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Perspective

Linking Pain and Motor Control: Conceptualization of Movement Deficits in Patients With Painful Conditions

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Abstract

When people experience or expect pain, they move differently. Pain-altered movement strategies, collectively described here as pain-related movement dysfunction (PRMD), may persist well after pain resolves and, ultimately, may result in altered kinematics and kinetics, future reinjury, and disability. Although PRMD may manifest as abnormal movements that are often evident in clinical assessment, the underlying mechanisms are complex, engaging sensory-perceptual, cognitive, psychological, and motor processes. Motor control theories provide a conceptual framework to determine, assess, and target processes that contribute to normal and abnormal movement and thus are important for physical therapy and rehabilitation practice. Contemporary understanding of motor control has evolved from reflex-based understanding to a more complex task-dependent interaction between cognitive and motor systems, each with distinct neuroanatomic substrates. Though experts have recognized the importance of motor control in the management of painful conditions, there is no comprehensive framework that explicates the processes engaged in the control of goal-directed actions, particularly in the presence of pain. This Perspective outlines sensory-perceptual, cognitive, psychological, and motor processes in the contemporary model of motor control, describing the neural substrates underlying each process and highlighting how pain and anticipation of pain influence motor control processes and consequently contribute to PRMD. Finally, potential lines of future inquiry—grounded in the contemporary model of motor control—are outlined to advance understanding and improve the assessment and treatment of PRMD.

Impact. This Perspective proposes that approaching PRMD from a contemporary motor control perspective will uncover key mechanisms, identify treatment targets, inform assessments, and innovate treatments across sensory-perceptual, cognitive, and motor domains, all of which have the potential to improve movement and functional outcomes in patients with painful conditions.

Keywords: Motor Control and Motor Learning, Movement, Pain

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Introduction

Pain, a complex experience in itself, is further complicated by its reciprocal interactions with movement.[1–5] In the presence or anticipation of pain, people move differently to minimize or avoid pain-causing or exacerbating movements.[6,7] During an acute episode of pain, adaptive movements may be beneficial; however, these adaptations may persist beyond the duration of acute pain.[8,9] Over the long term, such adaptive movements often lead to abnormal loading of tissues and reinjury and, as a result, perpetuate pain.[8,10,11] Pain-related movement dysfunction (PRMD) describes long-term maladaptive motor behaviors in the presence of chronic pain, anticipation of pain, or that persist as a habit despite relief from pain. PRMD, as conceptualized here, is not a symptom of specific painful conditions but instead learned behaviors that may manifest as subtle changes in muscle activity to a complete avoidance of activity and anything in between.[12–14] Abnormal movement patterns across multiple pain diagnoses have been described in detail[12,15]; however, scarce attention has been paid to the nature of the contributing motor control processes, including their underlying neuroanatomic and physiologic mechanisms, that contribute to "learning" abnormal movement patterns in response to pain.

Rehabilitation interventions to remediate PRMD exploit motor control processes. For example, impairment remediation (eg, strength training[16,17]), functional training,[18] and neuromuscular facilitation[19–21] predominantly target motor execution processes crucial to motor control and learning. However, the development of such interventions arose either from traditional models of motor control or through clinical exploration and reflection (which we believe are important). For example, proprioceptive neuromuscular facilitation techniques employed to improve movement performance in patients with chronic low back pain[22,23] have their roots in the reflex-hierarchical theory.[24] Historic motor control theories and interventions grounded in them often overlook the complex interaction between sensory-perceptual, cognitive, psychological, and motor systems that we now know are crucial in the contemporary understanding of motor control. Though the limitation of historic motor control theories cannot be denied, movement science, in the last few decades, has advanced from an early focus on reflexes and reactions at the level of the spinal cord and brainstem to a more complex interaction between task, individual, and environment that engages complex neural networks throughout the nervous system.[25,26] Pain effects on movement should be reconsidered within the contemporary understanding of motor control to better explain mechanisms of effective interventions and design more effective interventions.

Over the past decade, interest in motor control concepts to explain pain-induced changes in movement has surged. Hodges proposed a theory for adaptation to pain of changes in multiple levels of the nervous system that lead to redistribution of muscle activity and altered mechanical load.[1] More recently, Butera and colleagues proposed a new model that, for the first time, called for an integration of sensory, motor, and psychological factors involved in pain processing and motor adaptation.[3] Although both of these models have advanced our view to include neural control of movement in painful conditions, neither of them outlines the specific sensory-perceptual, cognitive, and motor processes that sequentially evolve in distinct neural networks to plan, execute, and adapt goal-directed actions. Contemporary understanding of motor control includes a set of relatively well-defined sensory-perceptual, cognitive, psychological, and motor processes, each with putative neural substrates, and underlies specific aspects of goal-directed movements, including action selection, planning, execution, and adaptation. With a set of delineated processes at hand, we can more systematically study the effects of pain on goal-directed actions, test and design rehabilitation interventions grounded in contemporary theory, and, consequently, improve patient outcomes.

This Perspective describes PRMD through the lens of motor control theories to provide rehabilitation clinicians and scientists with a contemporary account of motor control processes and putative neuroanatomical substrates that implement complex adaptive motor behaviors. First, we distinguish between nociception and pain as they relate to the control of movement. We then present a novel framework, the contemporary distributed model of motor control, that is grounded in the current understanding of sensory-perceptual, cognitive, and motor processes,[27–30] and corresponding neuroanatomic substrates that support goal-directed actions. Throughout the paper, we summarize recent pain research to elucidate how pain and/or anticipation of pain affects the neurobehavioral processes within the contemporary distributed model of motor control. To conclude, we recommend future research directions that may be necessary to better understand, characterize, and treat PRMD. Our global position is that conceptualizing the effects of pain using a systematic theory-driven lens of contemporary motor control will help outline neural and behavioral mechanisms that contribute to pain-altered movement patterns, shed light on individual differences in motor adaptations to pain, identify appropriate rehabilitation treatment targets, and improve clinical outcomes.

Nociception and Pain: Transmission and Processing

Nociception and pain, though related, are distinct phenomena.[14] Nociception refers to the peripheral and central transmission and processing of sensory information generated by the activation of nociceptors.[14] In contrast, pain is characterized as an unpleasant sensory and emotional experience that may or may not be associated with actual or potential tissue damage.[14,31,32] Sensory information from free nerve endings is relayed by the spinothalamic pathway to the primary somatosensory cortex for sensation and localization of nociception.[33] In addition to the spinothalamic pathway, nociceptive information is also relayed by the spino-reticulothalamic, spinomesencephalic, and spino-parabrachial-amygdala pathways to multiple cortical and subcortical areas such as the secondary somatosensory cortex, reticular formation, amygdala, insula, anterior cingulate cortex, and prefrontal cortex.[31,33] Processing at each of the cortical and subcortical levels, and subsequent interaction between nociceptive substrates and those that subserve emotions, cognition, and memory, together occasion the perception of pain. Nociception, then, describes sensation arising from activation of nociceptors, whereas pain describes a subjective perception modulated by patient-specific factors (eg, one's physiological and psychological state[34]).

The distinction between nociception and pain is relevant for the control of movement because each may have distinct, yet interacting influences on different levels of the neuraxis. Nociceptive pathways may preferentially interact with spinal segmental and multisegmental levels to control reflexive components of movement.[35,36] In contrast, pain may predominantly modulate motor control by influencing the higher-order cognitive, perceptual, and motor areas of the brain such as the prefrontal and motor cortices.[31] Although it is difficult to clearly delineate the precise neural border for the influence of pain and nociception, it is crucial to understand the influence of nociception and pain on the motor control processes and neural substrates involved in goal-directed actions. In the next section, we describe the contemporary model of motor control, delineate distinct sensory-perceptual, cognitive, psychological, and motor processes that contribute to goal-directed actions, and discuss the implications of pain on these processes.

Contemporary Model of Motor Control and Adaptation

Broadly speaking, motor control involves 2 mechanisms: feedforward and feedback control.[37,38] Feedforward (or anticipatory) control occurs prior to action onset and includes selection of task-goal, action, and planning parameters.[38] For example, when Lebron James prepares to shoot a free throw (task-goal), he selects the most appropriate action and assigns specific parameters (ie, force, timing) to that action—all before executing it. If feedforward control is impaired, a patient may demonstrate impaired action selection, or deficient timing and/or amplitude of muscle activation, and slower motor performance.[37,39] Feedback control, in contrast, uses sensory information about the executed action to correct the ongoing movements (online correction) and update the feedforward controller for future actions.[40] Reliance on sensory feedback and consequent online correction requires processing at spinal reflexive and supraspinal pathways.[41] Such continual response takes longer processing times and is mainly possible for slower actions that rely on feedback about the effect of action on ongoing motor performance.[38,42] Impaired feedback processes may reflexively modulate muscle activation, minimize correction of action over its course, or alter subsequent movements by changing the nature of feedforward control.[38]

The Table out lines the serial processes in motor control of goal-directed actions, underlying systems and neural substrates, and behavioral effects of pain on each of the processes. Figure 1 illustrates pain and nociception-related deficits in distinct sensory-perceptual, cognitive, psychological, and motor systems that underlie the behavioral impairments observed for each process in the contemporary model of motor control.

Sensing and Perception

Goal-directed actions rely on our ability to quickly gather information about the environment and task through multiple sensory systems. The exteroceptive information about the task and environment is integrated with interoceptive information (eg, proprioception) and the internal representation of body anthropometrics (eg, body schema) to help plan upcoming actions.[30] Primary sensory cortices (somatosensory, visual, auditory) and secondary sensory cortices implement localization and perception of sensory information. Unimodal and multimodal association cortices (parietal association cortex) help integrate varied sensory inputs to allow for recognition and planning necessary for action.[43,44] For example, a basketball player needs to gather and integrate visual information about the distance from the hoop, auditory information of play calls from coaches, and proprioceptive information about his or her body to decide about a jump shot attempt.

Pain Effects on Sensing and Perception

Musculoskeletal injury and surgeries that activate nociceptors often impair mechanoreceptor function and transmission, further blunting proprioception.[45–48] Chronic pain is also associated with reorganization of sensory cortices,[49,50] which likely interferes with discrimination, processing, and integration of tactile[51,52] and proprioceptive[53–56] sensations and, in severe cases, alters body schema and kinesthesia.[57,58] Further, processing of painful stimuli (ie, nociception) may also be altered in primary somatosensory and association cortex that may increase pain sensitivity.[59] Impaired sensory processing paired with altered body schema and kinesthesia contributes to deficits in motor coordination[60] and control.[61,62]

Assessment of sensations, discriminatory sensations in particular, may help to identify abnormal sensory processing and integration. Interventions such as sensory discrimination training have yielded less consistent evidence in improving pain perception in painful conditions.[63,64] Similarly, visual imagery, mirror therapy, and virtual reality have been successfully used for pain relief[65–68]; however, relatively fewer studies[68,69] have examined the effects of sensory-perceptual training on motor performance.

Goal Selection and Intent

Accomplishing a purposeful movement requires selecting a task-goal consistent with intent and aimed toward maximal success.[27] For example, a basketball player, when surveying the defense, may choose to pass the ball to an open teammate or try to score. Successful choice of task-goal requires attentive observation of environment and identification of the salient, meaningful goals that will maximize success. Multiple higher-order cognitive processes such as attention, motivation, and decision-making converge to support goal selection that complies with the rules of the environment and task.[27,70,71] Besides cognitive processes, psychological states such as emotional response and pain catastrophizing, also influence goal selection.[72] Prefrontal and parietal-occipital association cortices, including their interactions with the anterior cingulate cortex (limbic system) and the striatum, implement task-goals based on the performer's intent and values.[71,73–75]

Pain Effects on Intent and Goal Selection

Pain and/or anticipation of pain influence higher-order cognitive processes of attention,[76] motivation[77] and decision-making,[78,79] and psychological states, thus affecting the selection of appropriate action goals. In the cognitive domain, pain may redirect individuals' attentional resources toward an internal focus (ie, focus on joint or joint movement),[80,81] thus impairing their ability to attend to environmental cues for selection of task-goals. Pain or anticipation of pain, in noncompetitive or threatening environments, may bias individual's motivation toward minimizing pain rather than toward selection of the most appropriate goal.[82,83]

Table. Motor Control Processes, Underlying Neuroanatomical Basis, and Effects of Pain[a]

Motor Control Process	Systems Engaged (Sensory-perceptual, Cognitive, Psychological and Motor)	Neuroanatomical Basis	Effects of Pain on Motor Behavior
Sensing and perception	Sensory-perception: relevant task and environmental stimuli	Primary and secondary sensory, sensory association areas	Deficient integration of tactile, proprioceptive, and visual sensations
Goal selection and intent	Cognitive: attention, arousal, motivation, effort Psychological: emotional well-being, mood states	Prefrontal, parietal, occipital association cortexes, limbic system	Selected goal may not be most effective for task success; pain may influence decision making and attention
Action selection	Cognitive: motivation, reinforcement-based action selection Psychological: mood influences vigor	Premotor cortex, basal ganglia circuits (motor, executive, and emotional)	Inefficient actions may be selected. Pain or fear of pain during most efficient action may act as "punishment," minimizing probability of choosing it
Action planning	Cognitive: feedforward planning of timing, sequencing Motor: interactive torques	Premotor cortex, cerebellum, parietal cortex	Pain may lead to abnormal sequencing and timing of interactive torques, leading to compensatory movements
Action execution	Motor: force encoding and muscle synergies	Motor cortex	Slower inefficient movements with poor kinematics; deficits in force production persist during task performance
Feedback (internal feedback) processing	Sensory-perception: feedback-based online correction	Dorsal columns, Anterolateral system, primary and association sensory cortex, cerebellum	Inefficient movement correction and/or response to sensory feedback
Knowledge of results processing	Cognitive: motivational systems, error-based systems, reinforcement systems	Visual–auditory systems, basal ganglia, cerebellum	Error and reinforcement are influenced by KR

[a] KR = knowledge of results.

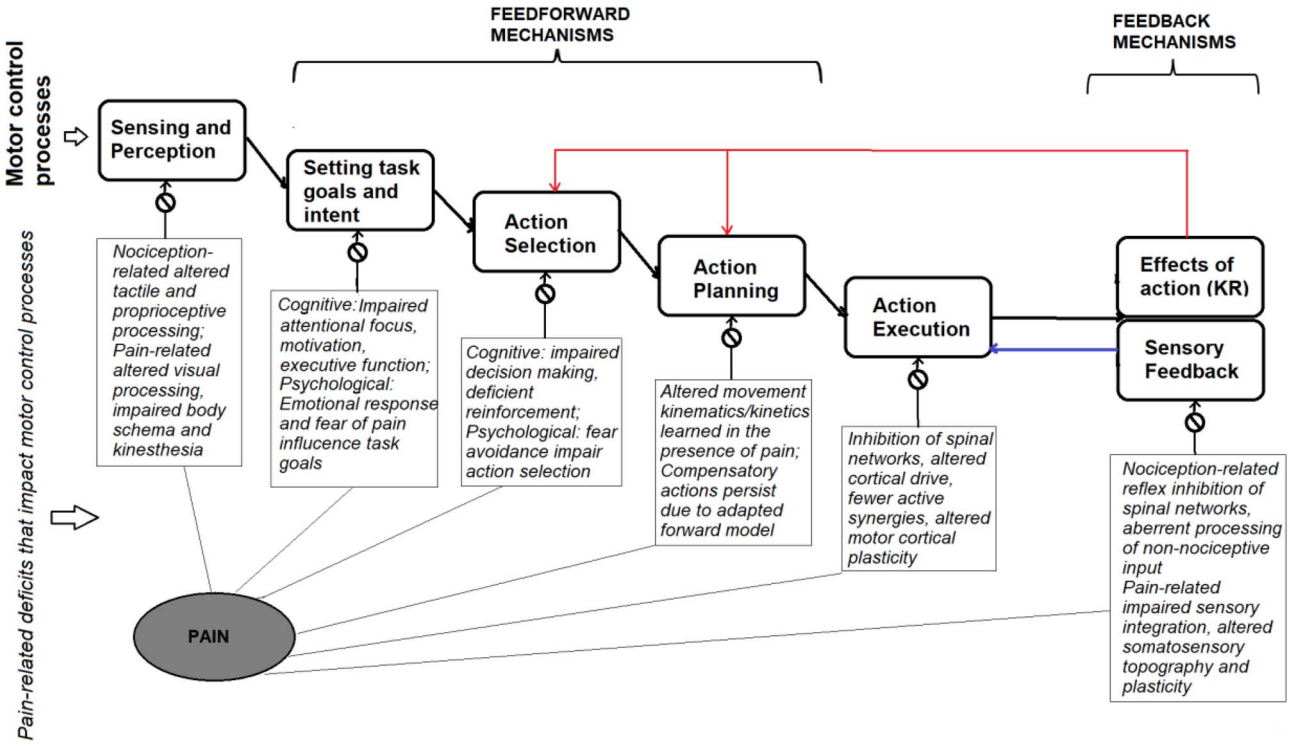

Figure 1. A contemporary model of motor control and the effects of pain on each of the processes: sensory-perceptual, cognitive, psychological, and motor processes that contribute to control and adaptation of goal-directed actions. Sensory systems help identify salient features of task and environment. Selection of goal, action, and planning of actions predominantly rely on feedforward mechanisms engaged prior to task execution. Feedback from somatosensory systems and effects of action on task-goals (ie, knowledge of results) influence subsequent actions (red arrows). In the case of slower actions, online feedback can be used to correct an ongoing movement (blue arrow).

Studies indicate that cognitive functions central to successful goal selection, such as task-switching, multi-tasking,[84] and working memory,[85,86] are impaired in the presence of pain. In the psychological domain, behaviors such as fear avoidance, catastrophizing, and poor self-efficacy may also influence goal selection.[87–89]

Assessing motivation and executive function may help identify factors that interfere with selection of appropriate goals for action. Further, identifying fear-avoidant beliefs and catastrophizing tendencies will not only provide insights into motor behaviors but also help direct appropriate psychological treatment targets.[90] Behavioral interventions that train attentional focus toward external task-relevant features for successful performance during practice may enhance motivation and curtail fear and anxiety.[80] Incorporating multi-tasking and decision-making[91,92] to select appropriate goals may optimize, challenge, and target cognitive processes necessary for goal selection.

Action Selection

Once a task-goal is identified, the individual must select the most appropriate action from a range of potential alternatives.[93] For example, to pass a basketball to a teammate (task-goal) in a noisy court (environment), how does a player (individual) choose a bounce pass over a chest pass or overhead pass? Action selection relies on knowledge of success probability of possible actions, developed with practice or experience through reinforcement learning.[94] In reinforcement learning, selection of a given action is modified by the probability of it receiving a binary (success or fail) form of feedback.[95] Actions with a high probability of reward are retained and executed with vigor; conversely, those with failure or punishment are avoided.[96–98] Reciprocal interactions between the prefrontal, premotor, and parietal cortices and basal ganglia implement reinforcement learning, with dopamine playing an important role in assigning the reward value to successful actions.[99–103] In particular, within basal ganglia, preferential activation of the caudate nucleus during early practice shifts to the putamen as learning progresses and skills become automatic.[104] Recent evidence suggests that neural networks subserving emotion processing (eg, amygdala, anterior cingulate cortex, and hippocampus) interact with the dopaminergic networks to influence action selection.[105]

Pain Effects on Action Selection

Acute and chronic pain influence cognitive control of motor behavior through interacting yet potentially distinct mechanisms. Acute, injury-induced pain often leads to immediate movement avoidance[106,107] to minimize the possibility of pain. Avoidance is thought to be implemented by modulation of cognitive control due to the fear of pain,[7,108] although reflex inhibition may also account for minimizing movement.[12] As pain becomes chronic, neuroplastic changes in cognitive and emotional brain circuits lead to increased fear-avoidance beliefs, impaired cognitive control, and reduced decision-making capability.[109–111] Work by Baliki and colleageus, for example, evidenced in individuals with chronic pain decreased connectivity between the medial prefrontal cortex (MPFC) and the parietal lobe as well as increased connectivity between the MPFC and insula.[112] MPFC and parietal lobe connections are crucial to the executive control of action selection[73,74,113]; therefore, decreased connectivity may contribute to deficits in action selection and planning.[78,79] Further, greater connectivity within the emotional circuitry, including the insula, may interfere with executive functioning and decision-making for action selection.[14,112]

At the level of action selection, pain accompanying a specific action may act as a "punishment," suppressing the likelihood of selecting a painful action by reducing its dopaminergic "value."[103,114] Subsequently, other feasible actions that allow task performance without pain may be more rewarding and learned through reinforcement learning.[115] There exists a clear interaction between the relative level of pain and the salience of task-goals in action selection[77] such that actions that serve the dual role of avoiding or minimizing pain and accomplishing task-goals are likely to be reinforced and habituated. Further research is needed to delineate neural networks that implement efficient and successful action selection with minimization of pain for accomplishment of task-goals.

Clinically, assessing fear-avoidant behaviors and movement analyses across a range of activities will provide insights into which actions are predominantly selected and which are avoided. Psychological strategies to target pain-related psychological deficits such as fear avoidance (eg, pain neuroscience education, cognitive behavioral therapy, or exposure therapy) are critical for promoting activity and behaviors necessary for best patient outcomes.[90,106,116] Besides pain relief, interventions that involve exploration of different movement strategies (eg, random-order practice) while interacting with complex environments provide richer opportunity to practice action selection.[117] Experiencing success in salient activities through pain-free, yet kinematically efficient and safe actions during task practice is more likely to reinforce desirable actions.[118,119]

Action Planning

Once an action is selected, motor commands are planned to specify movement parameters (ie, timing and force). Specification of movement parameters is well-conceptualized using the influential theoretical construct of an internal model.[29,39] Internal models explain how neural systems enable planning of motor commands to accomplish task-goals, predict the consequences of the preplanned motor commands, and update future commands. Two distinct types of internal models have been described: inverse internal models and forward internal models.[29,39]

Inverse models help to calculate the necessary motor commands to move the limb from its current state to a future desired state oriented toward the task-goal[39] (Fig. 2). To achieve the future desired state of the limb, the desired action trajectory is transformed to estimate joint torques, timing, and muscle activations needed to move the joints. Such transformation requires information about the current state of the motor system and an inverse model that specifies the motor command required (eg, how much force is needed to throw a ball) to accomplish the desired end-state of the motor system aimed toward a task-goal (eg, distance of the base from oneself). Feedforward specification of motor commands using the inverse internal model is implemented by neural networks that engage the association areas in the posterior parietal cortex, dorsal premotor cortex, cerebellum, supplementary motor area, and cingulate motor area.[120–127] These sensory-motor association networks help to plan motor

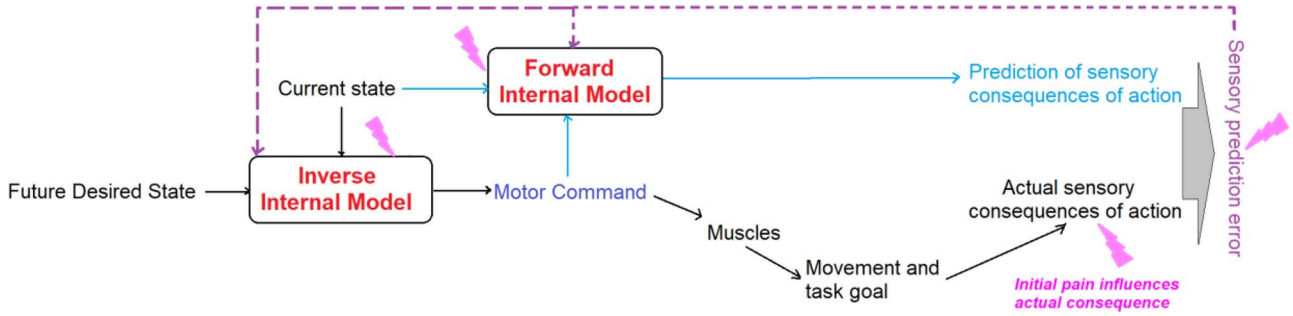

Figure 2. Inverse and forward models in feedforward control needed for action planning. Inverse models specify motor commands based on current status and the future desired state of the musculoskeletal system. Forward models help predict the sensory consequences (ie, the feel of movement as well as effects of the motor command on action goals). Pain influences both inverse and forward internal model due to changes in sensory prediction error (pink lightning bolts).

commands that, once relayed to the primary motor cortex, activate spinal motor networks subserving action execution.

Forward models predict the sensory consequences of the motor command specified by the inverse model.[39,128] As motor commands are relayed to target muscles, an efference copy is relayed to the forward model.[129,130] Forward models use the current state of the motor system and motor command to generate a predicted sensory consequence of the motor command prior to action execution.[39] As the action is executed, the forward model compares the predicted sensory consequence and actual sensory consequence to compute the sensory prediction error signal. Sensory prediction errors may arise from internal factors (eg, motor noise, impaired sensory input, or altered sensory input such as pain) or external factors (eg, environmental perturbation). The prediction error is then used to update the inverse and forward models for improving subsequent movements. Substantial evidence indicates that the cerebellum plays an important role in adaptation using the forward model.[41,128]

Pain Effects on Action Planning

Pain influences cognitive-motor processes that support inverse and forward internal models for adaptation of goal-directed actions.[35,131–133] Pain may interfere with accurate sensory prediction of motor commands via the forward internal model, thus yielding a sensory prediction error signal.[131,134] For example, as a patient without shoulder pathology generates a motor command to reach to an overhead shelf, the predicted sensory consequence during is a pain-free reach. However, in the presence of shoulder pathology, the actual sensory consequence is a painful reaching action. Mismatches between the predicted and actual sensory consequence in those with shoulder pathology may drive adaptive updates to the inverse model.[128] The resultant inverse model may thereafter specify more forces at the scapulothoracic joint while minimizing the forces applied at the glenohumeral joint, resulting in a new compensatory, pain-free reaching action. Thus, pain-driven updates to the inverse model may underlie compensatory actions observed in individuals with pain.

When pain-free compensatory action is repeated to accomplish a task-goal, the forward model also undergoes updates: it "learns" that the newly adopted compensatory action accomplishes the task-goal without pain—a rewarding outcome more likely to be reinforced. Once learned, compensatory action may persist even after the pathology is treated and pain subsides at the periphery because the updated inverse and forward models continue to support compensatory motor adaptations. Multiple clinical reports indicate that despite reduction in pain, decreases in inflammation, and improvements in range of motion and strength, patients continue to compensate with actions that, once adaptive and protective in nature, are unnecessary, even harmful if maintained.[8,9,135–138] For instance, adaptive movements that place greater loads on the non-operated limb after total knee arthroplasty may have consequences for the development of degenerative osteoarthritis of the non-operated limb.[10,11] The cerebellum, widely implicated in forward and inverse models, has recently been further implicated in the perception and processing of pain in relation to movement.[139] For instance, work by Ruscheweyh and colleagues found that individuals with cerebellar damage perceived increased pain and reduced analgesia compared with pain-free controls.[140] In a different study, parts of the lateral cerebellum were activated with an experimental pain stimulus delivered during a grip-force production task,[139] putatively suggesting a cerebellar substrate for multimodal (pain and movement planning) processing that underlies pain-related adaptations in motor control. The precise behavioral relevance of this overlap remains open to further research as does the role of cerebellar circuits in pain-related movement adaptation.

Compensatory actions are likely to persist if the forward model is not retrained through new prediction errors or if more stereotypic actions are not trained through reinforcement learning. Assessing the discrepancy between capacity and actual performance through movement analyses is critical to determine the nature of compensatory behavior. Interventions focused on augmenting capacity (eg, pain-free range of motion) and retraining fast, successful movements through systematic manipulations of task, environment, and feedback are likely to benefit action planning. Compensatory actions can be remediated in 1 of 2 ways: (1) through high-intensity, high-dose task practice that promotes successful and pain-free movement patterns with better kinematics and kinetics through reinforcement[141]; or (2) through education and graded exposure to pain during movements to encourage pain modulation with repetitive actions.[142] During graded exposure in the presence of pain, the prediction of pain during movement likely allows the forward model to predict some pain while continuing practice of desired movement patterns and activities. Use of technology in both strategies to improve to manipulate reinforcement, or error, provides external focus, and a frame of reference for kinematically better actions may

prove helpful. In basic behavioral studies, use of virtual reality to improve motor performance with practice has yielded success in healthy individuals[143–145] and individuals with ACL reconstruction.[146]

Action Execution

The motor plan for the selected action is finally relayed to the action execution system, which includes the primary motor cortex, corticospinal pathway, and the spinal motor neuron pool. The motor cortex generates movement-specific signals and transmits them to the brainstem, spinal cord circuits, motor neurons, and, finally, the muscles. Multiple lines of evidence indicate that the motor cortex may encode multiple features of movement such as kinematics[147–151] (spatial and motion aspects), kinetics[152,153] (muscles and forces), complex posture primitives,[154,155] and/or cooperative muscle synergies.[156–158] A muscle synergy, for example, constitutes multiple muscles activated in a specified order and amplitude; 1 muscle can be a part of different synergies. Each synergy, when recruited, results in a coordinated activation of constituent muscles with specific relative amplitudes and timings.[159] Neurophysiologic studies of primate and human motor cortex provide supplementary support to the notion of muscle synergies in the control of goal-directed action.[160] Massé-Alarie and colleagues used transcranial magnetic stimulation (TMS) to test the overlap between motor cortical representations of the forearm muscles at rest and during different tasks.[161] They observed that a single muscle had multiple representations. In addition, each representation was differentially more active during distinct motor tasks. Further, synergistic muscles shared more cortical sites with each other than with antagonist muscles. Together, their findings indicate that motor cortical representations may plausibly encode different muscle synergies with task-specific activation profiles. Thus, motor execution may be accomplished by activation and combination of different synergies in a task-specific manner. Finally, motor cortical drive is certainly crucial to activate the spinal motor neurons and muscles needed to produce volitional actions. Motor cortical drive to generate muscle force is strongly influenced by the sensory-perceptual system and cognitive-psychological processes such as motivation and fear.[162–166] Once activated, muscles act on the mechanical linkages to produce action to accomplish task-goals.

Pain Effects on Execution

Pain modifies the neural mechanisms underlying action execution. During bouts of acute muscle pain, studies consistently evidence reduced activity in the sensory and motor cortices (characterized by a range of functional imaging and neurostimulation techniques such as functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and transcranial magnetic stimulation (TMS),[167,168] which may reflect a protective mechanism to minimize movement. In contrast, chronic injury and pain have been associated with changes in cortical representations of muscles and increases in corticospinal excitability.[169–172] A recent meta-analysis suggests that increases in corticospinal excitability are accompanied and likely mediated by a reduction in GABA-mediated intracortical inhibition.[173] Long-term motor cortical changes likely contribute to volitional activation deficits[174–177] that persist even after pain relief and rehabilitation.[178,179] In addition to motor cortical changes, impaired spinal mechanisms (eg, reduced presynaptic inhibition and recurrent inhibition) and psychological states (eg, fear of pain) may also contribute to voluntary activation deficits in chronic pain conditions.[35,180] Despite reported changes in cortical and spinal activity, the influences of task, environment, and muscle specificity need further research to improve generalizability.

Chronic pain may further suppress certain muscle synergies and/or delay their activation, thus leading to abnormal and inefficient goal-directed movements (Fig. 3). For example, compared with pain-free controls, individuals with lateral epicondylalgia were found to demonstrate fewer synergies that were activated with longer delays when generating submaximal grip force.[181,182] A lesser level of synergy activation was associated with lower pressure pain threshold in these patients. Similar alterations in muscle synergies have been described in experimental pain models[183,184] and in patients with other painful conditions.[185] Muscle synergy deficits are often accompanied by neural changes. Using TMS, Schabrun and colleagues[171] mapped the motor cortical representations of the extensor carpi radialis brevis (ECRB) and extensor digitorum (ED) in individuals with chronic lateral epicondylitis and pain-free controls (Fig. 4). Controls demonstrated multiple motor representations for ED and ECRB in the motor cortex. In contrast, individuals with lateral epicondylitis demonstrated significant reduction in the number of "peaks" or motor cortical representations of ED and ECRB. Findings further indicated greater overlap between the contracted representations of the muscles in patients with lateral epicondylitis. Altered and smaller motor cortical representations align with findings, highlighted earlier, showing fewer synergies and thus may represent the physiological signature of pain-induced changes in the organization of muscle synergies.

Greater overlap within the reduced cortical muscle representations and subsequent fewer available synergies may help explain poor motor control for skilled hand function observed in patients with chronic lateral epicondylitis and other painful conditions.[171,186] First, decreased and delayed activation of synergies may interfere with the speed and accuracy of task performance. Second, fewer available synergies may constrain or limit functional task performance to abnormal, often stereotypical movements. Motor deficits are often augmented during repetitive tasks when fatigue sets in and additional synergies are needed to maintain task performance.[171] Deficits in activation of additional synergies during repetitive actions (eg, tennis) may further impair task performance, increase tissue overload on existing synergies, or both.

Assessment of strength and power deficits, fatigue, and motor performance provide an indicator of action execution deficits. Interventions that target neuromuscular mechanisms underlying force production may improve strength/power. Remediating motor deficits that arise from faulty synergies may require novel interventions that go beyond traditional strength training. For example, training of multiple movement combinations (synergies), and incorporating these synergies into functional tasks, would likely improve motor control.[187] Providing opportunities to practice varying movement patterns (practice variability) with verbal feedback and cueing may allow the patient to experience a range of actions without compensation. Incorporating technological advances such as virtual reality may reinforce efficient movements with better kinematics and kinetics in more motivating and varied environments.

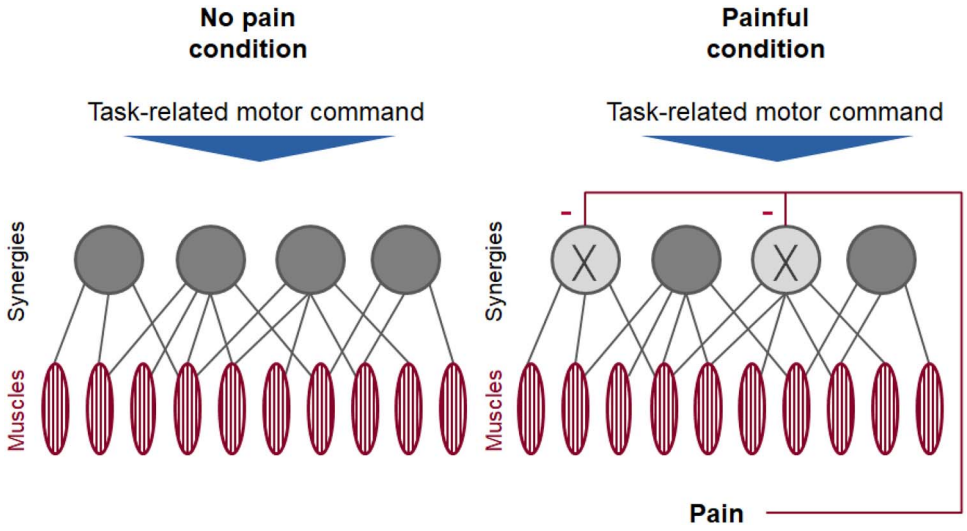

Figure 3. The influence of pain on motor execution and motor synergies in particular. (A) Motor commands activate task-specific synergies or motor modules. Each synergy consists of multiple muscles working together in a coordinated fashion; 1 muscle can be a part of multiple synergies. (B) Presence of pain may inhibit specific muscle synergies and contribute to movement dysfunction.

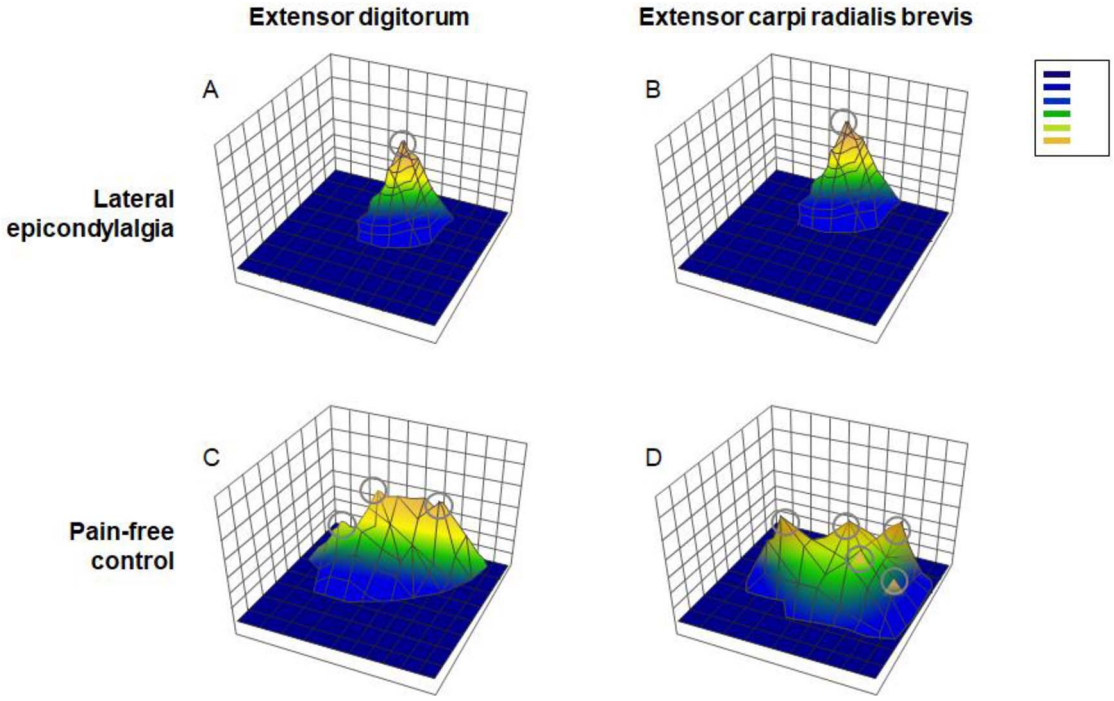

Figure 4. Adapted from Schabrun and colleagues. A 3-dimensional motor cortical representation of extensor digitorum and extensor carpi radialis brevis in a representative pain-free control (lower row) and an individual with chronic lateral epicondylitis (upper row) obtained using TMS. "Peaks" were identified if Motor Evoked Potentials (MEPs) were >50% of maximum map amplitude and at least 5% greater than MEP amplitude of 7 of 8 surrounding grid points. A peak represents the area of the muscle that is more responsive to TMS activation. A reduced number of discrete peaks in cortical representation is evident in the participant with lateral epicondylitis compared with the pain-free control. Group data (not shown here) supported this representative individual data from Schabrun et al[171]. TMS = transcranial magnetic stimulation.

Feedback Control

Actual sensory consequences of the executed action are relayed to the nervous system through multiple sensory systems (eg, visual, somatosensory, etc). When actions are slow, online feedback can be used to modify ongoing actions.[28] With fast actions (eg, throwing), the use of online feedback to modify an ongoing movement is inefficient due to long delays in sensory acquisition and processing. Instead, somatosensory feedback from the musculoskeletal system, together with the effects of action on task-goals (knowledge of results), update the inverse and forward models.[39] Updated inverse and forward models help plan and adapt subsequent actions to maximize success. Importantly, motor cortex excitability and plasticity are heavily influenced by sensory feedback.[188,189]

Pain Effects on Feedback Control

Nociceptive inputs modulate feedback-dependent reflexive spinal networks in unique ways to alter the motor neuron excitability, agonist–antagonist interaction, and processing of

1. **What are commonly observed deficits in sensory-perceptual, cognitive, psychological and motor systems for motor control that contribute to complex PRMD?**
   - What is the time course of the deficits that contribute to PRMD?
   - Are the deficits in motor control processes and the time course of their emergence different across diagnoses?
   - How are deficits in sensory-perceptual, cognitive, psychological and motor systems related to individual differences in patients with PRMD?
2. **What neural and behavioral mechanisms contribute to deficits in motor control processes in the presence of pain?**
   - What are the relative contributions of spinal and supraspinal networks in PRMD?
   - How do neural networks associated with altered motor control differ in localized pain (eg, lateral epicondylitis) compared to generalized pain syndromes (eg, fibromyalgia)?
3. **Which assessment strategies (sensory-perceptual, cognitive, psychological and motor tests, questionnaires, kinematic motion capture) can reliably and objectively detect motor control deficits in PRMD in a valid manner?**
   - Which of the assessments help predict long-term changes in motor control, performance, and re-injury?
   - Are the assessments sensitive enough to demonstrate clinically meaningful change with treatment?
4. **What are critical ingredients of treatment strategies that will help remediate the motor control deficits that contribute to PRMD?**
   - Can sensory-perceptual retraining strategies that help reduce pain remediate abnormal movements in PRMD?
   - Can action selection processes, including inverse and forward models, be retrained in the presence of pain to help normalize movements?
   - What are the best strategies to train feedforward and feedback control in individuals with pain?
   - What are optimal parameters (eg, intensity, dose, nature of feedback) of clinical interventions targeted at improving motor control in individuals with pain?
   - How can technological advances such as virtual reality and non-invasive brain stimulation) be used to remediate the deficits in sensory-perceptual, cognitive and psychological processes contributing to PRMD?
5. **How do we select patients to appropriately target our interventions to maximize efficacy and efficiency of treatments?**
   - What are potential modulating variables (eg, personality type, self-efficacy) that may interact with pain perception and motor control of goal-directed movements?
   - How do psycho-social factors impact different steps in action selection, planning, and execution?

Figure 5. Potential future research directions along the translational pipeline. PRMD = pain-related movement dysfunction.

non-nociceptive stimuli.[12,190–193] These physiologic changes may underlie volitional activation deficits, delayed activation of muscle responses, and abnormal co-activation around painful joints. Impaired sensory processing, integration, and motivation may significantly interfere with the use of error and reinforcement feedback to update goal and action selection, and motor planning. Finally, sensorimotor somatotopy is impaired in individuals with chronic pain, potentially leading to shunting of sensations to abnormal movement patterns.[194–196]

Determining how manipulation of augmented feedback (eg, visual feedback) and/or instructions to correct movement patterns influences movement kinematics may provide some insights for potential ways to improve motor control. Disrupting visual feedback using stroboscopic glasses led to alterations in vertical jump–landing kinematics in individuals with ACL reconstruction.[197] Compared with verbal instructions alone, visual feedback improved movement kinematics during side-step cutting in healthy athletes.[198] Visual feedback has also been used to reduce pain perception in individuals

with chronic low back pain[199,200]; however, the effects on movement performance remain to be tested.

Outstanding Questions, Future Directions, and Conclusion

Understanding PRMD is a complex, yet imperative undertaking for advancing evidence-based treatments. Experts have long recognized the importance of motor control in the management of musculoskeletal disorders[1,2,201,202]; a comprehensive framework that outlines sensory-perceptual, cognitive, and motor systems will help both research and clinical efforts to treat PRMD. Both nociception and pain may influence goal-directed actions at multiple levels of the neuraxis. The complexity of each level, interactions among levels, and changes to the levels over time render it challenging, if not impossible, to isolate a single mechanistic explanation of PRMD. Given its layered complexity, investigation of PRMD demands a systematic approach along a continuum of research—from basic mechanistic investigations to applied clinical intervention studies—to expose key mechanisms, identify appropriate treatment targets, shed light on individual differences, and guide development of evidence-based outcomes and interventions. The contemporary distributed model of motor control is an attractive framework through which to study pain and its effects on the cognitive, sensory-perceptual, and motor processes, and their respective underlying neural substrates, that contribute to PRMD. To that end, Figure 5 outlines potential future research directions to help address outstanding questions along the translational pipeline—from a theoretical contemporary model to effective clinical interventions.

Rehabilitation of movement in the presence of pain or after pain relief requires comprehensive assessment and treatment of pain as well as related movement dysfunction. Although movement reeducation and practice are increasingly incorporated in physical therapy and other rehabilitation interventions of PRMD,[141,203] identifying deficient sensory-perceptual, cognitive, psychological, and motor processes contributing to abnormal movement will allow targeted innovative interventions to remediate those processes. For example, both fear of pain and impaired sensory processing and integration may impair movement performance. Fear of pain may be targeted through pain neuroscience education and graded, structured task practice that provides opportunities for action selection and planning. In contrast, impaired sensory processing may be optimally targeted through sensory reeducation and virtual reality interventions that take advantage of multi-sensory integration in the context of task practice. We suggest that assessment and treatment of sensory-perceptual, cognitive, and motor processes contributing to the control of goal-directed actions will lead to individualized treatments for better patient outcomes. The contemporary motor control model thus provides a framework to advance research and guide clinical practice to help treat individuals with PRMD.

Author Contributions

Concept/idea/research design: S.S. Kantak, T. Johnson, R. Zarzycki
Writing: S.S. Kantak, T. Johnson, R. Zarzycki

Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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