

Neuromechanical Principles Underlying Movement Modularity and Their Implications for Rehabilitation

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<http://dx.doi.org/10.1016/j.neuron.2015.02.042>

Neuromechanical principles define the properties and problems that shape neural solutions for movement. Although the theoretical and experimental evidence is debated, we present arguments for consistent structures in motor patterns, i.e., motor modules, that are neuromechanical solutions for movement particular to an individual and shaped by evolutionary, developmental, and learning processes. As a consequence, motor modules may be useful in assessing sensorimotor deficits specific to an individual and define targets for the rational development of novel rehabilitation therapies that enhance neural plasticity and sculpt motor recovery. We propose that motor module organization is disrupted and may be improved by therapy in spinal cord injury, stroke, and Parkinson's disease. Recent studies provide insights into the yet-unknown underlying neural mechanisms of motor modules, motor impairment, and motor learning and may lead to better understanding of the causal nature of modularity and its underlying neural substrates.

Introduction

The principles of neuromechanics are a framework for understanding patterns of neural activity that generate movements in a healthy nervous system, as well as in motor deficits, and how these patterns change through rehabilitation. Neuromechanics is the study of interactions between neural, biomechanical, and environmental dynamics that give rise to meaningful motor behaviors and addresses the fundamental question, "How does the activity of a neuron, a motor unit, or a muscle affect behavior?" Neuromechanical studies reveal that the functional consequences of activity in any of these components cannot be interpreted independently but must be interpreted in the context of all the forces acting on the body, including those from the external environment, from body structures, and from other muscles (Dickinson et al., 2000; Hooper and Weaver, 2000; Nishikawa et al., 2007). Depending on the neuromechanical context, a movement could be unaffected by, or critically dependent upon, the timing and amplitude of a muscle's activity. As a consequence, our ability to functionally interpret neural motor signals is intimately entwined with the properties of the neuromechanical system (Chiel and Beer, 1997; Chiel et al., 2009; Tytell et al., 2011). Here, we explore how the following neuromechanical principles provide insight into how the nervous system constructs and learns movements:

(1) Motor abundance: for any given task, there are many functionally equivalent motor solutions.

- (2) Motor structure: the structure of motor patterns is shaped by biomechanical task relevance.
- (3) Motor variability: motor variability is high where the effect on motor output is low.
- (4) Individuality: individuals express different motor styles that depend on evolutionary, developmental, and learning processes.
- (5) Multifunctionality: muscles can contribute to many actions; a few muscles can be combined in many ways to produce a wide range of different actions.

In the first section, we hypothesize that these neuromechanical principles and plasticity in the nervous system support the development of motor modules, which are defined as coordinated patterns of muscle activity that flexibly combine to produce functional motor behaviors (Bizzi and Cheung, 2013; Bizzi et al., 2008; d'Avella et al., 2003; Ting and McKay, 2007; Tresch and Jarc, 2009). While there is general consensus that structure exists in motor patterns, how they arise, whether they reflect neural structure, and whether they are functionally relevant are sources of lively debate. We argue that motor modules arise from neural plasticity in spinal and supraspinal structures, which is shaped by regularities in biomechanical interactions with the environment. Different expressions of motor modules across individuals may reflect how each individual explores a potentially difficult-to-search and nonlinear set of neuromechanical solutions for movement. As motor modules are refined

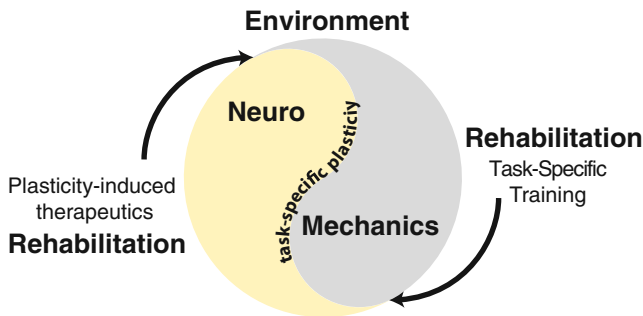


Figure 1. Neuromechanics and Rehabilitation

Movement is influenced by both the neural and biomechanical systems of the body and their interaction with the environment. Experience-dependent plasticity shapes the individual-specific patterns that determine how we move. Novel rehabilitation paradigms seek to restore motor function by enhancing endogenous neural plasticity through a number of mechanisms and to sculpt the plasticity via task-specific training.

over a lifetime, they may appear objectively optimal based on minimizing movement time, energy, or some other feature of the movement (Todorov and Jordan 2002; Scott, 2004, 2008; Todorov, 2004; Shadmehr and Krakauer, 2008). However, it is likely that motor modules are “sloptimal,” i.e., only locally optimal or just “good enough,” to balance competing costs of reliably generating motor actions versus exhaustive exploration or computation to produce new behaviors.

In the second section, we address how motor modules may provide a powerful framework to address current limitations that impede the development of more effective and individualized rehabilitation therapies (Giszter and Hart, 2013; Safavynia et al., 2011; Santello and Lang, 2014). Current clinical motor tests are focused on overall motor functions, such as walking speed, and are not intended to distinguish different task-specific deficits that underlie impairments (Cheeran et al., 2009; Mancini and Horak, 2010; Pardasaney et al., 2012). However, more directed task-specific training may be necessary to harness use-dependent neural plasticity, a common basis for rehabilitation across different neurological disorders (Figure 1). The level of motor disability may be most important for devising optimal strategies to fit individual patient needs (Dobkin, 2009). Here, we give three clinical examples showing how motor modules can help to (1) identify individual-specific motor impairments, (2) assess the effects of rehabilitation, and (3) provide a framework for development of targeted therapies that enhance neural plasticity and sculpt motor recovery. We postulate that motor module organization is altered after CNS injury and disease (i.e., spinal cord injury [SCI], stroke, and Parkinson’s disease [PD]) and that quantifying this disruption may provide tremendous insight into individual-specific motor impairments as well as mechanisms of learning and refining motor behaviors during rehabilitation (Figure 1).

Neuromechanical Principles Underlying Motor Module Organization

In this first major section of the essay, we elaborate on the characteristics of biomechanical systems that may lead to a modular organization for motor control. Modularity can be observed at many levels of motor performance, from muscle,

kinetics, and kinematic measures, and in both the spatial and temporal organization of such measures. We focus solely on what we consider to be the most basic level of modularity: time-synchronized activity of multiple muscles or motor units throughout the body. This level of modularity addresses a basic biomechanical constraint: muscle effects on motor output cannot be considered in isolation but require the coordination of multiple muscles throughout the body (Chiel et al., 2009; Dickinson et al., 2000; Hooper and Weaver, 2000; Nishikawa et al., 2007; van Antwerp et al., 2007). Upon this most basic level of modularity, structure and variability in timing, kinetics, and kinematics of movements can be constructed.

Typically, motor modules are characterized through linear decomposition techniques that are useful but may not fully capture the true complexity of motor modules. Using signal processing methods, such as principal-component analysis (PCA), independent component analysis (ICA), and nonnegative matrix factorization (NMF) (Lee and Seung, 1999; Ting and Chvatal, 2010; Tresch et al., 1999, 2006), motor signals can be decomposed into underlying motor modules, also referred to as muscle synergies, that reflect *consistent patterns of multi-muscle coordination that generate specific actions* (Figure 2). More physiological and feature-based representations have been found in both sensory systems (Lee and Seung, 1999; Olshausen and Field, 2004) and motor control (Ting and Chvatal, 2010; Tresch et al., 2006) when using techniques that do not assume orthogonality (e.g., PCA). In neural systems, non-negativity also appears to be important to reflect spiking activity of neurons. While all of the current decomposition techniques assume linear combinations of motor modules, it is unlikely that the motor modules are linearly additive in a global sense. However, using such methods can still be useful for revealing locally linear mechanisms that the nervous system may use to represent complex nonlinearities in the environment (Olshausen and Field, 2004). Although current computational methods to analyze motor patterns have many limitations (Burkholder and van Antwerp, 2013; Steele et al., 2013; Ting and Chvatal, 2010; Tresch and Jarc, 2009; Zelik et al., 2014) and may not be directly interpretable in terms of neural mechanisms, they still provide useful tools for describing and understanding structure in motor coordination. Advances in computational methods are ongoing but will not be discussed further here.

Principle of Motor Abundance: Motor Modules Reflect Specific Motor Solutions Selected from an Abundance of Possible Solutions. For any given motor task or behavior, there are generally a large number of “motor-equivalent” solutions that can produce similar or functionally equivalent behaviors. Because many motor solutions exist, there is no single correct or optimal motor pattern, i.e., different motor modules can equivalently perform the same motor task. This ability to choose from many solutions underlies the adaptability and robustness of biological systems. The concept of motor abundance (Latash, 2012) is critical for understanding the variations in movement solutions and variability in movements that are observed (Scholz and Schöner, 1999; Scholz et al., 2000; Valero-Cuevas et al., 2009). Within these “motor-equivalent” solutions, there may be some that are less desirable than others for any number of reasons, including energetics, stability, and generalizability

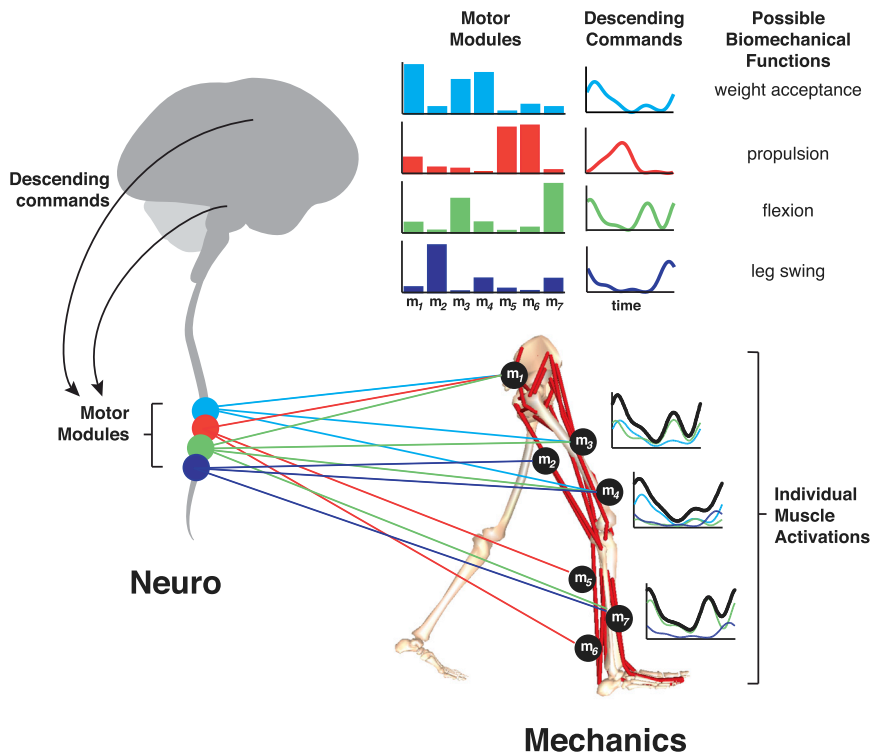


Figure 2. Motor Modules Define Functional Co-activation of Muscles

For walking, descending commands from the spinal cord, brainstem, and cortex can modulate spinal motor modules. Each motor module selectively co-activated multiple muscles with a characteristic level of activation (colored bars) to produce the mechanical output needed to achieve a given locomotor subtask (Clark et al., 2010; Neptune et al., 2009). The particular timing of recruitment (colored lines, top right) can vary across steps, across gait speeds, and environmental demands. The activity of individual muscles express unique temporal patterns of activity (black lines, bottom right) due to their different contributions to different motor modules (colored lines, bottom right).

structure and variability of motor patterns. Biomechanical *affordances* refer to the types of movements that are facilitated by body structure. Body structures define ways of moving that require little energy or neural control to produce. For example, simulations and robots that mimic the structure of the body can produce walking-like behaviors with little energy and without muscles or joint actuators (Collins et al., 2005; Kuo, 2007).

across tasks. However, finding optimal solutions may be challenging, as muscle activation patterns have complex and nonlinear relationships to biomechanical functions (Cullins et al., 2015).

Motor modules may reflect “good-enough” solutions for movement that provide stable and predictable motor outputs. Experimental evidence demonstrates that individuals exhibit consistent motor modules in seemingly variable muscle activation patterns across multiple muscles and motor behaviors, as well as across species (Bizzi et al., 2008; Chvatal and Ting, 2013; Chvatal et al., 2011; d’Avella et al., 2003; Giszter et al., 2007; Ting, 2007; Ting and McKay, 2007; Torres-Oviedo and Ting, 2010). Different stable solutions can be identified throughout a lifetime. For example, default patterns for movement are established in the embryonic stage, during which spontaneous motor activity, such as kicking and flailing, is observed (Bekoff, 2001). These movement patterns are available at birth and can allow a fawn to run minutes after it is born. Human infants are born with the capacity for stepping and kicking (Yang et al., 2004); through exploration (Smith and Thelen, 2003), movement patterns are refined, and more are created throughout development (Dominici et al., 2011). Models of spinal circuitry and biomechanics suggest that “good-enough” (i.e., suboptimal) solutions for movement can be found in just a few iterations of random searching (Tsianos et al., 2014); once found, these solutions are likely to be reinforced by use-dependent neural plasticity.

Principle of Motor Structure: Motor Modules Reflect Biomechanical Task Relevance. The biomechanical affordances and constraints of the body and environment shape the allowable

Biomechanical *constraints* refer to movements that may be difficult or impossible to achieve with a given structure, or they refer to the required neural input to achieve a movement, e.g., the precise timing or activity of a particular muscle. In walking, biomechanical constraints limit knee extension and place constraints on step length in backward walking. The basic structure of motor patterns during a particular gait is defined by the sequence of subtasks: placing the foot on the ground, pushing against the ground for propulsion, and swinging the limb forward. Each subtask defines certain co-activation patterns of muscle activation across the limb (van Antwerp et al., 2007; Zajac, 2002). Biomechanical affordances and constraints determine how precise or variable these motor patterns must be. For example, in a simulation of single-legged locomotion, biomechanical “bottlenecks” and “don’t-care” regions were identified that predicted the precision and variability of locomotor solutions found by a genetic algorithm. The highest fitness solutions all exhibited precise timing at the “bottleneck” of placing the leg and pushing it backward, which had a large effect on movement efficiency. In contrast, the solutions showed high variability in the “don’t-care” region late in the stance phase, during which the model leg continued to move backward but was no longer able to exert force (Beer et al., 1999). For example, distributions of motor neuron activation duration vary from one individual to another in *Aplysia* feeding behavior, but when motor neuron duration and timing play a critical role in a behavior such as the animal closing its grasper to retract food, the distributions become similar across all individuals (Cullins et al., 2015). In contrast, there is high variability in the duration of motor neuron activity to close the grasper if the animal fails to grasp food, as

the motor neuronal activity is no longer functionally relevant. Similar examples across many species and motor behaviors can be found where motor activity that does not directly contribute or interfere with the task at hand is found to be highly variable both within and across individuals (Bernstein, 1967; Scholz and Schöner, 1999; Valero-Cuevas et al., 2009).

Motor modules may reflect biomechanical structures and the required coordination of neural signals to perform motor tasks. Motor modules identified experimentally have been associated with biomechanical functions necessary for walking and balance (Allen and Neptune, 2012; Chvatal et al., 2011; Clark et al., 2010; Neptune et al., 2009; Safavynia and Ting, 2013; Ting and Macpherson, 2005; Torres-Oviedo et al., 2006). In simulations, motor modules have been shown to emerge based on optimal control of multi-jointed and multi-legged systems and produce near-optimal motor performance (Berniker et al., 2009; Chhabra and Jacobs, 2006; Kurtzer et al., 2006; McKay and Ting, 2012; Todorov and Jordan, 2002). Modular control can reproduce essential features of movement in simulations of a frog leg (Berniker et al., 2009), human walking (Allen et al., 2013; Allen and Neptune, 2012; Neptune et al., 2009), and cat balance control (McKay and Ting, 2012). Thus, motor modules may reflect an interaction between the neural and motor systems and may often align with coordination patterns that optimize energetic efficiency, given biomechanical constraints (De Groot et al., 2014; McKay and Ting, 2012; Steele et al., 2013). Because motor structure reflects biomechanical task relevance, similarities in motor modules for the same task will exist. For example, there are substantial similarities in the most active muscles of motor modules used for walking at different speeds and for different balance strategies, although inter-individual differences also exist (Chvatal et al., 2011; Clark et al., 2010). As discussed later, biomechanical constraints cannot uniquely determine motor module structure in most cases.

Principle of Motor Variability: Motor Module Variations across Individuals Are High if the Effect on Motor Output Is Low. Variations and variability in motor control also depend on biomechanical affordances and constraints based on the reasonable assumption that the nervous system only regulates motor outputs that are directly relevant to task goals. Using biomechanical models in conjunction with optimality principles has predicted higher variability in “good-enough” regions of behavior, e.g., the uncontrolled manifold, theory of minimum intervention, and optimal feedback control (Bernstein, 1967; Scholz and Schöner, 1999; Todorov and Jordan, 2002; Valero-Cuevas et al., 2009). Biomechanical models can be used to determine the degree to which variability can occur without having a deleterious effect on performance. For isometric force production, the degree of variation in muscle activity in the finger is relatively constrained, allowing for little variability (Kutch and Valero-Cuevas, 2012; Valero-Cuevas et al., 1998), whereas the range of possible variations is much greater in the cat hindlimb (M.H. Sohn and L.H. Ting, 2013, Am. Soc. Biomech., conference). These differences appear to match the variability in muscle activity measured experimentally. Variation in motor patterns may also endow a limb with other characteristics that may or may not matter to the movement. For example, increasing muscle activity to improve limb stability may reduce the need for precise neural

control (Bunderson et al., 2008; Franklin et al., 2004; M.H. Sohn and L.H. Ting, 2013, Am. Soc. Biomech., conference). Other equivalent solutions may be similar in energetics or stability yet differ in motor pattern, causing subtle differences in movement (M.H. Sohn and L.H. Ting, 2013, Am. Soc. Biomech., conference).

As a consequence of allowable variations to produce similar tasks, differences in the structure and number of motor modules that are specific to individuals have been identified across species and motor behaviors. The consistency of motor modules across biomechanical conditions within an individual suggest that they do not emerge from “online” optimization based on biomechanics but represent preferred patterns of muscle coordination that are modulated across a class of movements. For example, the structure of motor modules for walking share similarities in the most active muscles, but the contributions of other muscles can vary substantially (Chvatal and Ting, 2012; Clark et al., 2010). Moreover, these same motor modules are recruited across walking speeds and even in response to perturbations imposed during walking (Chvatal and Ting, 2012; Oliveira et al., 2012). Motor modules are used in kicking, swimming, and jumping in frogs and across different postural behaviors in cats and humans (Chvatal and Ting, 2013; Chvatal et al., 2011; Giszter et al., 2007; Hart and Giszter, 2004; Roh et al., 2011; Torres-Oviedo et al., 2006; Tresch et al., 1999), suggesting that they form a repertoire of whole limb actions. Motor modules in postural control can vary in structure and number across individuals and are preserved across different biomechanical configurations. Motor modules for weight support are characterized by extensor muscle activity, but the degree of activity in the hamstring muscles can vary substantially. Because motor variability is high where the effect on motor output is low, variations in motor modules may affect secondary characteristics of movement. Differences in motor modules can also reflect differences in kinematic strategies for postural control, and motor modules specific to one individual may not adequately reproduce muscle activity in another (Torres-Oviedo and Ting, 2010). Indeed, the accuracy of human walking simulations is improved when individual-specific motor modules are included (Walter et al., 2014).

Principle of Individuality: Motor Modules Are Shaped by History and May Generate Individual Movement Styles. It has recently emerged as a general principle that individual—and not averaged—motor solutions solve neuromotor problems. Individuals may have their own “motor program styles,” i.e., they may show significant individual variations in outputs of the motor system that are both consistent within a given animal and differ from one individual to another. Variations in motor program styles have been observed in a wide variety of animals (Calabrese et al., 2011; Golowasch et al., 2002; Marder and Goaillard, 2006; Prinz et al., 2004), as well as in humans (Nussbaum and Chaffin, 1997; Torres-Oviedo and Ting, 2010; Welch and Ting, 2008). Not all of these differences can be attributed to biomechanics, as the fidelity of human walking simulations using generic biomechanical models can be improved through the consideration of individual movement patterns (Ting et al., 2012; Walter et al., 2014), and differences in the weightings of joint torque production can be used to synthesize different styles of walking (Liu et al., 2005). This illustrates that biomechanics is

insufficient to determine motor patterns, allowing for many functionally equivalent solutions.

Developmental processes, motor exploration, experience, and training all play a role in shaping individual movement styles. Motor exploration and variability are essential to the discovery of movement patterns that produce useful motor functions and do not necessarily follow rules of engineering approaches (Herzfeld and Shadmehr, 2014; Huang et al., 2008; Loeb, 2012; Smith and Thelen, 2003; Wu et al., 2014). The properties of the neuromechanical system may be such that only a few variations are required to identify “good-enough” solutions (Tsianos et al., 2014). However, even after learning more optimal movement styles, subjects tend to revert to suboptimal, habitual patterns (de Rugy et al., 2012; Ganesh et al., 2010; Sntarse et al., 2011). Movement strategies for everyday tasks may appear optimal because they have been refined over both evolutionary time as well as a lifetime. Extensive, long-term training may be necessary to identify globally optimal movement strategies, which are sought by elite athletes, dancers, and musicians. Because motor history shapes individual movement styles, motor modules may differ and become different due to motor experience and training. Indeed, different movement patterns for grasping may be identified in musicians, shaped by their specific training (Gentner et al., 2010), and different musicians display different movement styles (Furuya and Altenmüller, 2013). This perspective on how we learn to move is consistent with activity-dependent plasticity after neural injury that is altered by the specificity, intensity, difficulty, and complexity of motor training (Adkins et al., 2006; Fisher and Sullivan, 2001; Will et al., 2004). Similar challenges are posed by sports or classroom learning, where stable, slop-timal solutions may be difficult to change (Chi and Roscoe, 2002; Handford, 2006). For example, changing movement patterns is a risky endeavor for elite athletes; Tiger Woods required 2 years without winning tournaments to reshape his golf swing (Eden, 2013). Understanding the costs of changing movement strategies is likely to play an important role in developing effective rehabilitation therapies.

As room for variability increases, the seemingly fixed and objective nature of motor modules dissolves. The more biomechanical constraints exist, the fewer opportunities there are for individual variation, and the more motor modules tend to look energetically optimal. When characterizing the optimality of motor patterns in both neurologically normal and motor-impaired individuals, it must always be asked: “with respect to what”? Although differences in walking style exist across gender, social status, and culture (Hall, 1976), these differences are much less than those observed in speech, a less biomechanically constrained motor task. Verbal communication can be equally good using different language-specific phonemes (Kuhl, 2004), which can be thought of as motor modules for speech. The degree of variability is directly related to the fact that variability in sound production does not cause the same devastating effects as in walking, where unfit variations may lead to a fall. Motor modules in speech production (Elemans, 2014; Gick and Stavness, 2013) may facilitate native-language speech but cause distinctive accents and pronunciation errors when speaking a foreign language. Similarly, motor accents in bodily movements may also cause differences in a person’s

ability to learn new motor tasks and thus be an important consideration during rehabilitation.

Principle of Multifunctionality: Motor Modules May Mediate Multifunctionality of Muscles for Movement. While motor modules themselves are invariant, they do not produce stereotyped actions. Rather than constrain the nervous system, the ability to combine modules flexibly actually facilitates adaptation and learning. Variability observed across different types of behaviors and trial-by-trial variability can be accounted for by varying combinations of motor modules (Cheung et al., 2005; Hart and Giszter, 2004; Roh et al., 2011; Torres-Oviedo and Ting, 2007; Tresch et al., 1999). Rather than random noise in individual muscles or trajectories, variability across instances of movement may thus reflect differences in the descending drive to stored movement patterns (Churchland et al., 2006) that could facilitate motor exploration (Huang et al., 2008; Wu et al., 2014). Indeed, learning to perform a novel task is faster if it can be achieved by altering recruitment of a smaller number of motor modules rather than learning new control strategies for individual muscles (Berger et al., 2013). Consistent with findings in spinal central pattern generators (CPGs) where temporal rhythms can differentially recruit groups of muscles (McCrea and Rybak, 2008; Stein and Daniels-McQueen, 2002), this suggests that the temporal commands to motor modules can be more readily adapted than the modules themselves (McKay and Ting, 2012).

Although modularity is often taken to mean a reduction in dimension, this is true only within the context of specific behaviors. Because a few muscles mediate many motor behaviors, many motor modules may exist to handle different motor behaviors or contexts. Considering the very large number of different tasks that an animal or human may engage in over a lifetime, many different patterns are required (Zelik et al., 2014). Dimensional reduction may be an artifact of current algorithms for identifying modularity that work by reducing the dimensionality of data. The multifunctionality of limbs and bodies is critical for facilitating a large motor repertoire. If one considers just the simple on/off combinations of muscle activation patterns among n muscles, one obtains 2^n possible joint torque patterns. Thus, the potential behavioral repertoire for coordination of multiple muscles is much greater than the total number of muscles or even motor units. (Chiel et al., 2009). When one further considers differences in level of muscle activation and relative timing of activations, the number of possibilities increases even further. If these possibilities are, in turn, combined with the effects of changes in posture, environment, or movement that can also modulate muscle function, the possibilities become very large. Consider the simple motor task of getting up from a chair, walking, turning, and then sitting down: the muscles of the body must be coordinated in a myriad of different patterns to accomplish all of the necessary subtasks. During challenging athletic activities or dancing, even more motor subcomponents must be mastered and properly deployed.

A large set of motor modules across the behavioral repertoire may facilitate multifunctionality, allowing the same muscles to perform different functions in different behavioral contexts. While having more motor modules than muscles may seem counterintuitive, a high-dimensional representation of actions defined by combinations of muscles may be more directly

related to the resulting motor output. In contrast, the effects of individual muscles are highly nonlinear, variable, and context dependent. Others have noted this previously: [Hughlings Jackson \(1889\)](#) noted that the muscles of the hand were represented in lower motor centers “in numerous different combinations, as simple and very general movements,” and in the highest centers, “the same muscles are represented (re-re-represented) in innumerable different combinations, as most complex and most special movements.” The implication is that these areas are not simultaneously active but represent the whole repertoire of hand movements. Physiologically, these many representations of movement could be mediated by neurons of the cortex, reticular formation, and spinal cord project to multiple muscles throughout the body. As an example, spinal motor neurons specialized for activating hip flexors in limb withdrawal reflex are not generally active in multiple types of limb movements ([Berkowitz, 2007](#)).

As a consequence, as representations of useful ensembles of muscles that produce actions, motor modules may improve the rapidity and robustness of searches for new movement patterns. Similar principles have been proposed to govern visual and sensory processing ([Olshausen and Field, 2004](#)) where different streams of visual input signals (e.g., retinal activity, or pixels) can represent the same object (cf. principle of motor abundance, discussed earlier). It has been proposed that sensory processing is facilitated by representations of the inherent structure, or features, in complex natural scenes (cf. principle of motor structure, discussed earlier). As the number of features far exceed the number of visual inputs, such representations form an overcomplete set of basis vectors that have more direct relationship to the objects in the environment than individual pixels (cf. principle of multifunctionality, discussed earlier); such principles have also been identified in signal processing as a way to handle nonlinearities ([Hastie et al., 2005](#); [Olshausen and Field, 2004](#)). In the motor system, the advantage is that motor modules can be recruited based on desired whole-limb or whole-body functions rather than requiring specific muscles activations to be computed ([Safavynia and Ting, 2012, 2013](#); [Ting and Macpherson, 2005](#); [Ting and McKay, 2007](#)). Moreover, among a vast dictionary of representations, only a few are used at one time to represent a given image or action, a phenomenon referred to as sparse coding ([Olshausen and Field, 2004](#)). Sparse coding is consistent with the existence of sensory and motor maps in which only neurons in small regions of the maps are active at any given time. Sparse representations have been proposed to enhance the efficiency of sensory processing and motor adaptation ([Fiete et al., 2004](#); [McKay and Ting, 2012](#); [Ting and McKay, 2007](#)), both of which are shaped by individual experience and developmental processes (cf. principles of variability and individuality, discussed earlier). Similarly across biology, arguments for modularity have been made based on their ability to improve adaptability and robustness while decreasing connectivity costs in neural networks ([Clune et al., 2013](#); [Wagner et al., 2007](#)).

Are Motor Modules Encoded by the Nervous System? While the arguments presented are largely theoretical and indirect, some evidence for motor modules at a neurophysiological level does exist. Although it is possible for synchronous activity of motor neurons to arise without being directly linked to the

same presynaptic neuron, the divergent structure of neurons in the cortex, brainstem, and spinal cord projecting to motor neurons and pre-motorneuronal pools can provide one type of neural substrate for the type of spatial modularity in muscle coordination discussed here. Studies stimulating the spinal cord and cortex reveal correlated outputs across motor pools ([Overduin et al., 2012](#); [Saltiel et al., 2001](#)). During natural movement, shared common drive to motor neurons of the eye ([Joshua and Lisberger, 2014](#)), leg ([Hart and Giszter, 2010](#); [Krouchev et al., 2006](#)), arm ([Holdefer and Miller, 2002](#)), and pelvic muscles ([Asavasopon et al., 2014](#)) has been demonstrated. Modularity in the temporal patterns of motor outputs ([d’Avella et al., 2003](#); [Flash and Hochner, 2005](#); [Hart and Giszter, 2004](#); [Ivanenko et al., 2003](#); [McCrea and Rybak, 2008](#)) likely have different, more dynamic representations in the nervous system such as in CPGs ([McCrea and Rybak, 2008](#); [Stein and Daniels-McQueen, 2002](#)) Proprioceptive sensory feedback can also play a role in the expression of motor modules, providing inputs that are structured by the mechanics of the musculoskeletal system and environment in some cases ([Cheung et al., 2005](#); [Kutch and Valero-Cuevas, 2012](#)). However, the existence of motor modules in the absence of sensory feedback ([Kargo and Giszter, 2000](#); [Kargo et al., 2010](#); [Cheung et al., 2005](#)), during the production of voluntary movements using visual feedback ([d’Avella et al., 2011](#)), or that is at odds with sensory inflow ([Chvatal et al., 2013](#); [Safavynia and Ting, 2013](#); [Torres-Oviedo et al., 2006](#)) provides some evidence for the neural encoding of some motor modules. Evidence suggests that sensory feedback can modulate temporal patterning of recruitment to relatively fixed motor modules across different types of behaviors ([Hart and Giszter, 2004](#); [Kargo et al., 2010](#); [McCrea and Rybak, 2008](#); [Stein and Daniels-McQueen, 2002](#)). Currently, the neural substrates for motor modularity remain largely elusive; however, studies of neuromotor impairments affecting the spinal cord, motor cortex, basal ganglia, and other neuroanatomical structures may help to reveal the mechanisms of motor modularity.

Neuromechanics of Motor Impairment and Rehabilitation

In the second major section of this essay, we turn to a consideration of the implications of motor modules for understanding motor impairment and their implications for rehabilitation. Although neurological pathologies affect neural mechanisms involved in movement, neuromechanical principles of motor abundance, motor structure, motor variability, individuality, and multifunctionality hold, whether in skilled experts or in individuals with motor impairments. Deficits in motor module organization can, in turn, provide a clearer understanding and assessment of the nature of the motor impairments and how they can be improved, providing rational targets for novel therapies. Many of the current outcome measures, diagnostic techniques, and clinical tests focus on overall motor function and lack the power to answer fundamental questions (i.e., why, what, and how) about a person’s deficits and ability to recover ([Mancini and Horak, 2010](#); [Pardasaney et al., 2012](#)). Testing the effectiveness of novel therapies requires more specific methods to reveal the heterogeneity of participants and characterize functional neurophysiologic adaptations due to treatments ([Dobkin, 2007](#)). For instance, why does a rehabilitation treatment help

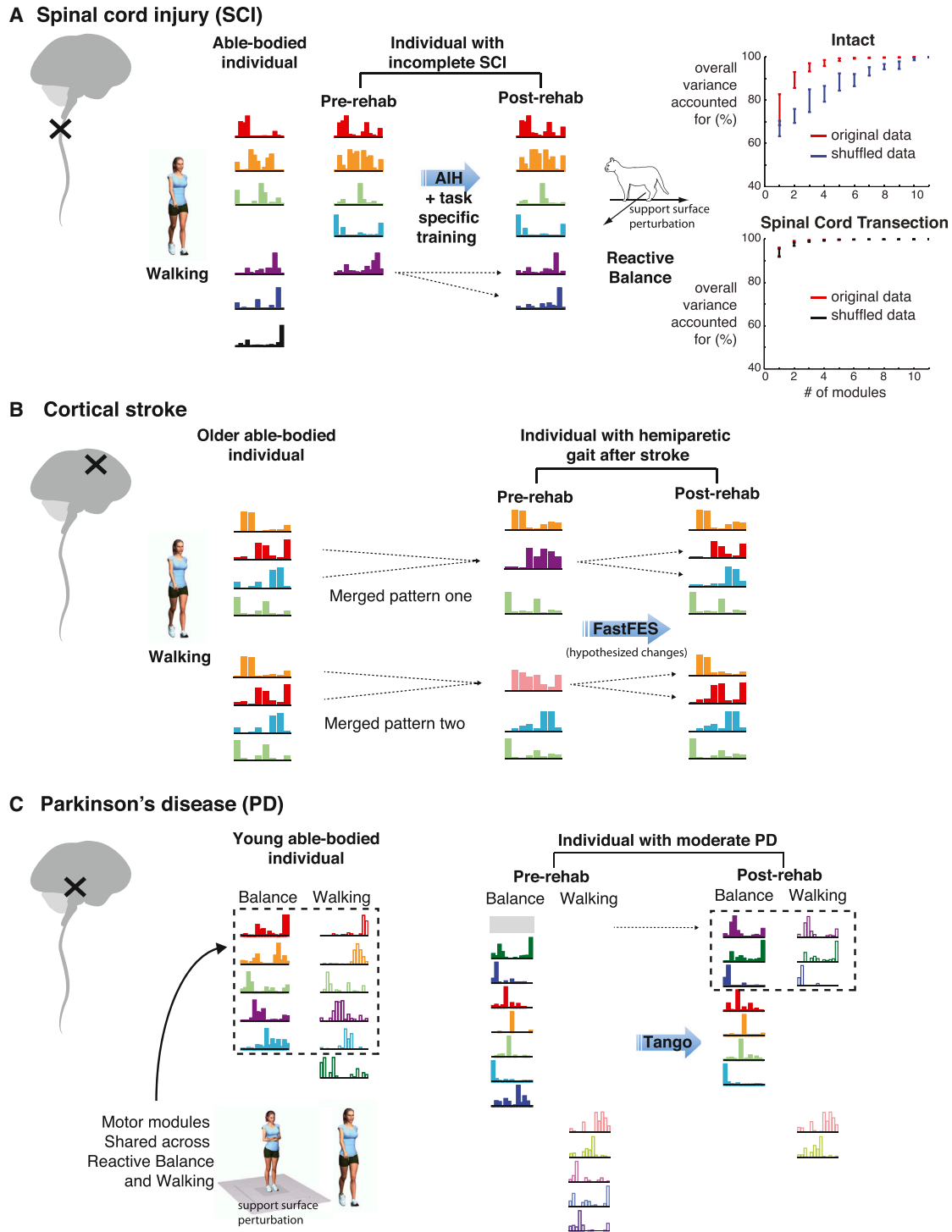


Figure 3. Different Motor Modules Deficits and Improvements in SCI, Stroke, and PD

Colored bars represent motor modules, with the height of each bar representing the extent to which an individual muscle is part of that motor module. Color of motor modules across conditions and/or populations (e.g., able-bodied to pre-SCI) represents similarity between motor modules.

(A) SCI disrupts both descending connectivity and spinal organization. Accordingly, motor modules resembling those found in able-bodied individuals are reduced after incomplete SCI, and additional motor modules characterized by co-contraction can emerge (data not shown) (Hayes et al., 2014a). After rehabilitation, motor modules may be reshaped and better resemble those in able-bodied individuals (H.B. Hayes et al., 2012, Soc. Neurosci., abstract). In animals with complete spinal cord transection, a few motor modules can account for a large degree of variance in muscle activity for reactive balance in response to support surface translations (Chvatal et al., 2013). In the intact condition, the 95% confidence intervals of the total variance explained by an increasing number of motor modules are significantly different from the 95% confidence intervals of the total variance explained in randomly shuffled data, indicative of consistent

(legend continued on next page)

some but not others? What motor strategies were changed due to recovery or treatment? Furthermore, motor modules provide a noninvasive assessment of the structure and variability of motor coordination that can be linked to scientific knowledge about the functions of the neural areas affected by injury or impairment. These can be combined with a neurophysiological measure of neural connectivity (Belda-Lois et al., 2011; Krakauer et al., 2012; Whittall, 2004) that cannot typically be identified during movements, especially gait and balance tasks. Tracking changes in motor modules through recovery and rehabilitation can provide assessments of improvement as well as insights into the neural mechanisms of motor plasticity (Giszter and Hart, 2013; Safavynia et al., 2011; Santello and Lang, 2014).

As individual differences in motor modules are shaped through experience, appropriate rehabilitative training may be necessary to target individual-specific motor deficits in conjunction with novel plasticity-enhancing adjuvant therapies (Hayes et al., 2014b; Lovett-Barr et al., 2012). Use-dependent neural plasticity, the capacity of the nervous system to adapt in response to experience, is a critical yet relatively unexplored mechanism underlying rehabilitation (Kleim and Jones, 2008; Nudo et al., 1996a, 1996b, 2001; Wittenberg, 2009; Wittenberg and Schaechter, 2009). While plasticity plays a role in rehabilitation, endogenous and injury-induced neural plasticity only enables partial spontaneous recovery of motor function (Goshgarian, 2003; Kaegi et al., 2002), and the extent of recovery is slow, variable, and frustratingly limited (Raineteau and Schwab, 2001). However, many exciting new developments in rehabilitation science are targeted at enhancing neural plasticity, including the use of stem cells (Isacson and Kordower, 2008; Lu et al., 2014; Takahashi and Yamanaka, 2006), neural stimulation (Benazzouz and Hallett, 2000; Hallett, 2000; Ruge et al., 2011; Stefan et al., 2000), therapeutic exercise (Courtine et al., 2009; Edgerton et al., 2006; Edgerton and Roy, 2009; Vaynman et al., 2003; Weishaupt et al., 2013), and acute intermittent hypoxia (Baker-Herman et al., 2004; Wilkerson and Mitchell, 2009). All of these therapies can provide a generalized enhancement of neural plasticity, either locally or profusely, enhancing the potential for individuals to reorganize relevant neural circuitry necessary to improve movement (Kleim and Jones, 2008), but all of these therapies require this plasticity to be appropriately directed to improve motor function.

In the sections that follow, we discuss motor modules for walking and balance in three neurological disorders affecting different parts of the CNS: SCI, stroke, and PD, each of which may provide insights to the neural bases of motor modules (Figure 3). Each of these neural impairments affects a specific

part of the nervous system that has a different detrimental effect on the walking ability, reflecting the distributed control of posture and gait throughout the CNS (Takakusaki, 2013). Interneurons in the spinal cord may encode motor modules for locomotion and other lower limb tasks (Hart and Giszter, 2010; Roh et al., 2011; Saltiel et al., 2001), which can be flexibly recruited by spinal structures regulating the timing of locomotor patterns (McCrea and Rybak, 2008; Stein and Daniels-McQueen, 2002). Motor cortical activity may be more heavily involved during forms of walking requiring cortical inputs, such as visually guided obstacle crossing (Drew et al., 2002). Cortical activity may encode motor modules as well (Capaday, 2002; Ethier et al., 2006), and/or recruit spinal motor modules (Rathelot and Strick, 2009). Spinal cord lesions affect both corticospinal connectivity, as well as the organization of the spinal cord below the site of the lesion, and can therefore affect the encoding and recruitment of modules in the spinal cord (Giszter and Hart, 2013; Roh et al., 2011; Tresch et al., 1999). It is also likely that there are separate and complementary motor modules encoded in cortical areas for both upper and lower limb movement (Hughlings Jackson, 1889; Rathelot and Strick, 2009) as well as in reticular formation in the brainstem for simple arm movements (Riddle and Baker, 2010; Zaaimi et al., 2012), and for postural control (Deliagina et al., 2008; Schepens et al., 2008). Stroke may impair cortical motor modules as well as cortical recruitment of spinal motor modules. The basal ganglia, which are affected by PD, may regulate the appropriate selection of motor modules in cortical and brainstem areas. In the following sections, we will discuss the different impairments in motor modules in (SCI, stroke, and PD), and describe how targeted rehabilitative therapies may improve modular organization.

Loss of Motor Modules in SCI. A few reports suggest that motor modules after SCI are lost or abnormally structured. The location of injuries to the spinal cord are highly variable, damaging and sparing different parts of the spinal cord and corticospinal connections that contribute to walking. Nearly 75% of persons with incomplete SCI regain some walking capacity (van Hedel et al., 2009) using assistive devices but show little progression to unsupported overground walking (Field-Fote and Roach, 2011; van Hedel and Dietz, 2010). After incomplete SCI, the number of motor modules used in walking is reduced (Figure 3A) in both children and adults (Fox et al., 2013; Hayes et al., 2014a). While some of the motor modules resemble those found in able-bodied individuals, incomplete SCI subjects exhibited a wider range of module compositions, reflective of the heterogeneity inherent in incomplete SCI. Many of the pathological modules were characterized by co-contraction of agonist

structure in muscle activity (red vs. blue lines). However, after complete spinal transection, the 95% confidence intervals of the variance explained by motor modules do not differ from that obtained by randomly shuffling data, suggesting that no consistent structure exists (red vs. black lines).

(B) Stroke disrupts corticospinal drive and impairs independent recruitment of joint actions. Motor modules for walking in the paretic leg are merged versions of those found in able-bodied individuals. Merging can occur between different modules that are associated with different motor deficits (Clark et al., 2010). After rehabilitation, splitting of motor modules is hypothesized to occur that would be associated with improved performance.

(C) PD impairs basal ganglia function and is associated with inappropriate selection of motor patterns as well as cortical hyperexcitability. Accordingly, in individuals with PD, the number of motor modules in walking and reactive balance are similar to those found in healthy individuals (Rodríguez et al., 2013; Roemmich et al., 2014). However, in young, healthy adults, motor modules for reactive balance to support surface translation and overground walking are similar, suggesting a common subcortical origin for the recruited motor modules. In contrast, in individuals with PD who have balance impairments, motor modules from reactive balance and walking can appear to be completely distinct, consistent with increased attention and cortical control of gait. After adapted tango rehabilitation, motor modules may become more similar across tasks, suggesting improved automatic, subcortical control of gait (J.L. Allen et al., 2014, World Congress of Biomechanics, abstract).

and antagonistic muscles (Fox et al., 2013; Hayes et al., 2014a), and many were statistically distinct from modules identified in healthy individuals (Figure 3A). Moreover, the expression of pathological modules may be specific to each individual's gait deficits (Hayes et al., 2014a). In contrast, in animals with complete spinal transection, modules for reactive balance responses were absent (Chvatal et al., 2013), consistent with the need for brainstem connectivity. In contrast, muscles could be vigorously activated in an alternating rhythm by paw shake, which can be spinally mediated. Although some modules were identified from successful balance trials, they were not statistically different from those extracted from randomly shuffled data (Figure 3A), suggesting that there was no meaningful motor structure in reactive balance after spinal transection (Chvatal et al., 2013).

Motor module analysis can provide insight into the motor deficits underlying impaired gait in SCI. For example, a module for eccentric braking was absent in all individuals with incomplete SCI, consistent with foot drop or slap that is often observed clinically. In general, motor modules exhibited abnormal co-activation of muscles and much broader temporal recruitment across the gait cycle (Hayes et al., 2014a). This suggests the use of a disorganized motor pattern, or patterns that stabilize the limb, rather than biomechanically efficient motor patterns that effectively achieve particular motor subcomponents during different phases of gait. It is interesting that the number of motor modules was reduced in able-bodied individuals when they used assistive devices that were matched to individuals with incomplete SCI. This suggests that the assistive devices provide biomechanical functions that may obviate the need to recruit particular motor modules. Analysis of such data could provide insight into the changes in motor module composition and recruitment necessary for improved motor function.

Neural plasticity induced by a novel breathing treatment may prepare the nervous system to be sculpted by task practice, which could then be assessed by motor module analysis. A promising strategy shown to improve respiratory and non-respiratory motor function in incomplete SCI is to induce spinal cord plasticity through exposures to modest bouts of low oxygen, e.g., acute intermittent hypoxia (AIH). In rodent SCI models, AIH induces motor plasticity (Dale and Mitchell, 2013; Dale-Nagle et al., 2010; Lovett-Barr et al., 2012; Mitchell, 2008; Vinit et al., 2009) through serotonin-dependent synthesis of brain-derived neurotrophic factor (BDNF) (Baker-Herman et al., 2004). Repetitive exposures to AIH elicits increased breathing capacity and locomotor performance in rodents with SCI (Lovett-Barr et al., 2012). In persons with incomplete SCI, a single bout of AIH increases plantar flexor muscle activity and torque output (Trumbower et al., 2012), and repetitive AIH over 5 consecutive days improves walking ability (Hayes et al., 2014b). Daily AIH just prior to walking training yields greater gains in walking function than either daily AIH or walking training alone (Hayes et al., 2014b). However, it is not known whether the effects of AIH simply boost the overall motor output or whether the combination of enhanced plasticity and training could improve the structure and recruitment of motor modules. Early evidence suggests that the number of motor modules is

increased and the composition of motor modules changes after AIH (H.B. Hayes et al., 2012, Soc. Neurosci., abstract).

Even when motor patterns are highly variable across repetitions of the same movement, different movements, and across individuals, motor modules provide a way to identify consistent motor structure and track individual progress in rehabilitation. Motor module analyses can distinguish completely random organization in motor outputs from highly variable recruitment of motor modules. The appearance of abnormal motor modules in SCI may be unstable and could reflect either inappropriate neural activity or a search process to re-learn useful motor coordination patterns. Tracking participants longitudinally across rehabilitation may inform how individuals search for and learn new motor modules.

Merging of Motor Modules after Stroke. Motor modules provide a valuable way to analyze the consequences of stroke, which have effects that are quite different from those of SCI. The number of motor modules in individuals post-stroke is reduced on the paretic side due to a merging of modules, revealing impairments in whole-limb muscle coordination that correspond to observed motor deficits in the leg (Cheung et al., 2012; Clark et al., 2010) and arm. Merged modules reflect a decrease in the independence of muscular control and are consistent with so-called "clinical muscle synergies" in stroke where abnormal coupling of muscles across the limb are observed in both the upper (Dewald et al., 1995) and lower extremities (De Quervain et al., 1996; Knutsson and Richards, 1979; Shiavi et al., 1987). In the lower limb, impaired motor modules appear to be due to a merging of two modules typically identified in the non-paretic and control legs (Figure 3B), consistent with a reduction in the independence of corticospinal drive to the spinal cord. The number of motor modules is correlated with reduced walking speed, clinical measures of balance and walking function, and biomechanical measures such as propulsion asymmetry and step length asymmetry (Bowden et al., 2010; Clark et al., 2010). Moreover, motor modules are better correlated with gait and balance function than are lower limb Fugl-Meyer assessments (Bowden et al., 2010) typically used to measure the severity of motor impairment. Even when the number of modules is not reduced, impairments in the ability to flexibly recruit motor modules is also observed, such as a reduced ability to take longer, higher, or quicker steps (Routson et al., 2014), suggesting deficits in the descending control of motor modules.

The characteristics of merged motor modules also predict differences in gait impairments that may necessitate different rehabilitation approaches. This is important because self-selected walking speed is a common measure of rehabilitation effectiveness, yet speed (a functional output) can be achieved through different strategies (e.g., improved mechanical output from the paretic leg, or increased reliance on mechanical output from the nonparetic leg); within these strategies, a subject may use different muscular coordination patterns (improvement in neural control). One of the most common impairments post-stroke is the inability to adequately recruit the ankle plantarflexors of the paretic leg (Lamontagne et al., 2007; Turns et al., 2007), which is important for directing ground reaction forces (Bowden et al., 2006) and hip and leg extension (Peterson et al., 2010) in walking. Among individuals with a reduction in motor modules,

two different types of plantarflexor impairment (Figure 3B) were found (Clark et al., 2010). Some were unable to independently activate the plantarflexors and the proximal extensors (hip abductors/extensors and knee extensors). In contrast, others could independently activate the plantarflexors but with inappropriate timing; these individuals also merged control of the proximal extensors with the hamstrings. Neuromechanical simulations reveal that both impairments lead to inadequate propulsion from the plantarflexors (Allen et al., 2013), suggesting that improving paretic plantarflexor recruitment is a critical component for rehabilitation. Furthermore, both groups also had impaired swing of the paretic leg. In the first group (merged plantarflexor control) this occurred *prior* to swing, whereas in the second group (independent plantarflexor control but merged proximal extensors and hamstrings), this occurred during *late* swing. These results suggest that distinct rehabilitation approaches may be prescribed based on neuromechanical impairments identified through motor module analysis.

A novel gait retraining tool that combines fast treadmill walking and functional electrical stimulation (FastFES) is being developed that is targeted to sculpting plantarflexor motor modules for walking propulsion. Fast walking can help improve motor function in several ways. First, moderate exercise can be a promoter of motor plasticity (Lamontagne and Fung, 2004). Second, it may encourage motor exploration by requiring participants to walk at more challenging speeds and provides opportunity for greater repetition (more steps) of practice, which enhances use-dependent plasticity. Third, it emphasizes biomechanical subcomponents of walking such as knee flexion and propulsion, promoting specific sculpting of motor modules. Further task-specific sculpting is provided through electrical stimulation of plantarflexors to improve paretic propulsion; stimulation also provides afferent feedback to enhance motor learning of new motor modules (Kesar et al., 2011; Reisman et al., 2013). FastFES has been shown to improve gait impairments, overground gait function, activity, and participation in individuals with chronic post-stroke hemiparesis (Awad et al., 2014a, 2014b; Knarr et al., 2013; Reisman et al., 2013) through improved plantarflexion (Knarr et al., 2013). However, changes in muscle activity, much less its structure, have not been measured after FastFES.

Motor module analyses performed before and after rehabilitation may provide a more in-depth and mechanistic evaluation of the treatment effects, and this analysis can be used to further optimize the dosage and ingredients of the intervention. For example, in FastFES, motor module analysis could reveal whether FastFES improves abnormal muscle coupling, e.g., an increase in number of motor modules, and/or inappropriate timing, e.g., improved motor module timing in both the targeted (ankle plantarflexors) and non-targeted (proximal muscles). Similarly, after a different gait training program, merging of the plantarflexor motor module with other motor modules was improved in some individuals but was still inappropriately timed (Routson et al., 2013), suggesting the need for further rehabilitation.

In the upper extremity, altered structure and temporal recruitment of motor modules have also been observed after stroke that may be related to altered neural pathways. Corticomotor-

neuronal cells in motor cortex can directly project to spinal motor neuron pools, coordinating multiple muscles. However, they can also project to spinal interneurons, which, in turn, coordinate motor neurons (Rathelot and Strick, 2009). After stroke, reticulospinal neurons in the brainstem can also provide a limited degree of gross arm and hand function (Riddle and Baker, 2010; Riddle et al., 2009; Zaaimi et al., 2012). Given this anatomy, changes in the timing of largely intact motor modules in the upper extremity may reflect altered corticospinal drive to interneurons (Cheung et al., 2009). Merged motor modules in the paretic arm that correlate to the degree of impairment (Cheung et al., 2012) could reflect a greater impairment of corticospinal drive so that modules can no longer be independently activated; alternatively, the merged modules could be due to compensatory arm control from reticulospinal neurons. It is interesting that, in the long-term chronic stroke survivors, even though some merged motor modules may still exist, other motor modules appear to fractionate, or split, perhaps as a compensation to improve performance. This may reflect greater capacity for experience-dependent plasticity in intact cortical areas in contrast to the brainstem or to the damaged cortical areas.

Altered Selection of Motor Modules in PD. PD affects the functioning of the basal ganglia, which project to both cortical and brainstem motor areas. In two studies, only moderate decreases in motor modules (Figure 3C) were observed in PD patients compared to healthy individuals. Since spinal and cortical structures remain primarily intact in PD, it seems reasonable that the structure and recruitment of motor modules is not as severely and obviously impaired as in incomplete SCI and stroke (Rodriguez et al., 2013). However (discussed later in this section), the relationship of this deficit to basal ganglia dysfunction remains unclear, as the number of motor modules in PD was shown to be insensitive to the presence of dopaminergic medication that enhances basal ganglia function (Roemich et al., 2014).

Deficits in walking and balance due to PD may reflect inappropriate selection of motor modules, which, in turn, may cause freezing of gait and postural instability. It has been proposed that the basal ganglia selectively inhibit competing motor programs, allowing the appropriate selection of motor pathways for movement (Mink, 1996, 2003). This hypothesis is consistent with evidence that individuals with PD have difficulty with set-shifting in both cognitive and motor tasks (Chong et al., 2000; Dirnberger and Jahanshahi, 2013). Moreover, impairments in cognitive set-shifting are associated with freezing of gait, which has been characterized as an inability to switch from gait initiation to walking (Factor et al., 2014). For postural control, this results in motor patterns that are inappropriate for a given biomechanical context. For example, after successful reactive balance responses during standing, individuals with PD continue to activate leg muscles when reacting to seated perturbations (Horak et al., 1992). This perseverance may also be related to other proposed functions of the basal ganglia, including reward prediction (Schultz et al., 1997) and habit formation (Yin and Knowlton, 2006). Therefore, it may be more important to examine the recruitment of motor modules in PD in different biomechanical contexts (Carpenter et al., 2004; Dimitrova et al., 2004a; Horak and Macpherson, 1996). For example,

individuals with PD fail to adequately decrease muscle activity when changing from narrow to wide stance (Dimitrova et al., 2004b) or in response to different perturbations (Chong et al., 2000). Neuromechanical modeling studies demonstrate that frontal plane balance necessitates a decrease in muscle activity to maintain postural stability (Bingham et al., 2011). This inflexibility in the ability to appropriately recruit motor modules may contribute to postural instability and explain why individuals with PD preferentially select a narrower stance (Dimitrova et al., 2004a, 2004b).

Adapted tango (AT) rehabilitation, specifically targeted at individuals with PD, may improve the appropriate recruitment of motor modules through exercise and practice of complex tasks. Increasing aerobic activity may enhance activity-dependent neural plasticity (Alberts et al., 2011; Hirsch and Farley, 2009). A link between activity, mental engagement, and neural pathways may be primed by dancing, which involves complex, unfamiliar tasks such as walking backward, problem solving, and movement improvisation. Furthermore, many individuals with PD have deficiencies in planning and executing complex, goal-directed behavior (Kliegel et al., 2005) and troubles with internally generating movement (Low et al., 2002). Therefore, alternating the leader and follower roles in AT may allow patients to focus on external cues, bypassing the dysfunctional basal ganglia and accessing circuitry involving the cerebellum, thalamus, and cortex. During dance, the need for creativity, the exposure to novel steps, and the complex movement patterns could, through the mechanisms of neural plasticity, expand neural areas and improve neural pathways that facilitate movement. Improvements in clinical measures of balance and gait, as well as in symptom severity, have been demonstrated after exercise for participants with PD (Corcos et al., 2013; Fisher et al., 2008; Hirsch et al., 2003; Li et al., 2012; Smania et al., 2010), including AT dance (Duncan and Earhart, 2012; Hackney and Earhart, 2010). These improvements in mobility, balance, spatial cognition, and disease severity may be retained for up to 3 months after AT in individuals with mild to moderate PD (Hackney and Earhart, 2009a, 2009b, 2010; Hackney et al., 2007; McKee and Hackney, 2013).

Our early results suggest that changes in motor modules identified after AT are consistent with an increased automaticity of gait, shifting control of gait from cortical to subcortical structures. Increased cortical hyperexcitability is observed in animal models of PD (Petzinger et al., 2010). This may result in decreased automaticity of gait as control shifts from subcortical to cortical structures in order to compensate for the impaired ability of the basal ganglia to regulate ongoing movement (Petzinger et al., 2010). The increased reliance on attentional, i.e., cortical, mechanisms for gait and balance could underlie difficulties in concurrently performing cognitive and motor tasks in individuals with PD (Hackney and Earhart, 2009b; Muslimovic et al., 2008; O'Shea et al., 2002). This inability to “walk and talk” is also impaired in some older adults (Woollacott and Shumway-Cook, 2002) and is associated with greater fall risk (Camicioli and Majumdar, 2010). Motor module analysis alone cannot directly reveal changes in the locus of motor control, but comparison of motor modules across behaviors mediated by different neural circuits can be instructive. For example,

young, healthy adults used a common set of motor modules for both overground walking and brainstem-mediated reactive balance responses (Chvatal and Ting, 2013), as well as visually guided anticipatory changes in gait that are likely to be mediated by cortical mechanisms (Chvatal and Ting, 2012). These motor modules may be organized in the spinal cord and then recruited by spinal, brainstem, and cortical inputs. In a small sample of individuals with mild to moderate PD, there were no obvious deficits in the number and structure of motor modules used in either walking or reactive balance. In contrast to young, healthy adults, however, these modules were not shared across behaviors. Moreover, after intensive AT, the number of motor modules common to walking and reactive balance were improved in some individuals (J.L. Allen et al., 2014, Soc. Neurosci., abstract). These results suggest that the automaticity of gait control by subcortical structures is improved by AT (Figure 3C).

Motor module analysis coupled with neuromechanical modeling may allow us to interpret muscle activity during gait and postural tasks in PD patients and provide insight into dysfunction in nondopaminergic brainstem areas implicated in gait control that are now known to degenerate in PD. Postural and gait impairments may be unresponsive to dopaminergic pharmacotherapy, implying that they reflect nondopaminergic pathophysiology—and likely result from interactions between disease processes and compensatory mechanisms and strategies (Bloem et al., 2004). Recent work has also revealed deficits in other brain regions necessary for locomotor control (Mena-Segovia et al., 2004) (Bloem et al., 2001; Bohnen and Albin, 2011; Factor, 2008; Grubli et al., 2012; Melton et al., 2006). In particular, recent attention has focused on the neuroanatomy of brainstem areas including the pedunculo-pontine nucleus (PPN), which degenerates in PD as well as in related disorders such as progressive supranuclear palsy (Lee et al., 2000). The PPN provides cholinergic input to the basal ganglia, brainstem, and spinal cord (Bohnen et al., 2009) and is closely localized to brainstem regions that have been identified in animal models as critical for regulating gait and postural tone (Takakusaki, 2013), and it has been implicated as an upstream cause of abnormal spinal reflexes in PD patients (Meunier et al., 2000). Recent results suggest that this region may represent a promising new target for deep brain stimulation for postural and gait impairments and falls (Moro et al., 2010).

In summary, motor module analysis in PD may facilitate an understanding of the mechanisms of motor dysfunction and rehabilitation in PD. By examining motor modules across different movement types, a patient's ability to appropriately select and modulate motor patterns may be evaluated. Changes in motor modules in response to various pharmacological and neural stimulation interventions may also reveal the neural mechanisms underlying motor deficits. Furthermore, they can be used in conjunction with neurophysiological measures to identify changes in the locus of neural control for movements due to neural degeneration and rehabilitation. As a consequence, the analysis of motor modules in PD and changes through AT may also provide insights into basic mechanisms of motor control and motor plasticity.

Clinical and Scientific Implications

We argue that examining motor modules in motor deficits and during recovery may provide more definite answers to the neural substrates of motor modularity. The degree to which motor modules are encoded by specific neuroanatomical structures or rapidly emerge from neuromechanical interactions remains an open question. Studying rehabilitation in specific neural deficits can help to reveal how motor structure is altered and re-learned through training, revealing processed underlying coordinated neural control of movement. Although motor modules as discussed in this essay may reflect only one aspect of neuromotor control processes, they provide a valuable first step toward analyzing motor patterns as a whole, allowing the previously impenetrable complexity and variability of motor signals to be managed. Computational methodologies that reveal the structure and variability of motor modules could lead to a powerful suite of diagnostic tools for movement that could be used for clinical, preclinical, and high-performance assessment of sensorimotor function. Ultimately, these insights may drive hypothesis-driven neurophysiological and behavioral experiments to identify how and where motor modularity arises in the nervous system.

AUTHOR CONTRIBUTIONS

All authors contributed to conceptualizing the organizational structure, content, and scope of the manuscript and approved the final document. L.H.T. was primarily responsible for writing the manuscript. H.J.C. and R.D.T. contributed to the writing of the scientific portion of the manuscript and editing the entire document. R.D.T., M.E.H., J.L.M., J.L.A., and T.M.K. all contributed to the writing of the clinical portion of the manuscript. L.H.T. and R.D.T. developed Figure 1. L.H.T., J.L.A., and J.L.M. developed Figure 2. L.H.T., H.J.C., J.L.A., and R.D.T. developed Figure 3.

ACKNOWLEDGMENTS

L.H.T. is supported by NIH grants R01 HD46922, R21 HD075612, and R01 HD081274 and by National Science Foundation (NSF) grant EFRI 1137229. H.J.C. is supported by NSF grant IIS-1065489 and NIH grant NS087249. R.D.T. is supported by NIH grants R01 HD081274 and K12 HD055931 and by the Wings for Life Foundation. J.L.A. is supported by NIH grants R01 HD46922 and T32 NS007480-14. J.L.M. is supported by NIH grant R21 HD075612 and by the Atlanta Clinical and Translational Science Institute (ACTSI) KL2-Mentored Clinical and Translational Research Program (NIH KL2TR000455). M.E.H. is supported by NIH grant R21 HD075612, Department of Veterans Affairs R&D Service Career Development Award Level-II (N0870-W), and NSF grant EFRI 1137229. T.M.K. is supported by NIH grant K01 HD079584 and American Heart Association (AHA) Scientist Development grant AHA 13SDG1332000.

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