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Neuroplasticity of Sensorimotor Control in Low Back Pain

SYNOPSIS: Low back pain (LBP) is an important medical and socioeconomic problem. Impaired sensorimotor control has been suggested to be a likely mechanism underlying development and/or maintenance of pain. Although early work focused on the structural and functional abnormalities within the musculoskeletal system, in the past 20 years there has been an increasing realization that patients with LBP might also have extensive neuroplastic changes within the central nervous system. These include changes related to both the structure (eg, gray matter changes) and function (eg, organization of the sensory and motor cortices) of the nervous system as related to processing of pain and nociception and to motor and somatosensory systems. Moreover, clinical interventions increasingly aim to drive neuroplasticity with treatments to improve pain and sensorimotor function. This commentary provides a contemporary overview of neuroplasticity of the pain/nociceptive and sensorimotor systems in LBP. This paper addresses (1) defining neuroplasticity in relation to control of the spine and LBP, (2) structural and functional nervous system changes as they relate to nonspecific LBP and sensorimotor function, and (3) related clinical implications. Individuals with recurrent and persistent LBP differ from those without LBP in several markers of the nervous system's function and structure. Neuroplastic changes may be addressed by top-down cognitive-based interventions and bottom-up physical interventions. An integrated clinical approach that combines contemporary pain neuroscience education, cognition-targeted sensorimotor control, and physical or function-based treatments may lead to better outcomes in patients with recurrent and persistent LBP. This approach will need to consider variation among individuals, as no single finding/mechanism is present in all individuals, and no single treatment that targets neuroplastic changes in the sensorimotor system is likely to be effective for all patients with LBP. *J Orthop Sports Phys Ther 2019;49(6):402-414. doi:10.2519/jospt.2019.8489*

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Low back pain (LBP) represents an important medical and socioeconomic problem.[34] Current treatments provide modest and generally short-term success, which may be due in part to our incomplete understanding of the mechanisms of nonspecific LBP.[12] Impaired sensorimotor control (which refers to all sensory and motor processes that control muscles and spinal alignment and movement to meet demands of healthy function and loading of the spine) has been suggested as one likely mechanism underlying development and/or maintenance of pain, at least initially as a result of suboptimal tissue loading.[10,29,82] Although early work focused on this "end-organ dysfunction" (the structural and functional abnormalities within the musculoskeletal system),[67] over the past 20 years there has been an increasing realization that patients with LBP might also have changes within the central nervous system. This can be considered from 2 perspectives: first, changes in processing of nociception and pain, which have been observed throughout the nervous system, and second, changes in the structure (eg, gray matter loss) and function (eg, organization) of sensorimotor regions of the brain cortex. Moreover, clinical interventions increasingly aim to drive neuroplasticity with treatments to improve sensorimotor function and pain.

This commentary aims to provide a contemporary overview of neuroplasticity in LBP. We specifically address (1) defining neuroplasticity in relation to processing of pain and nociception in LBP, sensorimotor control of the spine, and the potential of the system to adapt; (2) structural and functional nervous system changes as they relate to nonspecific LBP and sensorimotor function; and (3) related clinical implications.

Neuroplasticity and LBP

Neuroplasticity refers to the capacity of the nervous system to undergo functional

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and structural changes modulated by activity and reinforcement.[13] Neuroplasticity is a concept that, in its literal sense, is so broad that it is almost meaningless—it may just differentiate an alive neuron or nervous system from a dead one.[42] The capacity to learn new things, generate new outputs to perform new activities, generate new thoughts, create and remember entirely new visual scenes, and create new links between previously unlinked concepts demonstrates the extraordinary capacity of the nervous system to continue changing, in an ongoing "online" manner.

This online neuroplasticity can be conceptualized in terms of collaboration and competition between networks of neuronal and nonneuronal cells in the brain or spinal cord, which collectively exert an influence through neurobiological (ie, neuroneural, neuromuscular, neuroimmune, neuroendocrine) connections.[85] These networks might be more accurately termed *neuroimmune networks* because of the involvement of neural and immune (and immune-like) cells (see Hodges et al[28] for review). The influence of any given neural network depends on the principles thought to govern its operation, including the number of cells involved (called *neuronal mass*), the precision and efficacy of the connections within the network, and top-down weighting of the network by higher-order networks.[59] Each network consists of many cells, and each cell is in many networks—the principle of multitasking.[66]

The clinical construct of LBP involves a wide range of neural networks, including those that process pain and nociception (eg, regulation of descending nociceptive modulation),[61] sensorimotor function (eg, production of motor outputs, encoding of sensory inputs[21]), and cognitions and emotions (eg, encoding beliefs and thoughts). One can conceptualize neural networks that exert their influence in the body (eg, a movement) or in consciousness (eg, a feeling) as "action" networks and those that exert their influence inside the brain as "modulation" networks (see Moseley and Butler[53] for extensive review). The constantly varying mix of influences exerted by modulation networks on action networks allows for real-time neuroplasticity, and shifts within those networks allow for short-, medium-, and long-term neuroplasticity by virtue of shifts in their influence.

Research into neuroplasticity within the context of LBP considers the domain spectrum (from features of pain and nociceptive processing to sensorimotor control), the time spectrum (from online changes in function to long-term changes in function and structure), and the complexity spectrum (whole-human research, for example, investigating how people with LBP seek health care). It also considers systems (eg, investigating the features of neural networks that subserve movement or the brain's response to a somatosensory stimulus) and subsystems (eg, in vitro studies of changes in synaptic efficacy in spinal nociceptors, brain-grounded neurons, or immune cells).

Researching different targets requires different methods and involves researchers from different fields, inevitably leading to different interpretations and terminology by which these interpretations are articulated. **FIGURE 1** aims to capture the breadth of research targets and related methods that constitute the field of neuroplasticity research in LBP. The following sections introduce 3 domains relevant for LBP, considering how research has explained each in the time and complexity spectra and the interaction between domains.

Neuroplasticity in Processing of Pain and Nociception in LBP Neuroplasticity of processing of nociception and pain is increasingly recognized as a major contributor to LBP, with changes having been observed throughout the nervous system. Increased sensitivity of primary nociceptive afferents, a phenomenon termed *peripheral sensitization*, is common in many conditions, including LBP.[75] This can involve cutaneous receptors that respond to a range of noxious stimuli and/or receptors in deep tissues, such as those potentially impacted by low back injury. Deep tissue nociceptive fibers primarily respond to noxious mechanical and chemical (eg, inflammation) stimuli.[73]

Increased sensitivity and ascending projections of neural networks in the spinal cord or impairment in the function of descending inhibitory pathways[11] (termed *central sensitization*[89]) and increased sensitivity of brain-grounded neural networks that encode for nociception enable activation of these networks during a range of innocuous events. This neuroplasticity is mediated by biological processes that are themselves influenced by cognitions about pain and other psychological phenomena.[74] These biological processes have been observed in the short term and long term, and, when comorbid with depressive symptoms, increased sensitivity is associated with poor outcome after an acute episode of LBP.[37]

Although much research has been conducted at the cellular level in animal models to understand the biological processes at multiple levels of the nervous system (see Woolf[88] for comprehensive review), research in humans has been focused at a systems level, using methods to study endogenous pain inhibitory systems (often assumed to relate to descending noxious inhibition) such as conditioned pain modulation,[11] hyperalgesia in areas remote to the back,[38] receptive fields for spinal nociceptive reflexes,[57] and temporal summation.[20] Each method provides indirect evidence of the increased sensitivity assumed to characterize the central sensitization processes observed in animals.

Importantly, enhanced sensitivity will likely affect processing of other sensory signals. Motor control is modulated by the profound neuroplasticity of nociceptive networks. For example, peripheral sensitization means that nociceptive barrage, which modulates motor systems at the spinal and supraspinal levels, can be triggered by innocuous thermal and mechanical input and the presence of products of normal muscle activity (eg, lactic

acid). Further, sensitivity of the wide range of modulatory neural networks relevant to protection will expand the breadth of innocuous situations that can modulate the motor system to include those beyond somatosensory inputs—a situation captured in contemporary understandings of central sensitization.[90]

Neuroplasticity in the Motor System as a Modulator of Spinal Motor Control From a perspective of the motor aspect of sensorimotor control of the spine, neuroplasticity research has also covered the complexity and time spectra. An enormous diversity of regions of the brain and spinal cord (and beyond) (**FIGURE 2**) is involved in the generation of motor output, and, although neuroplasticity is possible at any level, research in LBP has focused on the motor cortex. For example, a shift in the stimulus-response profile of the trunk muscles, revealed by transcranial magnetic stimulation (TMS) over the primary motor cortex while recording their activity[78,80] (**FIGURE 3**), reflects neuroplasticity at a systems level. This is also reflected by changes in TMS-associated muscle activity in response to an exercise program, also reflecting neuroplasticity at a systems level. However, the former relates to a medium- to long-term course and the latter to a short- to long-term course.[79]

In contrast, both the altered activation patterns of the trunk muscles associated with the expectation of a noxious stimulus[54] and the avoidance of particular movements or behaviors because they are perceived to be dangerous reflect neuroplasticity at the whole-person level, in real-time and the long term, respectively. Each of these changes in the motor system has the potential to alter the biomechanics of the spine. Although one might argue that this biomechanical change is the objective of motor control change, and that it provides advantage to the individual, this is not straightforward. While altered biomechanics may have short-term benefit (eg, enhanced protection from increased muscle activation[29]), they may have long-term consequences[31] as a result of chronic suboptimal loading of spine tissues and consequent activation of nociceptors, either mechanically or via the sensitizing effects of inflammation.[31] At the whole-person end of the spectrum, avoidance of certain behaviors or withdrawal from activity[30] can lead to a descending spiral of health, social, and personal issues.

Neuroplasticity in the Somatosensory System as a Modulator of Spinal Motor Control Motor outputs generally depend on sensory inputs, including somatosensory information on the po-

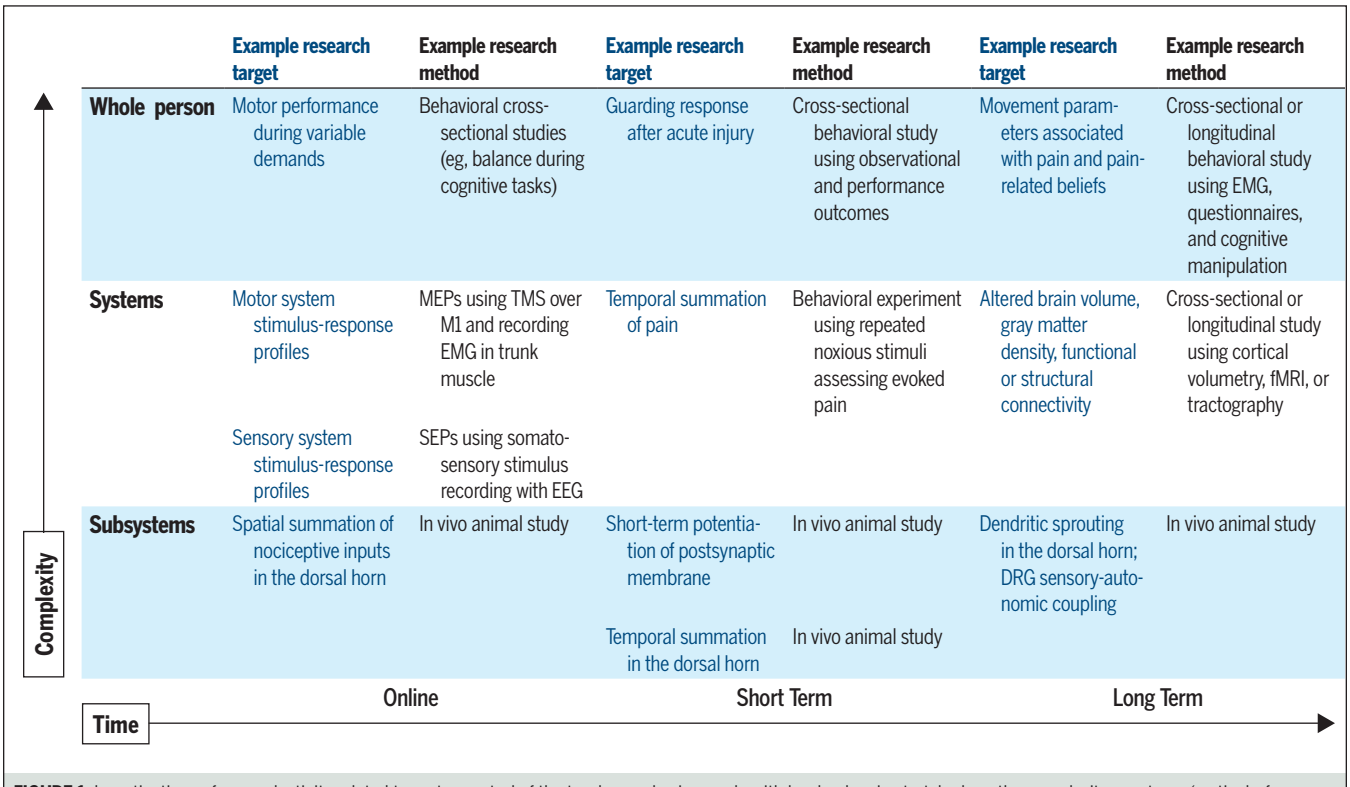

FIGURE 1. Investigations of neuroplasticity related to motor control of the trunk muscles in people with low back pain stretch along the complexity spectrum (vertical—from subsystems to systems and whole-person studies) and along the time spectrum (horizontal—from online changes in motor output to short- and long-term neuroplasticity-mediated effects). Example research targets are shown in blue font, and example research methods by which the target can be interrogated in black font. Abbreviations: DRG, dorsal root ganglia; EEG, electroencephalography; EMG, electromyography; fMRI, functional magnetic resonance imaging; M1, primary motor cortex; MEP, motor-evoked potential; SEP, somatosensory-evoked potential; TMS, transcranial magnetic stimulation.

sition and movement of the body and input from nociceptive networks as outlined above. As such, plasticity of the somatosensory system can modify motor behavior. The accuracy of interpretation of sensory input, which may be mediated by plastic change at the dorsal horn/spinal cord or higher centers (eg, primary sensory cortex excitability/organization), may change. Again, most human research has studied this at a systems level. For example, there is evidence of reduced proprioceptive acuity (see the review by Tong et al[77]), reduced weighting of proprioceptive input,[7] and higher-level interpretation of body schema,[6] without direct evidence of underlying neuroplastic processes or the involved level of the nervous system. Imaging[19] and electrophysiological[69] studies are currently providing additional insight.

Functional and Structural Brain Changes and LBP

There are multiple methods to study the function and structure of the nervous system, and each has been used to study changes or differences that are apparent between those individuals with and without LBP. As suggested above, most take a view of a small part of the complex whole that involves the interaction between pain and sensorimotor control of the spine. Each method measures different aspects of neural function and/or structure. The **TABLE** presents an overview of the information that can and cannot be gleaned from each of the measures, the pros and cons of the measures, and some examples of findings that have been reported with respect to LBP. This information is critical to interpretation of the findings presented below.

As highlighted above, it can be problematic and confusing to consider the evidence of neuroplasticity in the different parts of the brain and the sensorimotor control interaction separately, yet doing so is necessary, due to the nature of the studies that have been performed to date. The following sections separately discuss brain changes associated with pain and

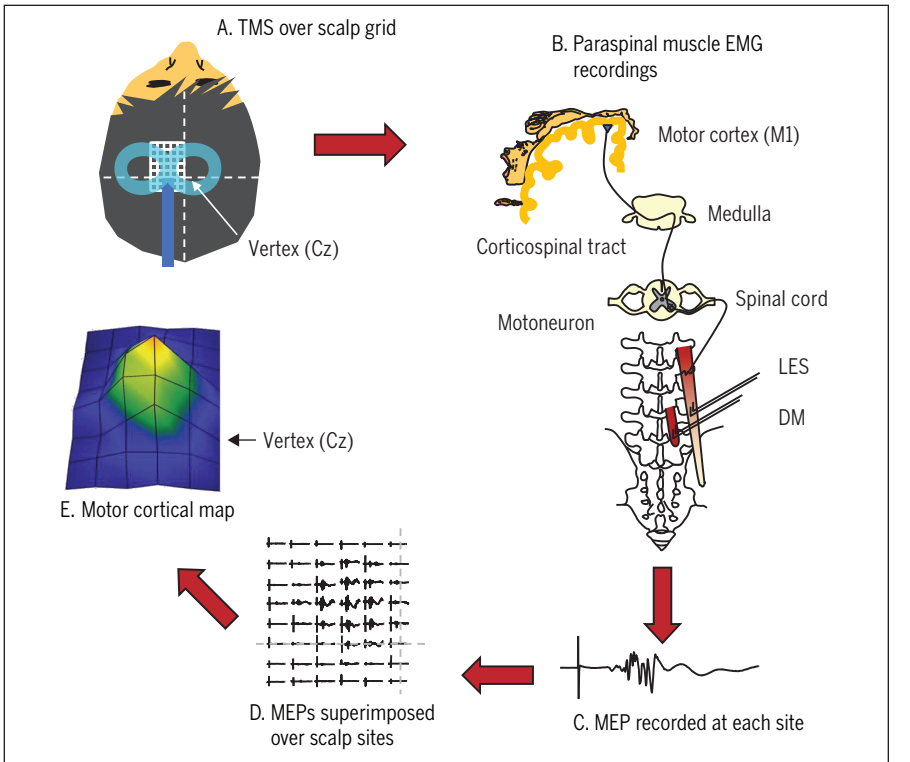

FIGURE 2. Mapping of the motor cortex using TMS. (A) Stimuli over the motor cortex excite intracortical neurons that provide synaptic input to corticospinal cells. (B) Recordings were made from the DM and LES at the L4 level. (C) The descending volley excites the spinal motoneurons and results in a MEP, mainly in the contralateral muscles. (D) The MEPs were recorded in both muscles from stimuli applied at each point on the grid, placed over the scalp and aligned to the vertex (Cz). (E) A 3-D map of MEP amplitude was created for each muscle from the individual and then group data. Adapted with permission from Tsao et al.[78] Abbreviations: DM, short/deep fibers of the multifidus; EMG, electromyography; LES, longissimus erector spinae; M1, primary motor cortex; MEP, motor-evoked potential; TMS, transcranial magnetic stimulation.

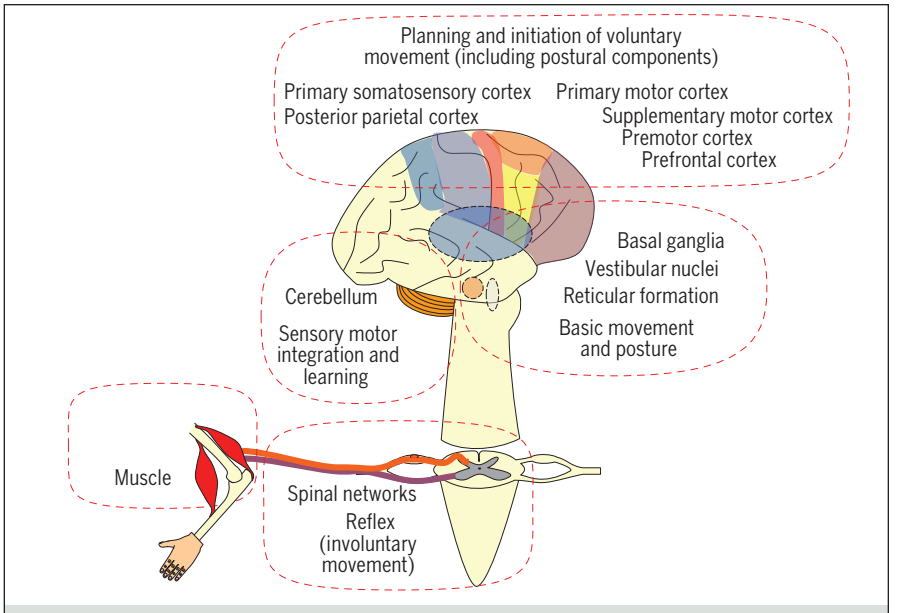

FIGURE 3. Areas of the brain, spinal cord, and peripheral nervous system involved in sensorimotor control.

TABLE Methods Used to Study Neuroplasticity in Low Back Pain

Method	Interpretation	Pros	Cons	Examples in LBP
Imaging				
fMRI	Measure of changes in BOLD signal related to CBF Interpreted as changes in regional brain activation Measures can be • At rest • Event-related activation associated with a stimulus or action (voluntary motor task, cognitive task, sensory input [nociceptive/nonnociceptive]) • Of functional and effective connectivity between brain regions in resting state or during task	Good spatial resolution	Relatively poor temporal resolution BOLD provides indirect measure of neural activation fMRI requires measures made in lying with a fixed head position, which limits investigation of functional tasks Analysis depends on identification of brain regions in separate images and involves substantial processing of data, which can impact results and interpretation Equipment for experimental tasks needs to be fMRI safe and compatible, which may limit possibilities	Reorganization of lumbar spine representation in the secondary somatosensory cortex is based on lumbar pressure stimulus or back muscle vibration (event-related activation)[23,24,33] Difference in functional connectivity between brain regions during motor imagery of daily activities and walking (task-related functional connectivity)[83]
Structural MRI	Measure of volume, thickness, density, and surface area of brain regions (eg, gray matter)	Good spatial resolution	Unclear which changes account for differences in volume (eg, cell number, water content, etc) Analysis can be affected by assumptions related to selection of regions, and preprocessing can affect the results	Decreased prefrontal and thalamic gray matter density in chronic LBP[3] Increased cortical thickness in the primary somatosensory cortex region is somatotopically associated with the lower back region in patients with LBP[39,64]
Diffusion tensor imaging	Measure of white matter microstructural changes with pathology Measure of structural connectivity between regions by analysis of water movement (white matter)	...	Measures can be affected by orientation of fibers (based on the assumption that fibers have a unique orientation, which is represented by the tensor's eigenvector. However, this is not valid for crossing fibers)	Microstructural changes in white matter are correlated with poor proprioception in LBP[62,64] Decreased structural connectivity is correlated with decreased performance of a postural task in LBP[62,65]
Functional near-infrared spectroscopy	Measure of brain oxygenation, which is interpreted to infer neural activity	Good temporal resolution Can be measured in any position, allowing for more functional tasks to be studied More robust against motion artifacts than fMRI	Poor spatial resolution Cannot measure brain activity more than 4 cm deep Difficult to interpret	Hemodynamic changes and oxygenation in the somatosensory association area and primary somatosensory cortex during painful and nonpainful pressure stimulus: no significant differences between LBP and healthy controls[84]
PET	Measures cell activity and populations by measurement of radioactively labeled molecules that bind to specific cells or cells in specific states	Good spatial resolution	Must be combined with brain imaging (eg, MRI) to interpret location Specificity of some molecules to the target cells varies Invasive Poor temporal resolution	Somatotopic organization of activated glial cells in chronic LBP[44]

Table continues on page 407.

nociceptive processing, the motor system, and the somatosensory system. Although these sections provide a way to compartmentalize information, they are not to be interpreted as competing theories of the importance of neuroplasticity in pain, but rather as different elements of the same whole. It is necessary to consider the extensive overlap between domains (eg, impact of central sensitization on motor output), which is highlighted below.

Functional and Structural Brain Changes Related to Pain and Nociceptive Processing From a perspective of pain and nociceptive processing, electroencephalography (EEG) studies show that patients with chronic LBP have larger cortical responses to noxious stimuli, including an enhanced N80 component of EEG, which is thought to reflect sensory cortex activation.[14] Behavioral studies

TABLE Methods Used to Study Neuroplasticity in Low Back Pain (continued)

Method	Interpretation	Pros	Cons	Examples in LBP
Arterial spin labeling magnetic resonance perfusion	Measures CBF by using magnetically labeled arterial blood water protons as an endogenous tracer • During resting state or during a stimulus • Can be used to investigate functional connectivity	Noninvasive as compared to PET Allows one to absolutely quantify tissue perfusion as compared to PET	Regional CBF is an indirect measure of neuronal activity Highly sensitive to head motion Signal-to-noise ratio inherently low, which increases total scan time	Physical maneuvers that induce pain are paralleled by changes in resting-state connectivity within default-mode network[45] Changes in ongoing chronic pain are associated with increases in regional CBF in, for example, the somatosensory, frontal, and insular cortices[87]
Electrophysiology				
TMS	Measures excitability and organization (eg, motor cortex maps) of motor regions of the cortex Paired-pulse methods investigate interaction between regions (interhemispheric) and excitability of intracortical networks	Good temporal resolution	Measures excitability of the corticomotor pathway, not only the cortex. Interpretation of changes at the cortex requires combination with other methods (eg, corticomedullary-evoked potentials to assess changes at the motoneuron) Cannot detect activation Poor spatial resolution Interpretation of responses of legs and trunk muscles is complicated by location near the brain midline	Shifted location of representation of the transversus abdominis on the motor cortex in LBP[80] Changes in intracortical inhibition in chronic LBP[48]
EEG	Provides measure of general brain activity (interpreted in relation to activity in different frequency bands that are thought to subserve different functions), event-related potentials (change in activation related to specific event), and contingent negative variation (change in brain activity after a warning stimulus provided before a stimulus to perform a task)	Good temporal resolution Can be used in functional contexts/tasks	Interpretation of spatial location of activity is complex and requires complex mathematical processing Analysis can be complex	Altered late-phase cortical processing of postural perturbations in LBP[36]
SEPs	Measures excitability and processing of sensory inputs Different components of the response are interpreted with respect to different brain regions and different processing events	Good temporal resolution	Multiple stimuli are required to capture the SEP, and this may affect the response to this and other measures	Functional reorganization in both the somatosensory and the motor system in chronic LBP[70]

Abbreviations: BOLD, blood oxygenation level dependent; CBF, cerebral blood flow; EEG, electroencephalography; fMRI, functional magnetic resonance imaging; LBP, low back pain; MRI, magnetic resonance imaging; PET, positron emission tomography; SEP, somatosensory-evoked potential; TMS, transcranial magnetic stimulation.

show allodynia and hyperalgesia to stimuli applied to the lumbar spine in people with LBP[22] and modified nociceptive reflexes. Further, some,[11] but not all,[38,47] studies show impairment of conditioned pain modulation in chronic or acute LBP, which suggests impaired descending inhibition as a feature of central sensitization. Functional magnetic resonance imaging (MRI) studies show that, in response to a noxious stimulus, patients with chronic LBP have lower regional cerebral blood flow in the periaqueductal gray and a higher increase in activation in the primary and secondary somatosensory cortices and the lateral orbitofrontal cortex. These findings suggest dysfunction in the descending inhibitory system subserved by the periaqueductal gray.[22]

Structural MRI studies suggest systematic differences between individuals with and without LBP, for example, in the dorsolateral prefrontal cortex, temporal lobes, insula, primary somatosensory cortex, corpus callosum, and internal capsule. Results of functional connectivity studies during rest imply

enhanced activation of the medial prefrontal cortex, cingulate cortex, amygdala, insula, and sensorimotor integration regions, together with disrupted functional connectivity in the default-mode network (a large-scale network of brain regions that maintain the brain's resting state and are involved in neurological functions that include the neural basis of self).[1,5,26,27,41] More specifically, results of imaging studies showing functional connectivity between the nucleus accumbens and medial prefrontal cortex[5] and structural connectivity between brain regions (white matter fractional anisotropy)[46] suggest that such connectivity patterns may be risk factors for nonrecovery. These findings add to the growing evidence of the critical role the corticolimbic system plays in the modulation of acute pain and mediation of chronic pain.[58] The corticolimbic system is central to reward and motivated behavior. Although primarily linked to modified sensory processing, this, too, cannot be separated from sensorimotor function, as motor behaviors will link with reward and punishment through relief or provocation of pain.

Furthermore, chronic pain is often characterized by predominance of the affective/emotional dimensions of pain (its "unpleasantness") over the sensory discriminative dimensions of pain.[53] Imaging studies corroborate that observation, as the pattern of brain activation during pain seems to shift toward affective/emotional relevant brain areas as LBP persists.[2,4] This can be conceptualized in terms of increased influence of neural networks that encode for unpleasantness and decreased influence of neural networks that encode for intensity and sensory features.

In summary, changes in function and structure are present throughout the nervous system and affect the processing of nociception and pain. Each has potential to change the interpretation of pain, the interpretation of somatosensory inputs, and the motor output. This result is considered in the following sections.

Functional and Structural Brain Changes Related to the Motor System Some neuroplastic changes have been interpreted from the perspective of motor control of the spine, which may affect tissue loading and motor patterns in the context of motor output of the neural networks associated with pain. Transcranial magnetic stimulation has been used to study the organization and neural network properties of the regions of the motor cortex associated with control of specific trunk muscles. These studies have found that in many individuals with chronic LBP, the area of peak excitability of cortical inputs to the deep abdominal muscles[80] is in a different location (more posterolateral) and there is greater overlap of the separate representations of longer (eg, longissimus) and shorter (eg, multifidus) muscles of the back (**FIGURE 4**).[71,78] In terms of neural networks, one can conceptualize these differences in 2 ways: (1) as a systematic difference in which primary motor cortex cells are involved in the action neural networks that drive certain trunk muscles,[80] and (2) as neural networks that drive specific muscles becoming less specific to those muscles,[78] a situation that implies reduced ability to differentially activate separate muscles.

An association has been identified between these differences in cortical organization and the duration and severity of pain[71] and features of motor behavior, such as the timing of recruitment of muscles in a postural challenge[80] and spine movement.[18] These latter observations have led to the hypothesis of a link with tissue loading. An alternative view is that the changes might reflect modified function of the system, which is not linked to pain by virtue of effects on tissue loading, but is nonetheless relevant as an expression of changed interaction between modulation (such as those related to altered afferent input or pain cognitions) and action networks.

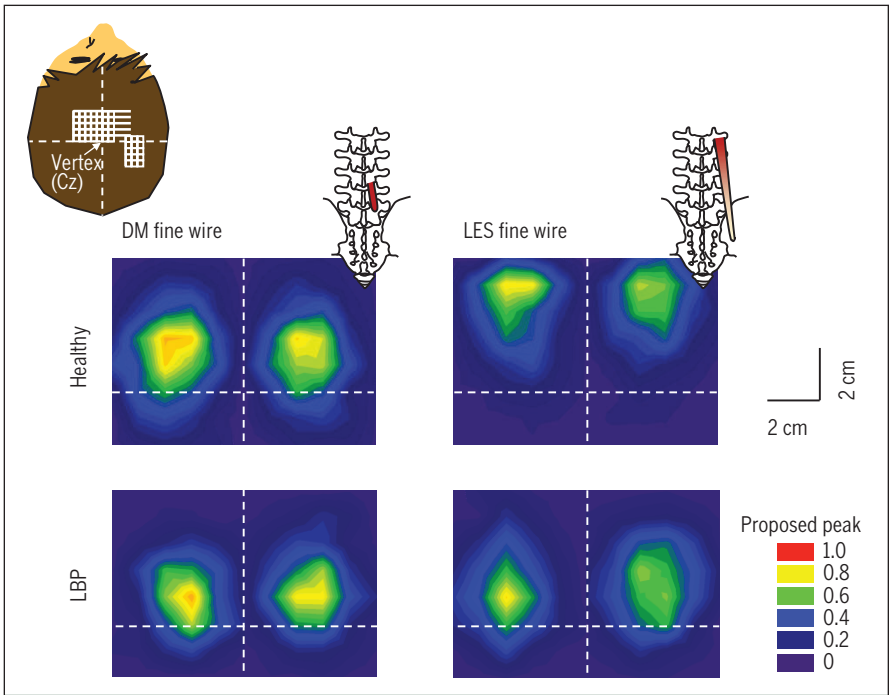

FIGURE 4. Reorganization of the motor cortex in LBP. Normalized maps of the left and right motor cortex for the DM (left panels) and LES (right panels) for healthy (top panels) and LBP groups (bottom panels). Dotted lines denote sagittal and frontal planes, intersecting at the vertex (Cz). Note that the motor cortical map for the DM overlaps that for the LES in the LBP group, whereas the DM is located posteriorly compared to the LES in the healthy group. Adapted with permission from Tsao et al.[78] Abbreviations: DM, short/deep fibers of the multifidus; LBP, low back pain; LES, longissimus erector spinae.

Evidence of increased responsiveness of corticomotor inputs to the bracing strategy (eg, superficial abdominal muscles[81]) and decreased inputs to muscles involved in subtle fine-tuning of spine control (eg, the transversus abdominis[81]) again raises the possibility of suboptimal tissue loading. One issue that remains to be resolved is whether these effects of neuroplasticity offer behavioral advantage akin to a shift in strategy to accommodate altered demands or incur behavioral disadvantage akin to a breakdown in the system.[31]

Changes in the response to TMS can be difficult to interpret because the response amplitude depends on the excitability of the cells in the cortex and those in the spinal cord (ie, motoneuron) (**FIGURE 2**). For instance, changes in threshold to evoke a response in the erector spinae in someone with LBP do not enable differentiation of changes at the spinal cord, the cortex, or both.[76] It is possible to evaluate excitability at the cortex using pairs of TMS pulses. Using these methods, intracortical inhibition and facilitation of corticospinal inputs to the abdominal muscles in individuals with LBP suggest modification of primary motor cortex synaptic function.[48] These observations confirm cortical involvement, but do not yet provide clear interpretation.

Recent work (reviewed in detail in Hodges et al[28]) also highlights novel changes in glial cell activity in motor regions of the brain.[44] Glial cells can influence neuronal activation in multiple ways. Increased activation of microglia in the somatotopically organized back and leg areas of the motor cortex has been identified,[44] but the functional consequences are not yet clear.

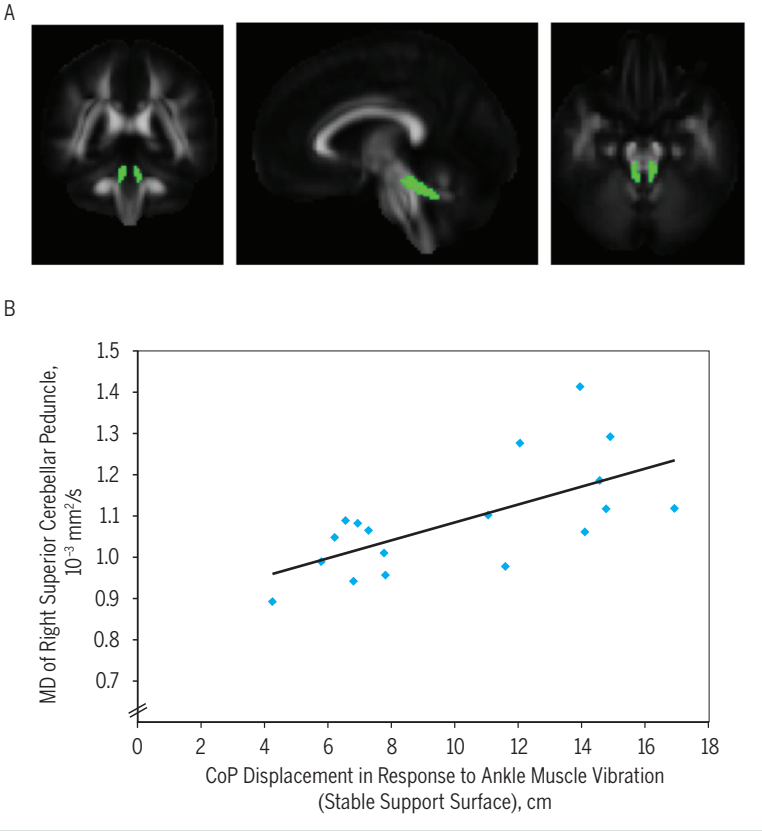

FIGURE 5. Association between white matter microstructure and proprioceptive weighting for postural control in individuals with nonspecific low back pain. (A) Visualization of the right and left superior cerebellar peduncle. (B) Scatter plot of the association between MD of the right superior cerebellar peduncle and the CoP displacement in response to ankle muscle vibration while standing on a stable support surface in individuals with nonspecific low back pain (r = 0.65, P = .003). Adapted with permission from Pijnenburg[62] andPijnenburg et al.[64] Abbreviations: CoP, center of pressure; MD, mean diffusivity.

Functional and Structural Brain Changes Related to the Somatosensory System In LBP, numerous observations have been made using MRI with respect to sensorimotor function. First, a relation between reduced white matter integrity (which has been interpreted to imply modified connectivity) of the superior cerebellar peduncle (a zone of relay for proprioceptive input to higher centers) and reduced utilization of proprioceptive signals from the back for standing postural control have been observed (**FIGURE 5**),[62,64] which may mean that information on back position/movement is ignored. Second, adding further support to this observation, functional MRI of brain regions involved in higher-order processing of muscle spindle input (specific somatosensory input) reveals less activity in response to back muscle vibration, and greater activation in response to ankle muscle vibration, in those with LBP than in those without LBP.[23,25] Third, the sensorimotor resting-state network is significantly reorganized, which may lead to modified utility of sensory signals from the back. Functional connectivity between brain areas related to the integration and processing of sensory and motor signals for movement is lower.[63]

Again, each of these differences/changes could imply impaired capacity to control movement (eg, lower functional connectivity of the sensorimotor network correlates with slower performance of a dynamic sensorimotor task, such as 5-time sit-to-stand-to-sit)[63] or a different interpretation related to competition between neural networks (those that serve sensorimotor function are losing influence, whereas those that serve pain and protection are gaining influence). Relevant to this is the observation that patients with recurrent LBP show greater cortical thickness than healthy controls in brain regions involved in cognitive regulation of

pain, and they also show a correlation between cortical thickening and pain intensity.[8] Again demonstrating the difficulty of disentangling the sensory processing and motor control aspects of neuroplasticity, there is a relationship between impaired sit-to-stand-to-sit performance and decreased cortical thickness of the rostral anterior cingulate cortex,[8] as well as correlations between regional changes in cortical thickness and gray matter volume and clinical tests of movement control, lumbopelvic control, and individual contraction of the transversus abdominis and multifidus muscles.[40]

Akin to the studies of motor cortex maps, several methods have been used to investigate the cortical organization of sensory cortices. Investigation of somatosensory-evoked potentials in response to acute noxious inputs shows modification of specific components of the response, including those interpreted to imply processing in the secondary somatosensory cortex and the anterior cingulate cortex, which are thought to reflect the affective/emotional components of the pain experience.[69] Note that central sensitization at multiple levels of the nervous system would lead to increased sensitivity to noxious inputs, leading to allodynia/hyperalgesia.

Electroencephalography reveals a greater area of cortical activity in association with postural perturbation from arm movements,[35] and greater amplitude of the late positive EEG response to unexpected postural perturbation that correlates with both the amplitude of displacement of the body's center of mass and the amount of catastrophizing.[36] The location of peak primary sensory cortex response to nonnoxious and noxious tactile stimulation to the back is expanded and shifted in people with chronic LBP (**FIGURE 6**).[19] Nonpainful pressure applied to individual lumbar vertebrae[33] evokes a secondary somatosensory cortex response that is smaller in those with LBP than it is in those without.[33] Some of these changes correlated with chronicity.[19] Functional MRI studies using mental imagery of motor actions show reduced brain activation within the left supplementary motor area and the right superior temporal gyrus and sulcus (areas associated with motor imagery), but diffuse and nonspecific enhancement of functional connectivity between motor imagery–associated networks, in patients with chronic LBP as compared to healthy controls.[83]

As motor performance was not changed, this result may be interpreted as compromised sensorimotor system function requiring greater neural involvement to complete the task or as central sensitization characterized by hyperexcitability.[83] Each of these differences between individuals with and without LBP might offer behavioral advantage akin to a revised strategy to promote protection, or a breakdown of the system. Either could have negative consequences at a tissue-loading level.

There is clearly extensive evidence of modified nervous system structure and behavior in people with LBP. Much of this evidence implicates sensory and motor processes associated with control of the spine and spine loading. However, this is not the only possible interpretation, and much can be drawn from the available literature by considering that the processes associated with motor control of the spine and sensory processing are parts of a whole that interact in the generation and maintenance of pain through multiple mechanisms.

Clinical Implications

Just as neuroplasticity enables mechanisms that change neural function and structure to generate and maintain pain, it also enables the capacity to restore the system to resolve or improve LBP. The integration of sensory and motor processes raises the possibility of several potential targets for restoring normal conditions. The following sections highlight some innovations for treatment of LBP that consider neuroplasticity.

Motor Control Training to Change Sensorimotor Neuroplasticity From the perspective of motor control of the spine, training that targets motor skill learning has been shown to normalize the location of primary motor cortex networks that are involved in activating specific trunk muscles, whereas general exercise such as walking does not (**FIGURE 7**).[79] These interventions also improve pain and disability, particularly with specific subgroups of patients.[68] Noninvasive brain stimulation has been suggested as an option to facilitate the recovery of organization of the motor cortex map, with positive preliminary results.[72] However, more recent work highlights that when applied to people with LBP, the neural circuits targeted with noninvasive brain treatments do not respond in the same way as they do in pain-free individuals.[70] Further work is required to understand how best to utilize these approaches.

Behavioral Approaches: Extinction Training Based on the evidence indicating modified balance between affective and sensory neural networks, there are preliminary findings that this balance can be normalized in people with LBP by a program of extinction training.[16] Extinction training focuses on the elimination of pain-related behaviors and the increase of healthy behaviors. It includes

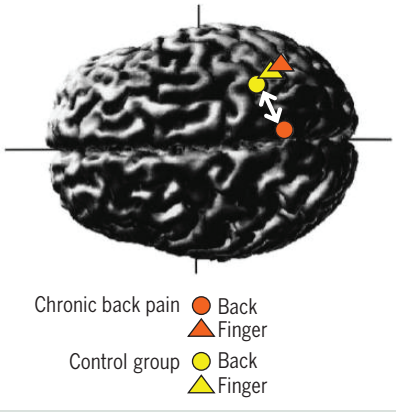

FIGURE 6. Reorganization of the somatosensory cortex in low back pain. Average location of the finger and back dipole was recorded by a 37-channel biomagnetometer from the hemisphere contralateral to the site of stimulation in the 70-millisecond range for patients with chronic back pain and healthy controls. Locations are superimposed schematically on a magnetic resonance image. Adapted with permission from Flor et al.[19]

video feedback of expressions of pain as well as training of pain-incompatible behaviors, increase of work-related and social activities, physical therapy, and medication management. The patients engage in role playing to reduce pain behaviors and increase healthy behaviors.

Sensory Discrimination Training A disrupted body image in patients with chronic LBP in the area of usual pain suggests the need for treatment options that focus on the reinstatement of normal body image or that strengthen body perception.[51] Until now, limited research has focused on treatments targeting the distorted body image often seen in individuals with chronic musculoskeletal pain. However, recently it has been shown that when patients with LBP are provided with visual real-time feedback of their own back during experimental painful stimulation at this site, the perceived intensity of acute painful stimuli applied to this site is reduced.[17] This approach works not only for acute experimental pain, but also for the clinically more relevant movement-induced pain.

Further, seeing the back during repeated lumbar spine movements reduces movement-evoked pain, at least in the short term.[86] Even habitual pain has been reduced by visual real-time feedback of the site of chronic pain,[15] and there is first evidence that treatments such as massage could be enhanced with this method.[43] The next challenge will be to investigate, in larger samples, whether pain treatment such as manual therapy or extinction training can be boosted by application of real-time feedback.

Cognitive Training Approaches Treatment of patients with LBP may also focus not on distraction and analgesia, but rather on precisely encoding the painful event by reducing the influence of protective neural networks through eliminating danger cues, differentiating safe cues, and increasing the influence of neural networks that encode performance of a task.[56,85] These initiatives (eg, graded motor imagery) are in their early days and remain to be fully tested but, importantly, have been developed according to the principles of neuroplasticity and the notion that there are many potential avenues by which to access the system.

Neuroplastic changes may be addressed by top-down cognitive-based interventions (such as education, cognitive behavioral therapy, motor imagery, specific motor training) and bottom-up physical interventions (such as peripheral sensory stimulation,[49] exercise, and manual therapy). An integrated contemporary neuroscience and clinical approach may combine intensive pain neuroscience education with cognition-targeted sensorimotor control training.[32,52,55,60]

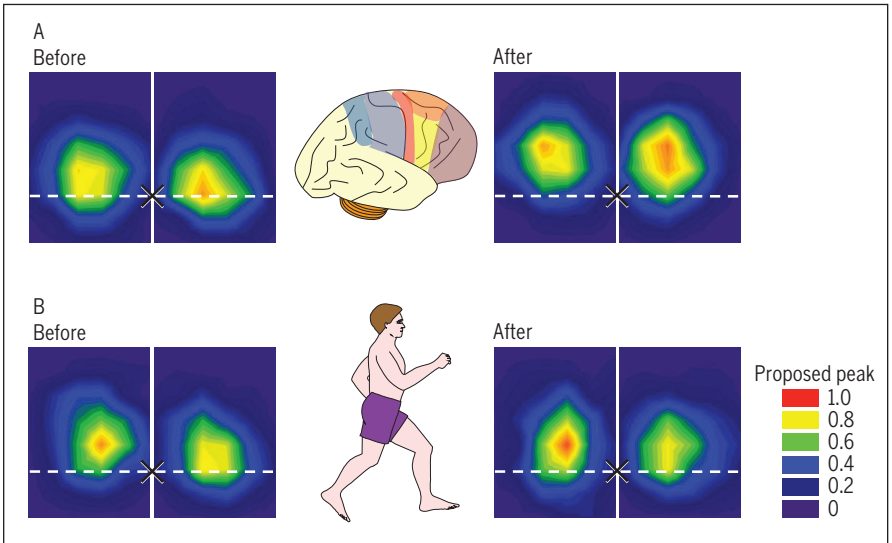

FIGURE 7. Effect of training on organization of the motor cortex in low back pain. Normalized transcranial magnetic stimulation maps of the transversus abdominis representation at the motor cortex before and after (A) skilled motor control training and (B) walking exercise are displayed. Dotted lines represent the frontal and sagittal planes and intersect at the vertex. Note that skilled motor training, but not walking training, induced a shift in the motor cortex map toward the location observed in pain-free individuals. Adapted with permission from Tsao et al.[79]

Summary

An important consideration is that, like most clinical features in LBP, there is considerable variation among individuals, and no single finding/mechanism revealed by imaging and electrophysiological methods is present in every case. As for other treatments, it is unlikely that any one treatment that targets neuroplastic changes in the sensorimotor system is likely to be effective for everyone with LBP. It is also critical to consider the importance of identifying aberrant pain mechanisms and choosing interventions that address the mechanism.[9] Overall, the complexity of assessment methods has generally limited the sample size used for studies of neuroplasticity, and larger studies, perhaps with alternative methods, are required.

CONCLUSION

People with recurrent and chronic LBP are different from those without LBP in several markers of the nervous system's function and structure as they relate to sensory and motor systems. Addressing these neuroplastic changes in a targeted manner may lead to better outcomes in patients with recurrent and chronic LBP, but this may require a combination of bottom-up and top-down approaches.

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