the hippocampus. The mechanism of long-term potentiation of brain synapses is crucial for (re)learning and developing new (pain/movement-related) memories, and hence for altering brain memories in the brain.

Results from clinical trials support the use of several components of the treatment presented here. There is some evidence that pain neuroscience education (Moseley, 2004; Moseley et al., 2004; van Oosterwijck et al., 2011) may be an effective sole treatment for people with chronic musculoskeletal pain. Some of the treatment principles as presented here are in line with those applied by psychologists during graded exposure in vivo (Vlaeyen et al., 2012), a cognitive behaviour treatment that has yielded good outcomes in patients with chronic low back pain (Vlaeyen et al., 2002; Leeuw et al., 2008), complex regional pain syndrome type I (de Jong et al., 2005), whiplash pain (de Jong et al., 2008), and work-related upper limb pain (de Jong et al., 2012). In addition, small-scale studies that combined pain neuroscience education with (an early version of) cognition-targeted exercise therapy suggest a strong synergistic effect (Moseley, 2002, 2003; 2005).

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