Addressing Neuroplastic Changes in Distributed Areas of the Nervous System Associated With Chronic Musculoskeletal Disorders

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Present interventions utilized in musculoskeletal rehabilitation are guided, in large part, by a biomedical model where peripheral structural injury is believed to be the sole driver of the disorder. There are, however, neurophysiological changes across different areas of the peripheral and central nervous systems, including peripheral receptors, dorsal horn of the spinal cord, brain stem, sensorimotor cortical areas, and the mesolimbic and prefrontal areas associated with chronic musculoskeletal disorders, including chronic low back pain, osteoarthritis, and tendon injuries. These neurophysiological changes appear not only to be a consequence of peripheral structural injury but also to play a part in the pathophysiology of chronic musculoskeletal disorders. Neurophysiological changes are consistent with a biopsychosocial formulation reflecting the underlying mechanisms associated with sensory and motor findings, psychological traits, and perceptual changes associated with chronic musculoskeletal conditions. These changes, therefore, have important implications in the clinical manifestation, pathophysiology, and treatment of chronic musculoskeletal disorders. Musculoskeletal rehabilitation professionals have at their disposal tools to address these neuroplastic changes, including top-down cognitive-based interventions (eg, education, cognitive-behavioral therapy, mindfulness meditation, motor imagery) and bottom-up physical interventions (eg, motor learning, peripheral sensory stimulation, manual therapy) that induce neuroplastic changes across distributed areas of the nervous system and affect outcomes in patients with chronic musculoskeletal disorders. Furthermore, novel approaches such as the use of transcranial direct current stimulation and repetitive transcranial magnetic stimulation may be utilized to help renormalize neurological function. Comprehensive treatment addressing peripheral structural injury as well as neurophysiological changes occurring across distributed areas of the nervous system may help to improve outcomes in patients with chronic musculoskeletal disorders.
Traditionally, treatments for chronic musculoskeletal disorders (CMSDs) such as chronic low back pain (CLBP) have been anchored in a biomedical model. This model is based on a structural-pathology paradigm where insult to anatomical structures is believed to be the sole driver of the condition. Over the last 2 decades, evidence has emerged of neurophysiological changes within the peripheral and central nervous systems associated with CMSDs. Studies suggest that CMSDs do not simply result from ongoing structural pathology to peripheral tissues but involve a complex interplay among peripheral structural injury; altered afferent information conveyed from peripheral receptors toward the spinal cord, brain stem, and cortical areas; changes in neuronal processing of noxious stimuli; and psychosocial factors. These neurophysiological changes are consistent with experimental and clinical findings of altered sensory transmission, including sensory amplification of pain; motor control changes such as altered muscle recruitment patterns; changes in perceptual processes, including altered body image; psychological traits such as catastrophization and somatization; and behavioral changes such as fear avoidance that appear to be implicated both in the clinical manifestation and the pathophysiology of CMSDs (Table).

Neurophysiological changes, or neuroplasticity, refer to changes in structure, function, and organization within the nervous system that occur continuously throughout our lifetimes in response to internal stressors such as cognitive processes, internal changes in sensory afference, and external stressors such as motor learning and peripheral sensory stimulation. Neuroplasticity is the method by which the brain encodes new experiences, learns, and develops new behaviors. Neuroplastic changes associated with CMSDs have been demonstrated in the: (1) peripheral nervous system and spinal cord, (2) brain stem, (3) sensorimotor areas, and (4) mesolimbic and prefrontal areas of the cortex. Neurophysiological changes occurring within peripheral receptors and the dorsal horn of the spinal cord include increased responsiveness to nociceptive stimuli resulting from anatomical insult to musculoskeletal structures and neuropathic stimuli in sensory amplification, a process called sensitization, resulting in hyperalgesia, increased pain perception, and allodynia; innocuous stimuli are perceived as painful. Peripheral sensitization, involving increased responsiveness of the peripheral nociceptors, and central sensitization, involving changes in the spinal cord amplifying the transmission of pain, are natural processes that have a biological advantage in helping to protect the injury from reinjury. However, sensitization should be transient, and peripheral and dorsal horn plastic changes should return to their preinjury state, with normalized afferent peripheral input associated with tissue repair.

Neuroplastic changes also occur within the brain stem, specifically in areas involved in the descending modulation of nociceptive and neuropathic stimuli, including the periaqueductal gray (PAG) and the rostral ventral medulla (RVM). The PAG and RVM are influenced by the mesolimbic and opioid systems, which, in turn, influence the transmission of noxious stimuli in the dorsal horn of the spinal cord. Evidence suggests that these descending modulatory systems are affected in chronic pain states and may perpetuate sensitization within the spinal cord.

The sensory discriminative areas involved in the transmission and processing of noxious stimuli include the primary and secondary somatosensory cortices (S1 and S2, respectively) and the insula. The insula appears to be at the crossroads between the sensory discriminative and affective aspects related to pain sensation in the caudal portion and pain affect in the anterior portion.

Changes in structure, function, and somatotopic organization of S1 and the primary motor cortex (M1) have been demonstrated in chronic pain conditions, including CLBP and complex regional pain syndrome (CRPS), and have been found in patellofemoral pain syndrome, patellar tendinopathy, osteoarthritis (OA), and rotator cuff pathology. Changes in pressure pain thresholds and bilateral findings, including decreased strength and range of motion and presence of inflammatory mediators in the contralateral homologous structure, also allude to the presence of altered neural transmission and processing in a number of CMSDs. The neuroplastic changes in the cortical sensorimotor areas are consistent with sensory disturbances (ie, changes in tactile acuity), perceptual disturbances (ie, altered body image), and motor disturbances (ie, motor control) apparent in different CMSDs. The neurophysiological changes in the sensorimotor cortical areas often correlate with pain intensity and symptom duration. Evidence suggests a 2-way causality between pain or injury and cortical plasticity in S1 and M1, as the elimination of pain may result in cortical reorganization, and interventions that address cortical reorganization may result in decreased pain and improved function.

The cognitive-affective-motivational areas involved in pain processing receive input from ascending projec-
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Table.
Areas of Neuroplastic Changes Associated With CMSD and Possible Signs and Symptoms Manifested by the Patient⁶

<table>
<thead>
<tr>
<th>Neurophysiological Changes Associated With CMSD</th>
<th>Possible Physiological Consequences of Neuroplastic Changes in These Areas</th>
<th>Signs and Symptoms That May Possibly Indicate Neuroplastic Changes in These Areas</th>
</tr>
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</table>
| Mesolimbic and prefrontal areas
  Areas demonstrated to have been affected include: insula, cingulate cortex, amygdala, medial and dorsolateral prefrontal cortex, and nucleus accumbens | Altered neuronal responses to pain, especially in regard to the “unpleasantness” associated with pain
  Implicit and explicit learning associating pain with movement and negative outcomes | Spontaneous fluctuations in pain
  Problems in affective, cognitive, and motivational aspects in relation to pain
  These changes may be associated with psychological aspects related to pain, including fear avoidance, anxiety, depression, catastrophization, somatization, worry, and increased vigilance |
| Descending pain modulatory systems, PAG-RVM pathway
  Descending modulatory systems receive input from prefrontal and mesolimbic structures, including the cingulate cortex, amygdala, and mPFC | Decreased descending inhibition of pain (disturbed conditioned pain modulation) | Central sensitization (hyperalgesia and allodynia)
  Pain thresholds may be decreased (pressure and thermal) |
| Peripheral receptors | Increased transduction of nociceptive stimuli | Increased pain transmission in the area of injury resulting from changes in input and output characteristics in peripheral nociceptors (peripheral sensitization)
  Contributes to central sensitization (hyperalgesia and allodynia) |
| Dorsal horn of the spinal cord | Increased transmission of nociceptive and neuropathic stimuli
  Results from changes in membrane permeability, decreased inhibition
  Influenced by descending modulation pathways, including the PAG-RVM | Central sensitization (hyperalgesia and allodynia)
  Pain thresholds may be decreased (pressure and thermal) |
| Somatosensory cortex | Altered somatosensory maps, including expansion, retraction, or shifting of representation | Increased 2-point discrimination
  Impaired performance of laterality recognition
  Change in perception of body image, including size of the limb, altered body midline |
| Primary motor cortex | Changes in muscle/movement representations in motor areas of the brain and corticospinal excitability | Changes in motor control, including co-contraction and loss of ability to selectively recruit individual muscles |
| Somatosensory associative areas | | Perceptual disturbances in body image, including altered size and altered body midline
  Impaired performance of laterality recognition |

⁶ CMSD=chronic musculoskeletal disorder, PAG-RVM=periaqueductal gray-rostral ventro-medullary, mPFC=medial prefrontal cortex.

The cognitive-affective-motivational areas involved in pain processing include the structures within the mesolimbic and prefrontal areas such as the insula, anterior cingulate cortex (ACC), amygdala, and prefrontal cortex (PFC).⁷ Arguably, the most important neuroplastic changes associated with CMSDs occur within the mesolimbic and prefrontal areas, regions associated with threat, fear, aversive conditioning, attention, motivation engagement or disengagement, and executive control.¹⁷ The best biomarker identified for the transition from acute to chronic conditions,¹⁸ and for the presence of chronicity in people with low back pain and OA, involves activity within these regions.⁴ Altered structure, function, and activity within the mesolimbic and prefrontal areas correlate with psychological traits that are often implicated in chronic conditions such as fear avoidance and catastrophization (a tendency to focus on and magnify actual or anticipated pain experience and to feel hopeless in the face of such experience¹⁹).²⁰,²¹ Mesolimbic structures, specifically the PFC, ACC, and amygdala, also influence motor areas and functioning of the descending modulatory systems, including the PAG-RVM pathway, that are affected in chronic pain states.⁶,⁷ The PFC and mesolimbic activity appear to lay the foundation for increased vigilance, attention, and salience attributed to the injury and, therefore, may contribute to central sensitization, resulting in hyperalgesia and allodynia, and provide conditions ripe for inducing neuroplastic changes in the sensorimotor and subcortical areas. Increasing attention...
and salience directed to the injury, threat, and perception of pain appear to result in implicit and explicit learning linking movement with pain.16

In summary, neurophysiological changes associated with CMSDs include alterations in structure (decrease in gray matter in mesolimbic and prefrontal areas),22,23 function, organization (ie, changes in response properties and cortical representation in S1 and M1),1 and neurobiology (changes in brain chemistry concentrations have been found in people with CLBP in an area of the PFC and in M1).24

**Implications of Distributed Neuroplastic Changes Associated With CMSD for Rehabilitation**

Neuroplasticity associated with CMSDs has important implications for the treatment of conditions such as CLBP, OA, and possibly other CMSDs.25 Conventional rehabilitation interventions, in large part, are directed toward input mechanisms (ie, mechanisms addressing inflammation, repair, and remodeling in peripheral structural injury) and output mechanisms (ie, muscle strength, endurance, motor control, and proprioception) associated with CMSDs.26 Although these interventions may have an impact on peripheral structures, they—in themselves—may not be sufficient to restore cortical properties and function and alleviate pain, particularly in chronic injuries.27 In musculoskeletal rehabilitation, limited resources have been directed to the problems of transmission, processing, and control mediating afferent stimuli and motor output.26 Failure to effectively treat conditions such as CLBP may stem from the fact that the central neuroplastic changes occurring across distributed areas associated with this condition have largely been ignored and may explain why treatment effects are consistently small regardless of the type of intervention.1,28

Principles of neuroplasticity emerging from animal and human studies can be harnessed to induce positive neuroplastic changes. Studies in people with and without neurological injury suggest that the stimuli necessary to promote neuroplastic changes, at least in sensorimotor cortical areas, must be repetitive, of sufficient intensity to stimulate adaptive changes, require attention and behavioral salience, and involve learning.2,29 These studies also suggest that changes will be specific to the neuronal structures implicated in the task.2,29 Neuroplasticity is stimulus driven, and the stimuli can be mediated by top-down (from higher to lower hierarchical structures within the nervous system) and bottom-up (from peripheral to central structures of the nervous system) processes.30 As CMSDs involve neuroplastic changes within distributed areas, it is logical to believe that treatment should be directed across the different affected structures in the nervous system, including the sensorimotor areas and the mesolimbic prefrontal areas. Although this area of study is in its infancy, it appears that rehabilitation professionals have at their disposal tools and resources to promote adaptive changes in the sensorimotor areas as well as the mesolimbic and prefrontal areas associated with CMSDs.

**Interventions**

**Top-down**

**Reconceptualizing pain.** Health care practitioners and people with CMSDs tend to view pain with a biomedical focus31 despite the failings of this model to explain clinical and experimental findings and to guide effective rehabilitative strategies. Studies indicate that the relationship between threat and tissue damage is altered in chronic pain states, the stimulus-response relationship between structural injury and pain perception is nebulous, and neuroplastic changes associated with chronic pain are maladaptive and no longer perform the biological function of protection.1,3,4,16 It is imperative that updated and current knowledge regarding pain and a biopsychosocial perspective stemming from the wealth of research findings that have emerged over the last 2 decades be transferred to health care professionals and the health care curriculum.32,33

Recognition of misguided beliefs, values, and behavioral strategies that people with CMSDs may display regarding pain and their injury that are incongruent with the rehabilitative principles of graded activity to promote mobilization and positive adaptive changes should be addressed early and continuously in the rehabilitative process.33 The conceptualization that pain and movement are associated with structural damage and the belief that the structural insult to anatomical structures is the source of all pain need to be reformulated.34

Experimental findings demonstrate that neurophysiology education of pain (NEP), which includes information regarding the anatomy, physiology, and processing of noxious stimuli; the perceptual nature of pain; and the altered processing with chronic pain, is associated with improvement in function and attenuation of pain.35 The information and concepts presented in the NEP programs are accessible to patients experiencing chronic pain36 and can have an immediate impact on behavior.35 Although the scientific literature is limited in regard to these programs, they would appear to perform better than educational programs that stem from a biomedical model to explain structural pathol-
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ogy and biomechanics as the drivers of the CMSD. A single session of neurophysiology education of pain in people with CLBP has proven to result in a transient decrease in pain and improvement in function and may be associated with changes in brain activation patterns. For more permanent changes in belief and behavior, the concepts stemming from neurophysiology education will probably need to be repeated consistently in the rehabilitation program. Although education has been demonstrated to be beneficial in outcome for chronic back pain, recent meta-analyses and systematic reviews of NEP demonstrate that these programs are promising but that results are currently tenuous due to the limited number of studies.

Addressing maladaptive thoughts and behavior. Cognitive-behavioral interventions (CBIs) seek to identify and address thoughts, ideas, and beliefs that are inconsistent, erroneous, and unproductive, resulting in maladaptive behavior patterns such as worry and avoidance. These interventions include traditional cognitive-behavioral therapy (CBT), which is a control-oriented treatment that attempts to address catastrophic thinking through cognitive restructuring, promotion of problem-solving skills, and addressing maladaptive behaviors through exposure-oriented interventions to address avoidance behaviors. Cognitive-behavioral therapy appears to result in improvement in function, decreased anxiety, and depression, which are correlated with increases in activation within the PFC. These findings suggest that CBT results in an increase in executive control that modulates dysfunctional activity in the mesolimbic areas. A prospective study of CBT in people with chronic back pain demonstrated decreased functional connectivity between the areas in the PFC and ACC with the amygdala/PAG, which positively correlated with decreased pain and improved self-efficacy. Systematic reviews of CBT in people with chronic pain indicate that CBT has small-to-moderate effects on mood, catastrophization, pain intensity, and, to a lesser extent, pain-related disability and avoidance behaviors for up to 6 months.

Acceptance-based interventions. Other forms of CBI also have been studied in regard to pain, including approaches that involve the development of awareness and nonjudgmental acceptance of pain in contrast to attempting to control or fight pain. Two such approaches are acceptance commitment therapy (ACT) and mindfulness-based stress reduction (MBSR). Acceptance commitment therapy involves the acceptance of positive and negative experiences, the elucidation of values, commitment to these values, and appropriate goals and actions that support these values. Pain is seen as an interference to goal-directed, value-driven action. Mindfulness-based stress reduction incorporates meditation, yoga, and a body scan/relaxation technique providing instruction on acceptance without cognitive assessment to minimize anxiety and its detrimental effects on pain processing. This approach also encourages movement and relaxation and the transference of these skills and mind-set to everyday life. Different variants have been developed, including mindfulness-based cognitive therapy, which incorporates principles of CBT within MBSR. Mindfulness-based stress reduction decreases stress, anxiety, and depression associated with chronic pain states and, similar to CBT, has an impact on prefrontal structures and their control of mesolimbic structures.

In healthy individuals, a 6-week program of MBSR resulted in neuroplastic changes in the insula and S1 and in changes in functional connectivity between the medial PFC and the insula (increased connectivity between these structures is found in patients with OA), changes that also correlated with the improvement on psychological indexes, including worry, anxiety, and depression. In healthy people exposed to a noxious stimulation, MBSR not only resulted in the activation of areas in the PFC involved in the reformulation of the contextual evaluation of the noxious stimuli but also influenced activity within S1 and the thalamus, areas involved in the transmission and sensory discriminative aspects of pain, alluding to possible gating mechanisms of noxious transmission.

There is positive evidence for the use of CBI in the management of chronic pain; however, outcomes are variable, and the effects are small for pain intensity, anxiety, depression, quality of life, and physical well-being. The beneficial effects are greatest for mood, catastrophizing thoughts, and disability, and there is evidence that effects are maintained at 6 months. In summary, reconceptualization involves education that challenges negative and faulty beliefs regarding pain. Issues regarding stress, anxiety, and worry that contribute to a heightened response to pain, guarding, and fear avoidance need to be addressed continuously, and patients should be provided with the tools to better understand and manage their pain and disability, including information regarding pain neurophysiology and a biopsychosocial formulation of CMSDs. Collectively, these interventions appear to improve self-efficacy, the ability of the person to self-manage through actions and interventions to cope with his or her pain and disability, and promote...
active coping styles. Greater self-efficacy is associated with better outcomes in patients with chronic pain. Cognitive-based interventions also address the mesolimbic and prefrontal changes associated with chronic pain, which, in turn, may affect descending pain modulatory systems within the brain stem (that perpetuate sensitization) and cortical sensorimotor areas. Neurophysiology education of pain and CBI should be addressed at the onset of treatment, even in acute and subacute phases, and should be continuously addressed during the rehabilitation process. Failure of these interventions to demonstrate more positive effects and for longer durations may stem from the fact that substantial changes in neurophysiological correlates of faulty beliefs and values have not been reconceptualized sufficiently.

**Primed the brain for movement.**
The creation of adaptive changes in musculoskeletal structures requires graded and progressive interventions, performed repetitively and with sufficient intensity. These principles appear to apply equally in addressing neuroplastic changes to promote positive adaptive outcomes.

Graded exposure can begin with interventions that require implicit activation of sensory and associative areas in the parietal cortical areas through interventions such as laterality recognition, where the patient is asked to determine the laterality of an anatomical image without moving the body part. Studies have shown that people with experimental and chronic pain, including CLBP, CRPS, OA, and CTS, make more errors, and the speed in the performance of this task is affected when visualizing the injured body part, reflective of altered somatosensory organization and processes in sensory areas, including S1 and the inferior parietal regions. Interventions incorporating implicit imagery result in changes in S1 properties and organization as well as decreased pain and improved function.

Explicit cognitive exposure involves motor imagery of painful or fearful movements. Motor imagery has a long history of use in kinesiology and has well-documented positive benefits for performance. In people experiencing chronic pain, motor imagery may help to improve physical performance and may help to address cortical changes in mesolimbic and prefrontal areas associated with physical performance of active movements and possible learned associations (implicit and explicit) of pain and movement. Motor imagery utilized for the learning of a new motor skill results in improvement in performance and changes in the motor areas similar to actual physical practice.

Cognitive-based interventions such as motor imagery can influence brain function and cortical processes, including sensorimotor areas. They may have an advantage in highly anxious and fearful patients, as they do not involve physical movement and should not elicit an anxiety response. The progressive nature of these interventions appears to be important, at least in certain pain conditions such as CRPS when pain severely limits the capacity for movement, and simply imagining movement can increase pain and swelling. To induce changes in properties and organization in sensorimotor cortical area tasks involving motor acquisition of new skills requiring sustained attention appears to be necessary.

**Novel approaches for promoting cortical neuroplasticity.** Direct noninvasive stimulation of cortical neurons to promote neuroplastic changes, both in isolation or in association with other modalities, has been investigated in a limited number of research studies. Noninvasive cortical stimulation includes transcranial direct cortical stimulation (tDCS) and transcranial magnetic stimulation (TMS). Transcranial direct cortical stimulation involves the application of a direct electrical current to the surface of the cranium. Combined tDCS and peripheral electrical stimulation (PES) in people with CLBP has resulted in a map reorganization in M1, improvement in sensory function, and decrease in pain that was superior to their individual application.

Transcranial magnetic stimulation involves an electrical current passing through a coil producing a magnetic field that traverses the skull and results in the depolarization of neurons under the coil. Repetitive transcranial magnetic stimulation (rTMS) applied at low frequencies (below 5 Hz) produces an inhibition of the area of stimulation, whereas rTMS applied at higher frequencies (greater than 5 Hz) results in a facilitation. Studies have been performed in people who were neurologically compromised, including patients with stroke, to help promote positive neuroplastic changes and improve motor function. Repetitive TMS over the somatosensory cortex also can result in improved tactile acuity. Repetitive TMS and anodal tDCS of the motor cortex help to attenuate chronic pain. A study by Stefan et al also combined PES with TMS to promote neuroplastic changes in M1.

**Bottom-up**
Addressing changes in sensorimotor areas of the brain. Bottom-up modulation of altered processing and organization in S1 includes interventions such as sensory discrimination training and PES. Tactile acuity, specifically 2-point discrimination utilized as a form of
Peripheral electrical stimulation can be utilized to affect neuronal properties in both S1 and M1 in healthy people. This form of electrical stimulation can cause alterations in the somatotopic map within S1 and improve sensory function. It can both augment and attenuate neural excitability in both S1 and M1, depending on the parameters of stimulation. Peripheral electrical stimulation of a mixed nerve for 120 minutes, at frequencies >10 Hz and an intensity of stimulation at or close to motor threshold, results in increases in corticospinal excitability and improvement of motor performance in healthy people. Higher stimulation frequencies appear to result in decreases in excitability of neurons in the motor cortex. Transcutaneous electrical nerve stimulation applied daily for 3 weeks to the hand in healthy individuals resulted in an increase in map volume and area of representation of muscles of the hand within M1.

To induce plastic changes in M1, active interventions need to focus on motor learning. The simple repetition of movement will not result in plastic changes in the motor cortex. Excellent reviews have recently been published on principles of neuroplasticity and motor learning and their utilization in patients with CMSDs. Principles including the utilization of motor learning, functional reacquisition, and external focus of attention can be incorporated into rehabilitation programs to address changes in the sensorimotor areas associated with CMSDs. Motor learning requires focused attention and salience and involves increased interaction and feedback. The importance of attention in promoting plastic changes in M1 has been demonstrated in a number of studies. Indeed, it is possible that effects related to motor learning may simply be mediated by the increased attention required to perform new tasks. Active movements to promote motor learning and associated cortical changes should involve functional progressions with increasing task complexity. Finally, an external focus of attention involved with motor learning may be beneficial to shift attention toward the accomplishment of a task, as distraction helps to modulate pain perception, rather than an internal focus, which results in increased vigilance toward pain and can exacerbate pain perception.

Clinical application of treatment addressing distributed neuroplastic changes with CMSDs. Active interventions addressing motor and mobility disturbances also should be graded and progressive. The use of laterality recognition training, motor imagery, and mirrors in an approach of graded motor imagery may be helpful in addressing neurophysiological changes associated with CMSDs. The question of whether to begin with painful movements to challenge the maladaptive changes in the nervous system or to progressively begin exercise in non-painful ranges and movements or with graded imagery before progressing to movements that are associated with fear and anxiety is a matter of debate. The choice may be dictated by patient’s attitudes, beliefs, and behaviors—the more fearful and anxious, the more non-threatening should be the progression of exercise as early pain may simply reinforce their existing values and operant learning linking movement to pain. However, pain should not be utilized as the sole measure of progression because of the nebulous relationship between pain and threat of impending further tissue injury in chronic pain states. Exercise should be guided by form, the ability to perform the movement correctly, and functional progressions in volume and intensity (resistance and difficulty of task).

The cognitive strategies reviewed earlier need to be addressed continuously in order to dampen the effects of anxiety and fear, to limit guarding, and to progressively integrate movements that were previously perceived as threatening. Patients’ beliefs, apprehension, and behaviors must be challenged repetitively. Graded functional progressions should, over time, help extinguish learned associations reflective of neuroplastic changes in the mesolimbic and prefrontal areas, and secondly address the cortical changes in the sensorimotor areas associated with CMSDs. Cortical and subcortical areas and the spinal cord have strong interconnections, and interventions targeting one area should affect the others, including sensorimotor and mesolimbic areas. Finally, the positive yet limited effects of many of these approaches in isolation suggest that a multimodal approach that is coherent, consistent, and incorporates interventions specifically targeting neuroplastic changes in the nervous system.
changes may yield more positive outcomes.

Reconceptualizing treatment provided to patients with CMSDs. The growing evidence for changes in distributed areas of the nervous system in chronic pain conditions also may provide greater comprehension of methods of action currently utilized by physical rehabilitation professionals and lead to more effective interventions, which may involve neurophysiological changes. Treatment goals in patients with CMSDs have largely been directed by a biomedical paradigm, which has proven to be limited in efficacy.\textsuperscript{28,74} Rehabilitation currently performed with patients with CMSDs may result in peripheral and central changes. The reconceptualizing of treatment provided to patients with CMSDs, therefore, would involve an approach that targets peripheral structural sources of pain, as well as interactions and specific interventions to encourage plastic changes in the nervous system, by addressing faulty values and beliefs regarding pain, attempting to minimize fear and anxiety, and performing exercises and interventions that target sensorimotor and perceptual changes.

It is imperative that the therapist remains consistent in the messages conveyed both explicitly and implicitly through his or her actions and behaviors. The message conveyed to the patient should not imply implicitly or explicitly that a structural pathology model of local biomechanical problems alone is the sole driver of the CMSDs. The implicit or explicit perception by the patient would be inconsistent with experimental findings and may perpetuate faulty beliefs and encourage fear avoidance, anxiety, and guarding, resulting in decreased movement and contributing to a biomedical focus of local tissue insult as the driver of the condition and possibly negatively affecting self-efficacy and outcomes.\textsuperscript{66,75} A consistent message conveyed by the therapist to the patient is important, as therapist-patient interaction and communication are important for treatment success.\textsuperscript{76} Our current understanding of principles of neuroplasticity may help understand the method of action of current interventions and develop interventions that help promote positive long-term adaptive changes within the CNS associated with CMSDs.

Conclusion

Chronic low back pain, OA, and probably other CMSDs are associated with neuroplastic changes across distributed areas of the nervous system, including structural as well as peripheral and central neurophysiological changes. These changes correlate with the clinical and experimental findings within this population, including psychological traits and perceptual and sensorimotor disturbances. Addressing the changes across the distributed network may help to yield greater understanding and outcomes for the treatment of these conditions. This approach involves cognitive-based interventions such as education to reconceptualize beliefs regarding pain and interventions to modify patients’ thoughts and reactions to help control anxiety and improve self-efficacy. Neuroplastic changes in the sensorimotor cortical areas also are affected in CMSDs, and interventions that modulate sensory input and involve motor learning need to be incorporated into existent rehabilitation programs. The focus of interventions oriented toward renormalization of distributed cortical areas is consistent with a biopsychosocial paradigm and may result in improved outcomes. Imaging studies of these cortical areas associated with CMSDs will help to determine how widespread these cortical changes are, to provide an additional means to address efficacy of these interventions, and to determine how well interventions correlate with positive outcomes and renormalization of cortical properties, processes, and organization. Musculoskeletal rehabilitation professionals are well positioned and have resources at their disposal to influence positive adaptive neuroplastic changes by addressing psychological and biological factors within the nervous system associated with CMSDs.

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All authors provided concept/idea/project design and writing. Dr Higgins provided consultation (including review of manuscript before submission).


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