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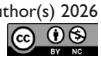

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Post-Stroke Abnormal Synergies Are a Resultant Behavior of the Interplay of Weakness, Spasticity, and Environmental Demands

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Abstract

Abnormal synergies coexist with primary motor impairments (weakness and spasticity) after stroke. They are observed during voluntary movements and are characterized by stereotyped movement patterns, a loss of independent joint control, and abnormal muscle coordination (eg, involuntary activation of distal muscles led by proximal joint movement). The structure and expression of abnormal synergies, however, are highly context-dependent (eg, influenced by gravity, body posture, and task constraints) and are not homogeneous across patients. Current evidence suggests that abnormal synergies are pathophysiologically related to damage to corticospinal tracts, upregulation of brainstem pathways (particularly the medial reticulospinal tract, but also involves the vestibulospinal tract), and maladaptive changes in spinal circuitry. These same mechanisms may overlap with those underlying spasticity and weakness. Spasticity is believed to result from overexcitability of descending excitatory brainstem pathways, the reticulospinal tract in particular, and the consequent exaggerated stretch reflexes, while muscle weakness is attributed to the reduction in corticospinal output. Recent research and clinical observations have advanced our understanding of abnormal synergies. Post-stroke abnormal synergies are not fixed motor impairments. A new framework is proposed that suggests post-stroke abnormal synergies could constitute the behavioral expression of primary impairments, including weakness and spasticity, arising from their interactions with environmental constraints, particularly antigravity control mechanisms. The term "synergy" has been used across various frameworks, with different definitions and quantification approaches. Identifying appropriate methods to quantify abnormal synergies is therefore essential to investigate their relationship with spasticity and muscle weakness, and evaluate potential abnormal synergy improvements following interventions, even if they primarily target other motor impairments.

Keywords

synergy, spasticity, weakness, motor control, motor recovery, stroke

Introduction

Stroke is a leading cause of permanent disability worldwide, with an approximate global prevalence of 94 million people.[1] The major motor impairments after stroke include muscle weakness, spasticity, and abnormal synergies.[2] Abnormal synergies limit independent joint control and directly impair functional movement in the upper and lower extremities.[3] In the upper extremity (UE), for instance, stroke survivors typically cannot move 1 joint (eg, the shoulder) without involuntary activation of others (eg, elbow or wrist), which severely restricts the ability to perform functional tasks such as reaching, grasping, or

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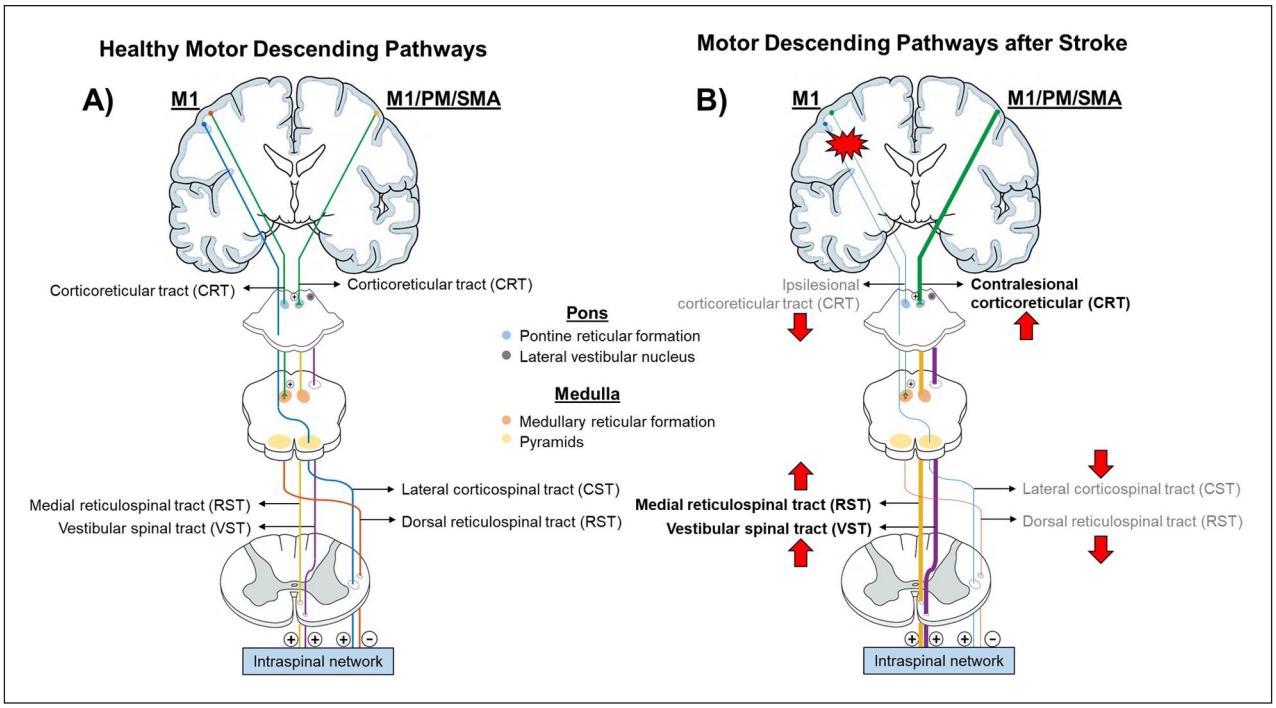

Figure 1. Modified from Li et al[11] on the unifying hypothesis. Major descending pathways for motor control in healthy individuals (A) and how stroke would negatively affect them (B). The corticospinal tract (CST) arises from various sensorimotor cortical regions, particularly the primary motor cortex (M1). The majority (90%-95%) of the CST fibers decussate at the level of the medulla (pyramidal decussation), forming the lateral CST. Main functions of the lateral CST include fine and precise movements. The reticulospinal tract (RST) originates in the pontomedullary reticular formation (PMRF), where it splits into the pontine tract, which forms the medial RST, and the medullary tract, which decussates to form the dorsal RST. The PMRF receives diffused inputs mainly from the ipsilateral motor cortex, including the M1, the premotor (PM), and the supplementary motor area (SMA). One of the main functions of the RST is gross movement and posture. The vestibular spinal tract (VST) originates in the lateral vestibular nucleus. The VST is primarily responsible for mediating postural reflexes and maintaining balance. In addition, the dorsal RST provides an inhibitory effect on the spinal stretch reflex, while the medial RST and VST provide excitatory effects on the spinal stretch reflex. After stroke, the balance of these motor descending pathways is negatively altered. Immediately after stroke, the lateral CST output is decreased, manifest as muscle weakness. During the recovery process, increased outputs from the medial RST and VST, combined with decreased output from the dorsal RST, upregulate the spinal stretch reflex, manifest as spasticity. Abnormal synergies after stroke have been associated with decreased lateral CST, increased descending brainstem pathways, particularly medial RST. Other descending pathways (eg, medial CST, rubrospinal, and tectospinal tract) are not shown here.

manipulating objects.[4] This loss of individuation is most pronounced in distal joints and correlates with greater disability in activities of daily living, such as writing, personal hygiene tasks, or dressing. In the lower extremity (LE), abnormal synergies result in impaired motor control, decreased walking speed, and compromised balance, as the ability to recruit the appropriate muscles for different phases of gait is diminished.[5] Here, abnormal synergies refer to post-stroke stereotyped multi-joint movement patterns characterized by a loss of independent joint control and abnormal muscle coordination during voluntary activation. These are also termed clinical, phenotypic, or post-stroke abnormal synergies. It is important to distinguish these from the term "synergies" widely used in theoretical motor control frameworks, such as modular organization or uncontrolled manifold. Overall, abnormal synergies are a major contributor to post-stroke motor dysfunction, limiting functional independence and recovery.

Muscle weakness and spasticity have been studied more extensively than abnormal synergies because they are more readily quantifiable, have standardized clinical and research assessment tools, and have established therapeutic approaches targeting these impairments.[6,7] In contrast, abnormal synergies after stroke are complex (eg, heterogeneous in their patterns), less easily measured, and lack universally accepted clinical assessment and interventions.[8] Additionally, the pathophysiology of muscle weakness and spasticity has been more characterized, with clear associations to corticospinal tract (CST) damage and altered spinal reflexes, respectively.[9-11] Meanwhile, the neural origins underlying abnormal synergies are likely to involve multifactorial changes affecting both various descending motor pathways (eg, corticospinal and reticulospinal tracts; Figure 1) and maladaptive spinal network plasticity.[4,9,12] Consequently, the neural mechanisms of abnormal synergies remain less characterized, and therapeutic innovations

are limited, although their negative impact on motor performance has been widely documented. Therefore, this article will examine the following topics to improve the understanding of abnormal synergies after stroke:

- Review the pathophysiology of abnormal synergies;
- Examine how abnormal synergies relate to muscle weakness, spasticity, and environmental demands;
- Propose a new framework for understanding how abnormal synergies arise and are expressed;
- Understand different definitions of synergies after stroke; and
- Describe various methods used to assess and quantify synergies after stroke.

Abnormal Synergies and Their Time Course Through Post-Stroke Recovery

More than half a century ago, stroke-induced movement patterns (ie, abnormal synergies) involving multiple joints were clinically described as flexor and extensor synergies.[13,14] In the upper extremity, flexor synergy often includes shoulder retraction/abduction and external rotation combined with elbow flexion, forearm supination, and wrist and finger flexion. In contrast, the extensor synergy typically involves shoulder adduction and internal rotation accompanied by elbow extension, forearm pronation, and wrist and finger extension.[4,13,15] Although stroke recovery trajectories are inherently dynamic and heterogeneous (eg, varying according to baseline patient profiles[16]), the Brunnstrom Recovery Stages remain a consistent framework for describing how movement typically returns after a stroke, regardless of the type of stroke (hemorrhagic or ischemic) or location of the lesion (cortical or subcortical).[13] Motor recovery starts with Stage 1 (ie, Flaccidity), where there is no voluntary movement, and muscles show little or no resistance to passive movement. In Stage 2, spasticity and abnormal synergies (either flexors or extensors) begin to appear. These synergies often happen as weak, uncontrolled reactions or during voluntary attempts to move. Abnormal synergies become most noticeable in Stage 3, where spasticity reaches its highest expression. Flexor or extensor synergies dominate movement, and patients often cannot move their joints independently, limiting functional ability, and coordination. If recovery stops at this stage, the abnormal movement patterns and spasticity will remain, leading to long-term difficulty with daily tasks. In Stage 4, spasticity begins to decrease, and patients start gaining limited control of movement outside of the abnormal synergies. In Stage 5, spasticity decreases further, and more complex and coordinated movements become possible. By Stage 6, spasticity is minimal, and patients can perform isolated joint movements with near-normal coordination. Not all stroke survivors reach Stage 6; many of them plateau in Stages 3 to 5.[17] This classical description provides a fundamental understanding of how abnormal synergies, in parallel with spasticity, emerge, evolve, and eventually are resolved throughout the course of stroke recovery, while also highlighting their interactions with other motor impairments (ie, weakness and spasticity).

Current Understanding of the Underlying Mechanisms of Abnormal Synergies After Stroke

Immediately after stroke, CST output decreases due to direct injury to the tract or its cortical origins, resulting in reduced transmission of voluntary motor commands, especially those required for fine, precise, and individuated movements.[18] The decrease in the CST function is strongly associated with deficits in dexterity, weakness, and muscle individuation, particularly in the distal muscles of the upper extremity.[18] Meanwhile, brainstem motor pathways such as the medial reticulospinal tract (RST) and vestibulospinal tract (VST) become upregulated, a process thought to involve both disinhibition from the lesioned hemisphere (eg, decreased signal from the lesioned corticoreticular tract) and compensatory plasticity from the contralesional hemisphere (eg, increased excitability and structural integrity of these alternative descending pathways).[19-21] Increased reliance on brainstem descending pathways, especially medial RST, could partially compensate for decreased CST function by supporting gross motor strength, particularly in the proximal muscles; however, it does not improve fine motor skills or precise control.[18,21,22] This progressive recruitment of cortico-reticulospinal pathways from the contralesional motor cortices is interpreted as an adaptive strategy that preserves gross motor control at the expense of fine motor control, potentially resulting in stereotyped multi-joint movement patterns.[20,21] Additionally, the RST has inherently broad and diffuse connectivity to multiple spinal motor neuron pools; therefore, its overexcitability in the context of reduced CST output after stroke could lead to the unintended activation of multiple synergistic muscles during attempted voluntary movement.[9] Multiple studies have shown a direct relationship between the alteration of these descending motor pathways with the development of abnormal synergies.[4,20] For instance, in moderate-to-severe hemiparesis, flexion synergy magnitude was proportional to the recruitment of contralesional motor cortices and excessive activation of their ipsilateral reticulospinal pathways, particularly when CST output is diminished.[20] Evidence of reticulospinal involvement is further supported by findings that head rotation, used to assess reticular formation excitability, selectively altered flexor synergy torques in stroke survivors, but not in healthy individuals.[23] Also, diffusion tensor imaging-based metrics, such as fractional anisotropy in the contralesional cortico-reticulospinal

tract, are used to quantify microstructural changes. Greater upper-extremity synergy severity was correlated with a higher RST integrity, which would reflect neuroplastic reorganization of the RST tract in response to CST injury.[24] Moreover, quantitative analyses of stretch reflexes in chronic hemiparetic stroke have shown that flexion synergy is associated with enhanced nonlinear neural connectivity and prolonged time lags in the spinal stretch reflex response, suggesting increased reliance on indirect pathways and maladaptive changes in the spinal circuitry.[12,25] Collectively, these studies showed evidence that after stroke, damage to the cortical descending tracts, upregulation of brainstem pathways, particularly the medial RST, and maladaptive changes in the spinal cord circuitry contribute to abnormal synergies and impaired fine motor control. Although these studies have advanced our understanding of neural substrates underlying post-stroke abnormal synergies, the precise mechanisms and their relation to other motor impairments remain unclear.

Abnormal Synergies and Other Motor Impairments

Abnormal Synergy and Muscle Weakness

Muscle weakness is a "negative" upper motor neuron (UMN) sign following a stroke, reflecting reduced voluntary force generation, while abnormal synergies are considered "positive" UMN signs.[10] Muscle weakness often emerges immediately after stroke and is primarily attributed to reduced CST output. Damage to the CST impairs spinal motor neuron recruitment and is strongly associated with pronounced weakness, particularly in distal muscles.[11,26] Although abnormal synergies could manifest independently of the degree of muscle weakness, and vice versa, the medical literature demonstrates these phenomena often co-occur and may share overlapping neural substrates, particularly damage to the CST. For instance, experimental studies showed that providing arm support reduces the expression of abnormal synergies during shoulder abduction tasks, likely by decreasing the demand on proximal muscles against gravity and altering neural recruitment, showing an indirect relationship between these 2 motor impairments.[27,28] Also, abnormal synergies may exacerbate functional weakness by limiting the ability to isolate joint movements, especially in the upper limb, where attempts to activate 1 muscle group involuntarily recruit others, reducing effective strength and control. Additionally, the overexcitability of the RST following the CST injury can contribute to impaired balance of the muscle strength across antagonistic muscles, potentially contributing to abnormal synergies.[21,29] For example, a non-human primate study reported that after recovery from CST lesions, the RST output increases in motor neurons innervating forearm flexor and intrinsic hand muscles, but not in forearm extensors.[22] Similarly, another study in healthy monkeys demonstrated projections of the RST facilitate activity of biceps and anterior deltoid fibers, but suppress triceps activity.[30] Together, these findings suggest brainstem pathways, particularly the RST, could promote partial functional recovery in specific muscle groups. Initially, muscle weakness after stroke results primarily from CST disruption. Later, as recovery progresses, maladaptive RST overexcitability, along with partial CST recovery, could enhance strength in some muscles (eg, forearm flexors). Nevertheless, other muscles (eg, forearm extensors) would depend mainly on CST recovery with limited or no support from the RST. In summary, muscle weakness and abnormal synergies could be interrelated consequences of stroke, potentially sharing mechanisms. For instance: (1) greater compensatory recruitment of brainstem pathways due to weakness, particularly against gravity, may elicit multi-joint coupling; and (2) the differential effects of RST overexcitability across muscle groups may simultaneously contribute to both imbalanced strength and stereotyped movement patterns. Nevertheless, the mechanistic interplay between both phenomena remains to be fully elucidated.

Abnormal Synergy and Spasticity

Spasticity and abnormal synergies are considered "positive" UMN signs, and they often co-occur after stroke, both contributing to deficits in voluntary movement and functional disability.[11] Li et al[11] proposed a new definition of spasticity:

> Spasticity is manifested as velocity- and muscle length—dependent increase in resistance to externally imposed muscle stretch. It results from hyperexcitable descending excitatory brainstem pathways and from the resultant exaggerated stretch reflex responses. Other related motor impairments, including abnormal synergies, inappropriate muscle activation, and anomalous muscle coactivation, coexist with spasticity and share similar pathophysiological origins.

This definition includes the pathophysiology of spasticity after stroke and its potential relationship with other motor impairments. Spasticity is commonly assessed with clinical scales such as the Modified Ashworth Scale and the Modified Tardieu Scale during passive movements.[31] Currently, there is no clinical assessment for spasticity during voluntary movement. In contrast, abnormal synergies are often assessed during voluntary movement. Clinical studies suggest that abnormal synergy is the predominant contributor to movement dysfunction during active tasks, whereas spasticity is more apparent during passive or supported movements and may be less functionally relevant in these contexts.[4,32] Spasticity has been associated with

hyperexcitability of descending brainstem pathways, particularly the medial RST, but also involves the VST and adaptations within spinal circuits.[10,33] Clinical and neurophysiological findings indicate that the loss of inhibitory cortical control leads to disinhibition and upregulation of these descending pathways, enhancing excitatory drive to spinal motor neurons and increasing the stretch reflex, manifesting as spasticity.[9,33] Emerging evidence suggests abnormal synergies and spasticity could partially share neural mechanisms,[12,25,34] particularly the RST, although other pathways are also involved.[11] For instance, a recent work showed that when stroke survivors voluntarily abduct their shoulder, involuntarily co-activating of the elbow flexors (ie, expression of post-stroke abnormal synergy), simultaneously potentiates stretch reflex hyperactivity at the elbow (ie, a hallmark of spasticity), providing convergent evidence of shared neural mechanisms between abnormal synergies and spasticity.[25] Also, hyperexcitability of brainstem pathways may simultaneously increase background muscle activity, contributing to spasticity, and promote coupled activation of functionally related muscles, giving rise to abnormal synergies. Electromyographic (EMG) studies show spastic muscles have higher baseline activity and more synchronous recruitment of motor units, with lower variability and increased activation in response to stretch, reflecting increased motoneuron excitability and prolonged excitatory postsynaptic potentials.[9,35] The heightened excitability makes spastic muscles more readily activated compared to non-spastic muscles, leading to involuntary muscle activation in response to minimal stretch or synaptic input.[36] Additionally, impaired reciprocal inhibition and persistent high excitability in spastic muscles reduce their ability to modulate activity in response to task demands, further promoting involuntary co-activation during attempted voluntary movement.[19,37] From a motor control perspective, the threshold control theory, for example, offers a complementary framework for understanding the relationship between spasticity and abnormal synergies. This theory proposes that the nervous system controls movement by regulating the tonic stretch reflex threshold (TSRT; ie, the muscle length at which the motoneuron recruitment starts at zero velocity of stretch[38,39]). After stroke, the range of TSRT regulation is reduced, falling within the biomechanical range (ie, muscles become involuntarily activated by stretch at joint angles where they should remain silent, manifesting as spasticity[38]). Notably, recent evidence showed that TSRT and the velocity-sensitivity (μ) explained a substantial portion of the variance in FMA-UE scores assessing in-synergy and out-of-synergy movements exclusively, providing further evidence of a close link between spasticity and abnormal synergies.[40] Overall, while abnormal synergy and spasticity often interact and may share neural substrates, the precise nature of their relationship (eg, whether they represent related yet distinct clinical phenomena or constitute different manifestations of the same underlying mechanism) remains to be elucidated. Thus, understanding this interplay is essential for advancing both assessment and effective rehabilitation strategies in post-stroke motor impairment.

Are Abnormal Synergies Fixed and Context-Independent Patterns?

Although flexor and extensor synergies are among the most common abnormal multi-joint patterns observed after stroke, research demonstrates abnormal synergies are not fixed but stereotyped, context-dependent patterns. Research demonstrates abnormal synergies can be selectively activated depending on context, and some individuals retain the ability to perform out-of-synergy movements, even for severely-impaired stroke survivors.[4,41,42] Also, rehabilitation and task-specific training can alter the structure and expression of abnormal synergies, showing they are dynamic and subject to neuroplastic change.[43,44] Overall, abnormal synergies are stereotyped but not fixed, varying according to multiple factors (eg, body posture, motor task, recovery phase, and level of impairment).

First, body position or posture can modulate the degree of abnormal synergy expression. For instance, abnormal synergy expression is typically less pronounced in the supine position (eg, lying in bed) but increases in sitting, with the greatest expression seen during tasks requiring antigravity control and postural stability, such as standing.[45] This is consistent with Brunnstrom's original descriptions, which emphasized that the ability to move out of synergy and perform isolated joint movements is context-dependent and often more restricted in positions requiring greater postural control or weight-bearing. In standing, the need for antigravity control and balance could further increase the intensity of abnormal synergies, often resulting in maximal expression of stereotyped joint linkages and reduced ability to isolate movements.[46,47] For example, a stroke survivor may show mild shoulder-elbow coupling (ie, flexor synergy) when lying in bed, but when sitting, elbow flexion might become more tightly linked to shoulder abduction, and in standing, wrist and finger flexion may also be involuntarily recruited as part of the synergy. For the lower limb, the extensor synergy links hip extension, adduction, internal rotation, knee extension, and ankle plantarflexion. In supine, a patient may be able to extend the knee with less involuntary hip adduction. In sitting, voluntary knee extension is more likely to be accompanied by involuntary hip adduction and ankle plantarflexion. In standing, these linkages are most intense, with attempts at knee extension resulting in strong, stereotyped activation of the entire extensor synergy pattern. Thus, the intensity and composition of these joint linkages increase with upright posture and greater postural demand.

Second, clinical studies using robotic exoskeletons and kinematic analysis have shown abnormal synergies after stroke are highly task dependent. A stroke study showed synergy-driven activation is typically stronger when elicited via proximal joints (eg, shoulder or elbow) and weaker when initiated at distal joints (eg, wrist or fingers).[4] Another study, which used a robotic exoskeleton, showed that the degree and pattern of abnormal joint coupling in stroke survivors varied depending on the specific reaching task, with multi-joint coordination impairment most pronounced during outward reaching movements, and the abnormal synergy expression varied between different movement directions and joint involvement, indicating that abnormal synergies are sensitive to task demands.[48] Recently, it was shown the ability to isolate joint movements and the manifestation of abnormal synergies differed between constrained (single-joint) and unconstrained (multi-joint) movement conditions, with more pronounced abnormal coupling in tasks requiring distal joint individuation.[42] Furthermore, by analyzing Fugl-Meyer assessment (FMA) scores, a study found some individuals with severe impairment could selectively suppress abnormal synergies depending on the voluntary activation context (eg, keeping the elbow extended during shoulder loading), demonstrating abnormal joint-coupling could be selectively excited or inhibited based on task conditions.[41]

Furthermore, the expression of abnormal synergies can change over time and with rehabilitation. Longitudinal studies have demonstrated that with targeted therapy, patients can achieve greater joint individuation and reduced abnormal joint coupling, indicating synergy patterns are not static but can be tuned or altered through motor learning and recovery processes. A randomized clinical trial found that adding robotic therapy to standard rehabilitation resulted in greater improvement in UE flexor synergy compared to adding self-guided therapy at the beginning of the training in moderately impaired subacute stroke survivors.[49] Moreover, robotic-assisted therapy could improve shoulder and elbow movements and reduce abnormal joint coupling in chronic stroke survivors, suggesting reduced abnormal synergy expression.[43]

In summary, post-stroke abnormal synergies are stereotyped but dynamic, context-dependent patterns rather than fixed deficits. Collectively, these findings underscore that abnormal synergies vary with body posture and environmental demands, highlighting the need for further study of their interaction with other motor impairments and contextual factors that may influence abnormal synergy expression, to inform more precise assessment and targeted interventions.

Pathophysiology of Abnormal Synergies after Stroke

Based on the previous information, it can be stated that abnormal synergies:

- Often co-occur with other motor impairments (ie, spasticity and muscle weakness);
- Are observed only during voluntary activation;
- Their structure and expression are highly context-dependent (eg, influenced by gravity, body posture, and task constraints); and
- Are not homogeneous across patients.

Therefore, muscle weakness, spasticity, and task/environment demand appear to be key contributors to the phenomenon where multiple muscles are activated together (ie, abnormal synergies), some voluntarily and others involuntarily. First, the damage to the cortex and to its descending CST may lead to a lack of individuation of muscle control and limited joint mobilization. Second, spasticity is associated with hyperexcitability of the stretch reflex circuits and decreased inhibitory control, which often lowers the threshold for involuntary motor unit firing of synergistic muscles, promoting stereotyped multiple muscle activation. Third, gravity imposes a constant load on the musculoskeletal system, and the neural control of posture and movement compensates for or exploits this load to maintain stability and efficiency.[50] The medial RST and VST are key descending pathways to control posture and balance for gravity and antigravity control. After stroke, their excitability is increased, compensating to some extent for posture and balance but sacrificing individual muscle and joint control. From this perspective, the expression of abnormal synergies may not represent an isolated motor impairment, but rather the result of other fundamental impairments and their interaction with environmental constraints.

In patients with spasticity, the lowered threshold of spinal reflex circuits and increased coactivation of functionally related muscles can result in stereotyped postures that reflect maladaptive antigravity control during standing and walking.[4,45] These postures are not optimal but could represent a maladaptive strategy to ensure joint and postural stability in the presence of impaired selective motor control and weakness.[51] The medical literature demonstrates that both neural and biomechanical factors interact with gravitational forces to shape postural and movement patterns in individuals with UMN syndromes, including those with spasticity and abnormal synergies.[52,53] Here, we provide 2 case examples showing that nerve blocks aimed at reducing spasticity in the upper extremity can lessen the expression

Figure 2. Two clinical observations illustrating changes in abnormal synergy as a result of joint postures. (A) Decrease in involuntary activation of elbow flexors after nerve block for spastic shoulder abductors (supraspinatus muscles). (B) Decrease in involuntary activation of shoulder extensors after nerve block for spastic elbow flexors.

of abnormal synergies during standing and walking. In the first case, the primary problem of this stroke survivor was a spastic supraspinatus muscle, which causes abnormal shoulder abduction during standing and walking. Shoulder abduction is accompanied with the involuntary activation of elbow flexors. Elbow flexion, instead of full extension, generates less torque to the shoulder joint. After effective reduction of spasticity on the supraspinatus muscle following the block of the suprascapular nerve, involuntary abnormal elbow flexor activity was greatly decreased, and the elbow joint was immediately in a more extended position. As such, the arm generates less torque acting on the shoulder joint (Figure 2A). In this case, no intervention targeted the elbow flexors. Reduction in involuntary elbow flexion (abnormal synergy) occurs as a result of a change in shoulder joint posture after nerve block for the management of the supraspinatus muscle spasticity. Similarly, in the second case (Figure 2B), a stroke survivor with left spastic

hemiplegia had involuntary shoulder extension in the presence of elbow flexor spasticity and spastic elbow flexion. After elbow flexor spasticity was reduced by nerve block to the musculocutaneous nerve, the shoulder joint immediately returned to the neutral position without any intervention. In this case, the shoulder extension was involuntary and reactive to minimize the torque the arm may generate in the frontal plane before the nerve block. In these 2 examples, involuntary activations of elbow flexors (Figure 2A) and of shoulder extensors (Figure 2B; ie, abnormal synergies) present to minimize mechanical consequences from the interactions between spastic muscle activation, weakness, and gravity. Similar cases are seen in the lower extremity as well.[54]

Proposed Framework: Abnormal Synergies as the Interplay of Primary Impairments and Antigravity Control

Several studies have examined post-stroke motor impairments—such as weakness, spasticity, and abnormal synergies—typically treating them as separate clinical entities. Contemporary research, however, increasingly recognizes these features as interrelated components of a complex syndrome,[9,55] though the precise nature of these interactions and the degree to which their underlying mechanisms overlap remain incompletely understood. While these impairments often coexist, they may behave differently under varying conditions (eg, passive vs. voluntary movements). Based on the existing literature and our clinical case examples, we propose a new theoretical framework suggesting that post-stroke abnormal synergies are not isolated phenomena, but rather could constitute the behavioral expression of primary impairments, including weakness and spasticity during voluntary activation arising from their interaction with environmental constraints, particularly antigravity control mechanisms.

Clinically, the proposed framework would imply that the management of weakness, spasticity, and abnormal synergies should be integrated rather than addressed in isolation, considering biomechanical constraints—such as gravity and postural load—within assessment and treatment planning. Ultimately, understanding how these impairments interact will allow clinicians to refine diagnostic accuracy, tailor treatment plans, and promote more meaningful functional gains. From a research perspective, this integrated perspective could generate future hypotheses and offer new methods of quantitative exploration of abnormal synergies that would go beyond stating their presence or absence. In addition, subsequent protocols should be carefully designed to account for the interplay of impairments within intervention strategies or assessment studies. Nevertheless, to translate this integrated perspective into future research, it is first necessary to identify the quantification methods established in the literature and evaluate which could capture these complex interactions. This naturally raises an important question: what can be an appropriate method to quantify abnormal synergies?

Quantification of Synergies After Stroke

Synergies after stroke have been quantified using a variety of approaches, which largely depend on how "synergies" are defined. From a phenotypic perspective, abnormal synergies are stereotypical, multi-joint movement patterns; thus, clinical and objective assessments have been proposed to evaluate them (Figure 3A). Meanwhile, different theoretical frameworks offer alternative definitions of synergies and suggest distinct, quantifiable methods for their investigation (Figure 3B). Consequently, approaches to quantify and investigate synergies after stroke vary according to the underlying definition, reflecting the absence of a standardized consensus.

Clinical and Objective Assessment Methods

As recommended by the American Heart Association/American Stroke Association, the FMA is widely used in stroke rehabilitation and is considered the gold standard to assess generalized sensorimotor impairment after stroke, as supported by systematic reviews and consensus in the rehabilitation literature.[41,56] Following the description of how voluntary movement returns post stroke by Twitchell's and Brunnstrom's studies, the FMA was proposed to track the recovery stages after stroke. Consequently, while the FMA provides a broad measure of motor impairment, it has been considered as an indirect indicator of abnormal synergies in multiple studies.[41,50,57] Indeed, the FMA-UE (section A) and the FMA-LE (section E) include specific synergy-related assessments (ie, volitional movement within synergies [flexor and extensor synergies], volitional movement mixing synergies, and volitional movement out of synergy). Higher scores on the FMA often reflect less abnormal synergies and better voluntary motor control, making it a clinical useful indirect assessment to characterize abnormal synergies.

Meanwhile, abnormal synergies from a phenotypic perspective can be more objectively quantified by measuring involuntary joint activity during voluntary activation of a target joint, using tools like EMG, robotics, and motion capture systems. For example, one of the most common approaches in the UE involves measuring involuntary torque or EMG activity at the elbow, wrist, or fingers during progressive shoulder abduction loading, often using robotic or instrumented setups. These methods precisely measure

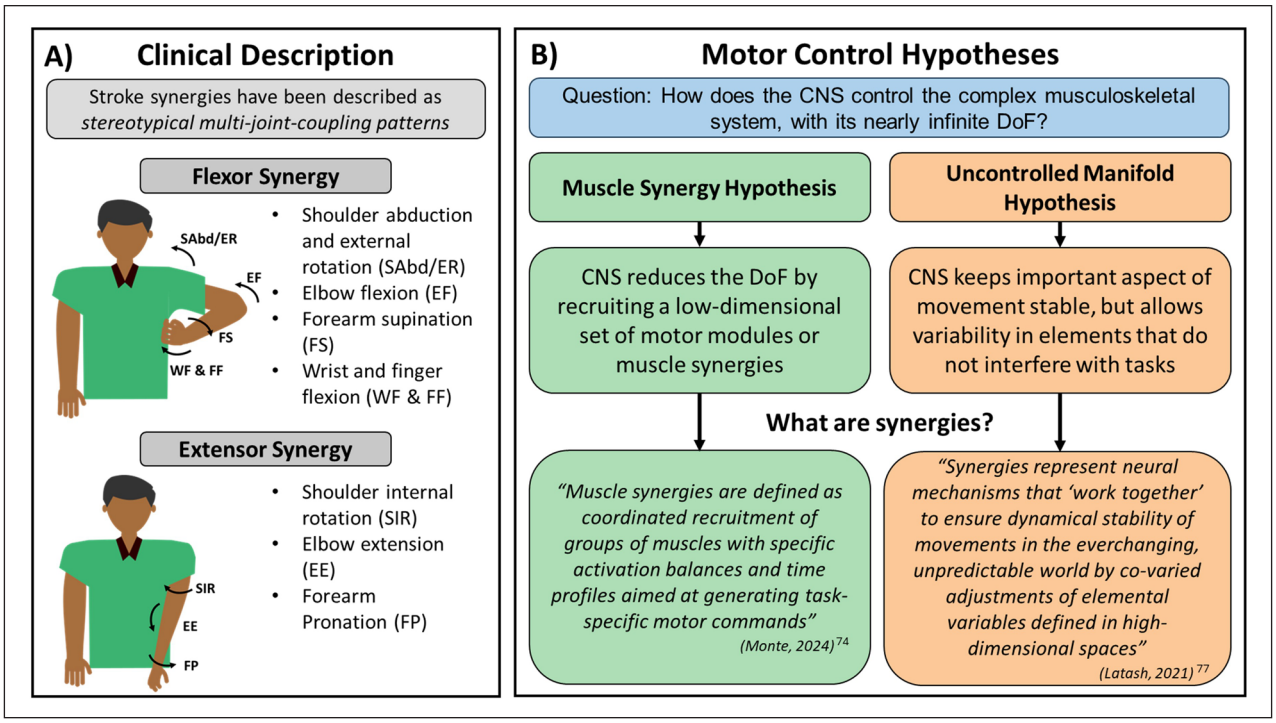

Figure 3. Different approaches to investigate synergies after stroke. (A) Clinical description of the pathophysiology expression of abnormal synergies after stroke and the 2 most common abnormal multi-joint-coupling patterns (ie, flexor and extensor synergies). (B) Two common theoretical frameworks based on motor control theory that aim to explain how coordinated movement is achieved in healthy individuals and how it is negatively affected after neurological injury. These theoretical frameworks represent computational constructs that can provide a deeper insight into the organization and neural control of movement and may reveal pathophysiological mechanisms not accessible by standard clinical scales (eg, Fugl Meyer Assessment). However, they are not direct measures of phenotypic abnormal synergies; therefore, they should not be treated as interchangeable measures of the same phenomenon.
Abbreviations: CNS, central nervous system; DoF, degree of freedom.

the extent of involuntary flexion at the elbow or wrist, frequently expressed as a percentage of maximum voluntary torque or EMG activity, to quantify synergy severity.[15,58,59] Additional innovations, like the abnormal flexor synergy index derived from 3D motion capture, have enhanced this evaluation by correlating motion data with clinical scales (eg, FMA-UE).[60]

Research Approaches Based on Theoretical Frameworks

Beyond clinical and classification-based assessments, different theoretical motor control frameworks have been employed to investigate synergies after stroke. Understanding how the CNS controls the complex musculoskeletal system, with its nearly infinite degrees of freedom, has led to the development of different motor control hypotheses.[61,62] These frameworks aim to explain how coordinated movement is achieved in healthy individuals and how it is negatively affected after neurological injury, offering valuable insight into mechanisms of motor impairment and recovery.[63,64] Among these, 2 common frameworks for investigating motor control after neurological injury are the modular organization (ie, muscle synergy) and the uncontrolled manifold (UCM) hypotheses.[3,62,64,65]

The Muscle Synergy Hypothesis

This hypothesis states the CNS controls movements by recruiting coordinated groups of muscles (ie, muscle synergy patterns), which function as motor modules to simplify control of the complex musculoskeletal system during different motor tasks.[66-68] Muscle synergies are often investigated using computational methods such as non-negative matrix factorization or principal component analysis applied to EMG data.[69,70] Research on muscle synergies began with the observation that the CNS might simplify motor control by activating groups of muscles together as functional units, rather than controlling each muscle independently. Early work in neurophysiology and motor control identified these coordinated patterns, termed "muscle synergies," as motor primitives that could be flexibly combined to produce a wide repertoire of movement.[68,71]

The muscle synergy concept (see definition in Figure 3B) has been supported by more than 2 decades of experimental and computational studies in animals and humans, showing that a small number of synergies could successfully account for most of the variability in muscle activation during complex tasks.[68,72-74] Muscle synergy consists of 2 components, which together characterize the modular organization of motor control[67,68,73]: (1) muscle synergy patterns, defined as a fixed ratio of muscle coactivation across multiple muscles required to perform voluntary movements; and (2) their activation profiles that describe how each of these patterns is recruited over time to produce movement. Muscle synergy analysis offers a powerful framework for understanding how stroke affects motor control. While healthy individuals and stroke survivors exhibit low-dimensional patterns of muscle activation, stroke often alters the structure, number, or activation of these synergies, leading to impaired motor function.[65,75] Some of the muscle-synergy-based metrics have been correlated with standardized clinical scores (eg, the FMA), and with functional outcomes.[3] Therefore, the muscle synergy hypothesis has become a valuable tool for quantifying post-stroke motor deficits, tracking recovery, predicting rehabilitation outcomes, and developing novel interventions.[3,76]

The Uncontrolled Manifold (UCM) Hypothesis

The UCM hypothesis is another leading framework in motor control, explaining how the CNS could orchestrate movement. It proposes the CNS takes advantage of the musculoskeletal system's natural abundance to stabilize relevant aspects of movement, while allowing variation in other elements.[77] This hypothesis reframes the "degrees of freedom problem" by suggesting that instead of the CNS reducing the degrees of freedom to achieve a "unique" solution, the CNS exploits the abundance of available elements (eg, muscles, joints, or motor units) to create flexible, stable, and adaptive motor behaviors.[62,77,78] Within this framework, synergies are not merely patterns of muscle co-activation but reflect a purposeful neural organization that manages variability along dimensions that do not interfere with motor performance (see definition of motor synergies in Figure 3B).

These motor synergies can be quantified using the UCM framework by partitioning the total variance of elemental variables across repeated trials into two components: variance within the UCM (V_{UCM}), which does not affect the performance variable, and variance orthogonal to the UCM (V_{ORT}), which affects the performance variable, reflecting instability.[79] The synergy index is typically calculated as ($V_{UCM} - V_{ORT}$)/total variance. A higher value (strong synergy) indicates greater flexibility, meaning that multiple movement patterns are available to achieve the same task. This flexibility is beneficial for support adaptation to changes due to external perturbation or intrinsic system properties.[80] In healthy individuals, predominance of V_{UCM} over V_{ORT} demonstrates the CNS effectively organizes variability to stabilize task performance. This approach has been validated across various motor tasks, including finger force production, multi-joint coordination, and postural control.[78]

In stroke, the UCM framework explains altered synergies after stroke as a loss of flexibility in motor coordination: the nervous system may fail to exploit the uncontrolled manifold, resulting in stereotyped, task-constraining coactivation patterns and diminished independent joint control. Variability from joint or muscle activity can be separated into "good variability" (V_{UCM}), which preserves task performance, and "bad variability" (V_{ORT}), which destabilizes it. In healthy individuals, V_{UCM} typically exceeds V_{ORT}, reflecting strong synergies and stable performance. After stroke, this balance may shift, leading to lower synergy indices and reduced ability to stabilize movement outcomes. For instance, in bilateral isometric force control tasks, stroke survivors show decreased V_{UCM} and increased V_{ORT}, particularly at higher force levels, resulting in greater force errors and poorer coordination between limbs.[81] Similarly, during upper limb reaching, they exhibit lower synergy indices for both kinematic and kinetic coordination compared with healthy individuals, indicating a reduced capacity to use redundancy for successful movement.[48] Recently, the UCM has been suggested as a novel biomarker of movement quality in neurorehabilitation due to its ability of describing movement in spatial and time domains.[82] Overall, the UCM framework demonstrates stroke may compromise motor variability organization, which can result in weaker synergies and a reduced ability to exploit the motor system's abundancy, potentially decreasing movement stability; however, this disruption is not consistently observed across all stroke survivors or tasks, as some studies report unchanged synergy indices post-stroke.[80]

Both theories converge on the idea that altered synergies following stroke reflect disrupted neural organization and impaired motor control, with the muscle synergy hypothesis emphasizing changes in the composition and activation of muscle groups, and the uncontrolled manifold hypothesis highlighting loss of adaptive variability and increased rigidity in motor output. These frameworks are widely used to interpret physiological and biomechanical data (eg, EMG, kinetics, or kinematics) in stroke research and guide the development of targeted interventions. Although theory-based methods can provide a deeper insight into the organization and neural control of movement, the relationship between theoretical frameworks (eg, muscle synergy or UCM hypotheses) and phenotypical abnormal synergies (eg, flexor and extensor synergies) and environmental constraints is not yet well understood.

Concluding Remarks

In summary, understanding and accurately characterizing post-stroke abnormal synergies is essential for research and clinical practice. Here, we highlight four principal considerations to guide future post-stroke abnormal synergy studies. First, due to the lack of a consensus in the definition and quantification of synergies after stroke, it is imperative to clearly define them and how they are quantified in any synergy study. Second, we proposed that from a pathophysiology perspective, abnormal synergies may represent the observable manifestation of the interplay of primary motor impairments (weakness and spasticity) and their interaction with the environmental constraints, especially antigravity control mechanisms, rather than an isolated motor impairment. Naturally, the manifestation of this interplay might vary across individuals depending on several factors (eg, lesion characteristics, CST integrity, chronicity, level of motor impairment, and the motor task under examination). This model is intended to provide a unifying framework that can guide the interpretation of existing findings, support the formulation of future research questions, and facilitate the development of targeted rehabilitation strategies aimed at modulating abnormal synergies and related motor impairments. Third, if the goal of a research study is to investigate the phenotypic presentation of abnormal synergies itself, or its relationship with other motor impairments (eg, weakness, spasticity, and impaired dexterity, among others), clinical assessments and simple objective measurements are preferable, as they are grounded in the underlying pathophysiology. On the other hand, although theoretical motor-control frameworks (eg, motor module and UCM) can provide a deeper insight into the organization and neural control of movement, potentially revealing pathophysiological mechanisms not accessible through standard clinical scales, they do not directly quantify phenotypic abnormal synergies. Rather, they provide complementary information such as coordination patterns, variability structure, task stabilization, and movement quality after stroke. Therefore, these frameworks should not be treated as interchangeable with measures of phenotypic abnormal synergies. Finally, if the goal is to develop novel interventions, both simple objective metrics and theory-based methods have shown the potential to promote the development of customized rehabilitation strategies reducing motor impairment by modulating synergy characteristics.[3,58,76]

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