Pain Treatment for Patients With Osteoarthritis and Central Sensitization

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Osteoarthritis is one of the most frequent, disabling, and costly pathologies of modern society. Among the main aims of osteoarthritis management are pain control and functional ability improvement. The exact cause of osteoarthritis pain remains unclear. In addition to the pathological changes in articular structures, changes in central pain processing or central sensitization appear to be involved in osteoarthritis pain. The latter calls for a broader approach to the management of patients with osteoarthritis. Yet, the scientific literature offers scant information addressing the treatment of central sensitization, specifically in patients with osteoarthritis. Interventions such as cognitive-behavioral therapy and neuroscience education potentially target cognitive-emotional sensitization (and descending facilitation), and centrally acting drugs and exercise therapy can improve endogenous analgesia (descending inhibition) in patients with osteoarthritis. Future studies should assess these new treatment avenues.

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Osteoarthritis (OA) is one of the most common rheumatologic conditions,[1,2] affecting more than 80% of the population beyond the age of 55 years.[3] Two of the most commonly affected joints are the knees and the hips, sharing a predominantly load-bearing function.[4] Individuals with OA often have chronic pain, which causes a great deal of disabilities and results in significant health care costs.[5] Unfortunately, at present, both the causes of the pain and the most effective treatment have not yet been established.[6,7]

Historically, OA pain has been considered a nociceptive pain related to the degree of structural damage to the affected joint. Because the cartilage, under normal physiological conditions, is an avascular and aneural tissue, the issue of whether pain could come from other joint structures was raised. Thus, OA pain has been attributed to deformation of the periarticular tissues[8] and the subchondral bone,[9] increased intraosseous pressure,[10] synovial inflammation,[11] and injuries to the bone marrow.[12] Osteoarthritis pain also has been described as a chronic inflammatory response,[13] partly caused by an up-regulation of sodium ion ($Na+$) channels[14] and local production of nitric oxide, associated with the degeneration of the joint cartilage.[15]

Recently, OA has been considered as a hypertrophic arthritis[6] to differentiate it from the atrophic arthritis typical of rheumatoid arthritis. This differentiation is due to the fact that, apart from cell death of chondrocytes and loss of joint cartilage, the production of new tissue has been observed in OA, including fibrocartilage. Hence, in an attempt of the cartilage to regenerate, an increase in protein synthesis by the chondrocytes has become evident, especially in the initial stages.[16] Moreover, the osteochondral angiogenesis derived from expression of growth factors (eg, vascular endothelial growth factor, platelet-derived growth factor) has been proposed as a factor that could facilitate the chronicity of pain in OA.[17,18] Furthermore, the literature has described cases of patients with OA with satisfactory results after treating myofascial trigger points, which indicates that musculoskeletal tissues also may play a part in the pain related to OA.[19]

Because OA is an incurable pathology, therapeutic objectives usually focus on maximizing the patient's function and quality of life, while keeping pain under control and minimizing the adverse effects derived from the use of medication.[6,20,21] Nonsteroidal anti-inflammatory drugs can be beneficial in initial stages, but in time they become inefficient, and the administration of other medications such as amitriptyline or gabapentin is more advisable.[22] This phenomenon might be related to the fact that chronic pain in people with OA is related more to neuroplastic changes in the nervous system than to an inflammatory condition of the joint.[22] Those who do not respond well to conservative treatment usually end up with a prosthetic restoration of the affected joint.[20,21] However, surgery does not always imply a complete resolution of symptoms.[23]

OA Pain

The understanding of pain in OA and of its modulation and treatment is central to physical therapist practice, as physical therapists usually manage patients affected by this disease. Although pain is a very common complaint in people with OA, there is scarce knowledge of the etiology and mechanisms of OA pain and its treatment by health care professionals.[24] The general trend is for health care professionals to consider OA pain as a reliable "informant" of what is happening at the peripheral tissue level. Thus, greater joint degeneration is considered to be associated with greater pain. Nevertheless, there are different arguments that make it difficult to explain OA using exclusively a "peripheral model" of pain. It has been reported, for instance, that radiological changes identified in patients with OA are not always consistent with pain,[25–28] although some studies have demonstrated this correlation.[29,30] The great inter-individual variability in pain severity and the unclear relationship between pain and structural damage have raised the issue of the existence of other mechanisms responsible for the pain in OA. At present, peripheral sensitization and especially central sensitization have been proposed as 2 of the mechanisms underlying pain in OA,[24,31,32] as in other chronic musculoskeletal pain conditions.[33,34] Indeed, there is a growing body of research involving pain mechanisms in OA being central pain mechanisms, an issue discussed in several recent reviews.[6,24,31,32,34,35]

Mechanisms involved in central sensitization have been shown across several chronic conditions, which recently have been grouped together under the term "central sensitivity syndromes" (CSS).[36,37] This novel unifying concept is now emerging as a single common set of central nervous system (CNS) processes[38] and has been proposed to include chronic painful conditions that are based on central sensitization such as fibromyalgia, irritable bowel syndrome, and temporomandibular disorder. Osteoarthritis pain is not currently included in the group of CSS because the role of central sensitization in OA is still in its infancy. Yet, here we advocate that increasing evidence supports the inclusion of OA in the group of CSS. The hallmark of these "centrally driven" pain conditions is a diffuse hyperalgesic state

identifiable using experimental sensory testing (ie, quantitative sensory testing[39]) and corroborated by functional neuroimaging.[40] The characteristic symptoms of these central pain conditions include multifocal pain, fatigue, insomnia, memory difficulties, and a higher rate of comorbid mood disorders.[36]

Central sensitivity syndromes is an important new concept that also embraces the biopsychosocial model of disease. In this sense, the OA pain experience is multidimensional, fitting well with the biopsychosocial model, which reflects the influence of biological (ie, structural changes), psychological (ie, mood and coping), and social (ie, social support) factors in the individual's symptoms and suffering. Several psychosocial variables (eg, catastrophizing, high level of depression, cognition about pain) have been suggested as influencing OA pain and disability.[41] Psychosocial interventions such as cognitive-behavioral therapy (CBT) or activity pacing may decrease OA pain and disability.[42–45] Some studies addressing the effects of combined physical and psychological approaches in OA pain have been conducted,[46] and other studies are still in progress.[47]

OA and Central Sensitization

In the last few decades, great progress has been made in the knowledge of pain. Currently, it is clear that the majority of chronic musculoskeletal pain conditions are characterized by an alteration in pain processing by the CNS.[34] More specifically, sensitivity of central neurons to inputs coming from the unimodal and polymodal receptors increases, which results in a physiopathological condition called "central sensitization," characterized by a general or extended hypersensitivity. *Central sensitization* is defined as "an increased response of CNS neurons which inform of pain when faced with inputs coming from low threshold mechanoreceptors."[48] However, central sensitization not only refers to spinal cord sensitization or amplification of the afferent impulses coming from the periphery. It also includes an alteration of sensory processing in the brain,[49] loss of descending antinociceptive mechanisms,[50] enhanced facilitatory pain mechanisms, increased temporal summation or wind-up,[51] and long-term potentiation of neuronal synapsis in the anterior cingulate cortex.[52] Pathophysiological mechanisms underlying central sensitization are complex and numerous, but the net effect is an amplification of neural signaling within the CNS that elicits pain hypersensitivity.[34]

Central sensitization is present in different chronic musculoskeletal conditions such as whiplash trauma,[53] chronic low back pain,[54] and fibromyalgia[55] and, more recently, in OA,[6,24,31,32,35] which concerns us here. One of the factors that favor the development of central sensitization in OA is the massive and repetitive nociceptive input coming from peripheral joint nociceptors and transmitted to dorsal horn neurons in the spinal cord. Therefore, intense and continued nociceptive input proceeding from an OA joint may cause central sensitization, as shown in different studies.[56–58] The presence of central sensitization entails greater complexity of the clinical picture[59] and fewer possibilities of achieving positive results with physical therapy treatment.[60]

Patients with OA often present referred pain and changes in skin sensitivity in remote areas with respect to the affected joint. There are various theories on referred pain, but they all include a higher centers misinterpretation of the peripheral origin of nociception.[61] Referred pain is a phenomenon attributed to central sensitization, so its presence in OA is highly indicative of changes in pain processing in the CNS.

Another phenomenon associated with central sensitization is secondary hyperalgesia. Although primary hyperalgesia or peripheral sensitization involves an increased sensitivity of peripheral nociceptors in response to tissue damage, secondary hyperalgesia corresponds to increased sensitivity of dorsal horn neurons located in the spinal segments corresponding to the primary nociceptive source. Peripheral sensitization is a local phenomenon, whereas secondary hyperalgesia is a central process of the nervous system. Regarding OA, different studies have shown an increase in nociceptive transmission in dorsal horn neurons, typical of secondary hyperalgesia.[62,63] Im et al[7] provided key in vivo evidence that OA pain is caused by central sensitization through communication between peripheral OA nociceptors and the central sensory system. They observed that structural changes in components of the peripheral knee joint correlated with alterations in the central compartments (dorsal root ganglia and the spinal cord) and symptomatic pain assessed by behavioral hyperalgesia.

Apart from referred pain and secondary hyperalgesia, there is further evidence in the scientific literature that shows how pain in OA can be modulated through mechanisms related to the CNS. It has been found, for instance, that OA causes a decrease in pain thresholds in not only the affected joint, but also far from it in remote and over extended areas.[64,65] Loss of descending pain inhibitory mechanisms,[64,66] increase of temporal summation (increase of painful response to repetitive stimulation),[66] and the presence of extended areas of hyperalgesia in patients with OA[66–68] further support the role of central sensitization in OA pain.

Moreover, it is important to remember that patients with chronic musculoskeletal pain conditions usually present generalized hyperalgesia in deep tissues and an increased response to experimental painful stimulation.[69,70]

Recent evidence of the role central sensitization plays in OA pain comes from a study by Graven-Nielsen et al,[71] who conducted a protocol of pain assessment in people with knee OA. Widespread hyperesthesia, enhanced spatial summation, and loss of conditioned pain modulation were observed, which imply sensitized central pain mechanisms in these patients. Moreover, all of these measurements were normalized following joint replacement which implies that these central pain processes were maintained by peripheral input.

An animal study has shown the contribution of the spinal glial cells to central sensitization associated with OA.[72] Glial cells are crucial in the onset and maintenance of central sensitization, especially in relation to neuropathic pain. Activated glial cells (microglia and astrocytes) in the spinal cord can contribute to central sensitization by producing proinflammatory cytokines, complement factors, and cyclooxygenase (COX) type 1 and 2 inside the CNS. Their participation in OA pain indicates that mechanisms underlying neuropathic and OA pain might be similar[22] Still, these animal observations require confirmation in human studies.

One of the characteristics of central sensitization is that, once installed, it can persist in time despite the lack of new painful stimuli from the periphery. In clinical practice, it is not uncommon to find patients with OA who show symptoms even after prosthetic substitution. It has been noted that patients suffering with OA and a high degree of pain and low pain thresholds before surgery run a greater risk of continued pain after getting a prosthetic knee, which has been interpreted as an accurate reflection of central sensitization.[23]

The effect of certain centrally acting drugs such as duloxetine on OA pain[73,74] and the result of various studies carried out with functional magnetic resonance imaging (fMRI) have further consolidated the role of central sensitization in this pathology. Duloxetine is a serotonin and norepinephrine reuptake inhibitor drug that activates descending noradrenergic descending pathways together with serotonergic pathways.[75] Functional magnetic resonance imaging is a valid test that identifies how and where the pain is processed in the brain and how this process varies for different patients.[76,77] Studies using fMRI have shown an increased activity of the periaqueductal gray in patients with OA in comparison with individuals who are healthy.[78] This finding has been interpreted as increased activity of descending facilitatory pain mechanisms (a mechanism with the same net effect as decreased descending analgesia). Pain of knee OA is processed in areas related to emotions and fears[79] and activates pain areas of the prefrontal limbic region,[80] which also is typical of other chronic musculoskeletal conditions such as low back pain.[81] These areas are involved in the emotional evaluation of a person's surroundings,[82] thus confirming that chronic pain is an emotional state. This view applies to OA pain, as noted by Kulkarni et al.[79] The Table summarizes the currently available evidence regarding central sensitization in OA pain.

With regard to central sensitization in patients with OA pain, there is still much to discover. Notably, we need to determine which contributing genetic and environmental factors increase the risk of developing central sensitization, precisely what triggers and maintains this phenomenon, and what is the responsible factor of its persistence in some individuals.[34] However, identifying the contribution of central sensitization to many painful clinical conditions, "inexplicable" until the last couple of years,[34] has marked an important shift in physical therapists' clinical reasoning and has favored the development of new therapeutic strategies.[83]

Identification of Central Sensitization in Patients With OA

For some physical therapists, central sensitization is a theoretical concept, difficult to apply in daily clinical practice. Some therapists have even come to believe that it is a phenomenon that can rarely occur in their patients, which contradicts reality. Unfortunately, there is currently neither an international consensus definition nor a set of valid clinical criteria for the diagnosis of central sensitization. In other words, the diagnosis of central sensitization in patients with chronic musculoskeletal pain cannot be given directly, and clinicians should rely on symptoms and signs suggestive of central sensitization pain.

A recent study has shown how physical therapists can use information obtained from the medical diagnosis, patient's medical record, physical examination, and treatment response to clinically identify central sensitization in patients with musculoskeletal pain.[84] Not all patients with OA are characterized by central sensitization, thus probably constituting a subgroup within this pathology.[85] Murphy et al[85] identified, in a heterogeneous sample of patients with hip and knee OA, a small sub-

Table.
Summary of Current Evidence Regarding Central Sensitization in Osteoarthritis Pain

Study	Year of Publication	Experimental Model	Joint Under Study	Evidence of Central Sensitization
O'Driscoll and Jayson[65]	1974	Human	Hip	Extended and remote areas of hyperalgesia from affected joint
Neugebauer et al[57]	1993	Animal	Knee	Dorsal horn sensitization (secondary hyperalgesia)
Kosek and Ordeberg[64]	2000	Human	Hip	Extended and remote areas of hyperalgesia from affected joint Loss of descending pain inhibitory mechanisms
Bajaj et al[67]	2001	Human	Lower extremity	Extended and remote areas of hyperalgesia from affected joint
Sharif Naeini et al[63]	2005	Animal	Ankle	Dorsal horn sensitization (secondary hyperalgesia)
Ivanavicius et al[22]	2007	Animal	Knee	Contribution of spinal glial cells to pain
Kulkarni et al[79]	2007	Human	Knee	Functional magnetic resonance imaging (fMRI)
Martindale et al[56]	2007	Animal	Knee	Dorsal horn sensitization (secondary hyperalgesia)
Pinto et al[62]	2007	Animal	Ankle	Dorsal horn sensitization (secondary hyperalgesia)
Imamura et al[68]	2008	Human	Knee	Extended and remote areas of hyperalgesia from affected joint
Lundband et al[23]	2008	Human	Knee	Persistence of pain after prosthetic substitution
Chappell et al[73]	2009	Human	Knee	Positive effects of centrally acting drugs
Gwilym et al[78]	2009	Human	Hip	fMRI
Arendt-Nielsen et al[66]	2010	Human	Knee	Extended and remote areas of hyperalgesia from affected joint Loss of descending pain inhibitory mechanisms
Im et al[7]	2010	Animal	Knee	Communication between peripheral OA nociceptors and the central sensory system
Hochman et al[97]	2010	Human	Knee	Neuropathic pain descriptors of symptoms
Abou-Raya et al[74]	2011	Human	Knee	Positive effects of centrally acting drugs
Parks et al[80]	2011	Human	Knee	fMRI
Murphy et al[85]	2011	Human	Knee/hip	Identification of subgroup of patients with symptoms suggesting central sensitization
Murphy et al[86]	2011	Human	Knee	Identification of subgroup of patients with symptoms suggesting central sensitization
Sagar et al[72]	2011	Animal	Ankle	Contribution of spinal glial cells to pain
Hochman et al[98]	2011	Human	Knee	Neuropathic pain descriptors of symptoms
Graven-Nielsen et al[71]	2012	Human	Knee	Widespread hyperesthesia, enhanced spatial summation, and loss of conditioned pain modulation

group (36%) with symptoms suggesting central sensitization (widespread pain, fatigue, sleep disturbance, and cognitive difficulties). However, no attempt was made to determine whether those symptoms were manifestations of OA or other comorbid conditions such as fibromyalgia. In a recent study, Murphy et al[86] showed how 27% of the variance in pain severity in women with knee OA was explained by age, radiographic severity, and centrally mediated symptoms. Centrally mediated symptoms explained an additional 10% of the variance in pain severity after the other 2 variables were entered into the analysis. Both radiographic severity and centrally mediated symptoms were independently and significantly associated with pain severity. In addition to more severe radiographic features, women with higher centrally mediated symptoms had greater pain severity.

Although the studies by Murphy and colleagues[85,86] have provided some evidence that patients with greater central pain contributions can be identified in routine clinical practice, the implications of this involvement in OA are just starting to be realized, and larger longitudinal studies are needed. Evidence-based strategies are needed to more readily and systematically identify these patients. Guidelines for the recognition of central sensitization in patients with musculoskeletal pain such as OA pain have been presented[84] and are currently being updated and upgraded toward the first international diagnostic criteria for central sensitization in patients with musculoskeletal pain. Development of these diagnostic criteria should represent an improvement in the field and constitute an important step toward facilitating the acknowledge-

ment and recognition of central sensitization as a disease.

Some classification systems based on pain mechanisms are described in scientific literature.[87–91] In them, a classification of the patient's pain is attempted according to the neurophysiological mechanism responsible for the generation or maintenance of pain.[90–93] Therefore, starting with a set of signs and symptoms, patients are classified in 3 groups: (1) those with nociceptive pain, (2) those with peripheral neuropathic pain, and (3) those with pain due to central sensitization. This classification system, in theory, allows us to establish the most adequate treatment strategy and improve outcomes.[87] One of the advantages of such classifications is that they offer a better explanation of variations observed in the nature and severity of many clinical presentations of musculoskeletal pain disorders such as OA, where pain can be present without pathology, pathology without pain, or persistent pain despite resolution of pathology. Reliability and discriminating validity of these classification systems have been documented recently in relation to lower back and lower-limb pain.[94–96] However, whether these results can be extrapolated to a population with OA is unknown.

Central sensitization also has been inferred from OA in humans in terms of neuropathic pain descriptors of symptoms. Hochman et al[97] recently identified in a sample of people with chronic pain due to knee OA, a small subgroup who used subjective descriptors of pain suggesting neuropathic pain. The neuropathic pain subgroup mainly comprised young women with greater pain intensity and severity and longer duration of pain.[97] Using specific questionnaires also allowed identification of a neuropathic pain component in patients with OA.[98]

In order to understand exactly the role central sensitization plays in patients with OA, it could prove useful to evaluate the response to interventions specifically addressing alterations in central pain processing. Moreover, patients with OA having clear signs and symptoms of central sensitization (eg, a patient with hip OA having widespread pain, hypersensitivity to bright light, and intolerance to stress) can be treated differently. Once the physical therapist concludes that central sensitization rather than the local joint destruction dominates the clinical picture of the patient with OA, the treatment focus should be reset on the CNS (ie, diminishing the hypersensitivity of the CNS). Apart from pharmacological treatments mentioned above (ie, centrally acting drugs), other treatments addressing cognitive-emotional sensitization such as CBT or neuroscience education should be take into consideration.[99] However, until now, these types of interventions have been underestimated in patients with OA.[100] Finally, education can be combined with graded exercise therapy/graded activity and stress management to design a comprehensive rehabilitation program targeting central sensitization in patients with OA. These interventions are explained below.

Neuroscience Education: A Future Tool in OA?

Traditional rehabilitation treatments for OA typically are directed to the periphery (ie, joint and surrounding structures) through interventions such as joint injections, joint protection, analgesic medication, manual therapy, exercise, or transcutaneous electrical nerve stimulation. Techniques used to manage pain such as manual therapy,[101,102] exercise, or transcutaneous electrical nerve stimulation[103] can potentially target central sensitization by modulating pain and desensitizing the CNS,[35,99] although their effects on central sensitization are unclear. Moreover, therapeutic strategies addressing the symptoms that accompany OA pain (ie, sleep disturbance, depression, and fatigue), such as CBT or CBT-guided and activity pacing, could act on central factors contributing to pain in OA.

One intervention recently used to desensitize CNS is neuroscience education. Neuroscience education is an educational intervention aiming to reduce pain and disability by explaining to the patient the biological processes underlying his or her pain condition. Its use is recommended in central sensitization conditions, where the patient presents maladaptive cognitions, behavior, or coping strategies in response to pain.[104] In contrast to educational programs commonly used in rehabilitation that apply pathoanatomical and biomechanical models to explain the pain (focusing on the tissues and tissue damage), neuroscience education describes how the nervous system interprets information coming from the tissues through peripheral sensitization, central sensitization, synaptic activity, and cortical processing. Conventional biomedical models not only have a limited efficiency in decreasing pain and disability,[105,106] but they also can be counterproductive because they increase the patient's fear, anxiety, and stress, which also can increase the pain.[107–109]

From a clinical perspective, it is a challenge to put into practice scientific knowledge related to central sensitization and chronic pain. Clinical guides are now available that provide information for explaining central sensitization, describing how to perform a neuroscience education session with patients with chronic musculoskeletal pain.[104] A systematic review of the effect of neuroscience education on pain, disability, and stress in patients with chronic

musculoskeletal pain has recently been published.[110] In this review, it was concluded there is convincing evidence that neuroscience education has positive effects on pain, disability, catastrophizing, and physical performance in patients with chronic musculoskeletal pain. Moreover, structure, content, and evidence of treatment with neuroscience education for different chronic conditions are described in detail elsewhere.[104,110] Nonetheless, one of the limitations of this review is that evidence exists only for very specific pathologies such as chronic low back pain, chronic fatigue syndrome, fibromyalgia, and chronic whiplash trauma. It remains to be established whether these findings can be extrapolated to other musculoskeletal pain conditions such as OA. Hence, future studies should specifically evaluate efficacy of interventions addressing psychosocial aspects in OA such as neuroscience education as has already been done with CBT or activity pacing. Moreover, one of the challenges clinicians are faced with is to find the perfect balance, for each patient with OA, between interventions directed at musculoskeletal tissues and "hands-off" approaches.[111]

It should be emphasized that neuroscience education is not a treatment but rather a strategy targeting cognitive barriers for behavioral change and hence effective physical therapy. Neuroscience education aims at reconceptualizing chronic pain in a way that it is no longer regarded as threatening (ie, the patient should understand that pain in case of central sensitization no longer reflects tissue damage but rather reflects "noise" in the sensory system). This approach opens the avenue for a time-contingent approach to exercise therapy and activity management, which is explained below.

Exercise Therapy and Graded Activity

Exercise is frequently encountered as a central component of the management of OA pain. Although the clinical benefits of exercise therapy in OA are well established (ie, evidence based),[112] it is currently unclear whether exercise therapy has positive effects on the processes involved in central sensitization. From a theoretical perspective, exercise has the potential to "treat" the process of central sensitization: exercise activates brain-orchestrated endogenous analgesia (reviewed in Nijs et al[113]). From a clinical perspective, clinicians are advised to use a time-contingent approach when exercising patients with OA and central sensitization. This approach implies that the patient does not cease exercise bouts once local pain severity increases. Instead, the patient adheres to the predetermined exercise modalities (including the time-contingent variable exercise duration) and interprets pain increases as nonthreatening.

Such a time-contingent approach is unlikely to be effective unless the patient applies this time-contingent approach in daily life as well. Indeed, graded activity is a behavioral therapy applying such a time-contingent approach in the daily life of patients with OA. Increased physical activity is effective for managing pain in patients with OA who are overweight,[114] and graded activity therapy is effective for patients with OA in general.[115,116] Moreover, graded activity results in better exercise adherence and more physical activity compared with usual care in patients with hip or knee OA, both in the short term and the long term.[117]

Conclusions

Osteoarthritis is a frequent chronic musculoskeletal pathology that usually causes great disability and results in significant health care costs. Even though patients with OA present structural anomalies, the severity of these changes is not always proportional to the degree of pain or disability. A significant proportion of these patients show signs of central sensitization, with pain modulation and processing altered at the CNS level. Substantial scientific evidence indicates a role for central sensitization in OA pain, yet it is necessary to develop strategies to allow reliable and systematic recognition of patients with OA whose pain has a central sensitization component. Central sensitization management is an area of great interest, at least in the subgroup of patients with OA pain having central sensitization. Interventions such as CBT and neuroscience education potentially target cognitive-emotional sensitization (and descending facilitation), and centrally acting drugs and exercise therapy can improve endogenous analgesia (descending inhibition) in patients with OA. However, to date, evidence on both identification and treatment of central sensitization in OA is still scarce, and more human research is needed.

Optimum treatment for people with OA pain requires a multidisciplinary approach and determination of how peripheral and central factors are contributing to pain in each patient in order to enable individualization of treatment strategies. Physical therapists are well positioned to deliver an individualized intervention because they are cognizant of the need for a biopsychosocial approach to management. In addition, they can perform systematic assessment and choose to utilize a more peripheral or central-based therapy.

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Lluch Girbés and Professor Torres-Cueco provided data analysis and project management. Professor Torres-Cueco provided facilities/equipment. Professor Lluch Girbés, Dr Nijs, and Professor Torres-Cueco provided consultation (including review of manuscript before submission).

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