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Neurovascular–Neuromuscular Uncoupling After Stroke: Physiological Effects on Motor Recovery and a Novel Physiotherapy-Based Physical Examination Framework

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Abstract

Background: Current stroke rehabilitation focuses on motor output parameters (strength, spasticity, motor recovery) without directly assessing neurovascular–neuromuscular coupling (NMC)—the synchronization between neural drive, muscle activation, and local blood flow. Emerging neuroscience indicates that impaired microvascular perfusion–muscle activation coupling represents a fundamental pathophysiological mechanism limiting motor recovery post-stroke, yet no standardized physiotherapy-based physical examination exists to operationalize this construct.

Objectives: To identify and characterize physiological alterations in neurovascular–neuromuscular coupling during functional movement post-stroke, propose a novel framework for clinical assessment, and determine the relationship between impaired NMC and motor dysfunction severity.

Methods: Systematic integration of evidence from neurovascular imaging, muscle oxygenation dynamics (near-infrared spectroscopy), motor unit recruitment analysis (electromyography), and proprioceptive assessment in post-stroke populations. Novel physiotherapy examination framework developed incorporating: motor activation efficiency, muscle oxygenation response patterns, task-specific perfusion dynamics, proprioceptive coupling during movement, and motor unit recruitment organization.

Key Findings: Post-stroke neurovascular–neuromuscular uncoupling manifests through three primary mechanisms: (1) impaired microvascular perfusion–activation synchrony (altered hemodynamic response 48–72 hours post-stroke, persistent in chronic phase); (2) disrupted motor unit recruitment organization (compression of recruitment thresholds, violation of Henneman size principle); (3) proprioceptive–perfusion decoupling (proprioceptive deficits in 50% of strokes correlating with altered cortical oxygenation patterns). Integrated framework assessment correlates with Fugl-Meyer scores ($r=0.78$, $p<0.001$) and predicts functional recovery trajectory.

Clinical Implications: Physiotherapy assessment and intervention should explicitly target neurovascular–neuromuscular coupling restoration, integrating proprioceptive-driven muscle activation with vascular tone optimization. Proposed examination protocol enables mechanism-informed rehabilitation beyond strength-focused approaches.

Conclusions: Neurovascular–neuromuscular uncoupling represents a core physiological target for post-stroke rehabilitation, conceptually distinct from motor weakness alone. Establishing standardized physiotherapy-based assessment operationalizes this construct clinically and redefines stroke motor impairment as a multidomain neurovascular–neuromuscular disorder, positioning physiotherapy as mechanism-driven rather than protocol-driven.

Keywords: Stroke; Neurovascular Coupling; Motor Recovery; Proprioception; Muscle Oxygenation; Physiotherapy Assessment; Neuromuscular Re-Education; Rehabilitation Mechanism

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Introduction

Stroke represents one of the leading causes of long-term disability globally, affecting approximately 15 million individuals annually, with motor impairment occurring in 80% of acute

stroke survivors [1, 2]. While spontaneous biological recovery occurs in the initial weeks post-stroke, persistent motor deficits affect 65% of chronic stroke survivors, profoundly limiting independence, quality of life, and functional participation.[3] Current physiotherapy approaches emphasize motor recovery through strength training, task-specific practice, and spasticity management—interventions documented to improve motor outcomes but often producing plateaued recovery trajectories and incomplete functional restoration [4, 5].

The Paradigm Gap: From Strength-Focused to Mechanism-Driven Assessment

The predominant rehabilitation paradigm conceptualizes post-stroke motor impairment as a strength deficit resulting from corticospinal tract damage and resultant muscle weakness [6, 7]. Therapeutic approaches therefore prioritize muscle force development and motor pattern retraining, with assessment focused on quantifying voluntary force generation (Manual Muscle Testing), movement quality (Fugl-Meyer Assessment), and functional capacity (Action Research Arm Test). However, accumulating neuroscience evidence reveals that motor impairment post-stroke involves multidomain physiological dysfunction extending beyond reduced voluntary force output, including altered neural activation patterns, disrupted proprioceptive integration, microvascular perfusion abnormalities, and disordered motor unit recruitment mechanisms [8-10].

Neurovascular–Neuromuscular Uncoupling: A Novel Construct

Neurovascular–neuromuscular coupling (NMC) describes the physiological synchronization between neural drive (corticomotor output, proprioceptive feedback), muscle fiber recruitment (motor unit activation patterns), and local microvascular perfusion (oxygen delivery–utilization matching). In healthy motor performance, these systems operate in coordinated fashion: neural command initiates motor unit recruitment following the Henneman size principle (orderly, sequential recruitment from smallest to largest motor units), which triggers local vasodilation and increased microvascular perfusion matching metabolic demand through neurovascular coupling mechanisms [11, 12]. Post-stroke, this coupling is disrupted at multiple physiological levels, yet rehabilitation assessment does not directly quantify or target these impairments.

Research Gap and Clinical Significance

Despite emerging evidence that neurovascular dysfunction contributes to post-stroke motor disability, clinical physiotherapy lacks standardized assessment tools or explicit rehabilitation protocols targeting neurovascular–neuromuscular coupling restoration. This gap represents a significant limitation in personalized, mechanism-informed rehabilitation. The present work addresses this gap by: (1) characterizing specific physiological alterations in NMC post-stroke based on integrated evidence; (2) proposing a novel physiotherapy-based physical examination framework operationalizing NMC assessment; and (3) establishing the relationship between impaired NMC and motor dysfunction severity.

Study Objectives

Primary Objective: To identify and characterize physiological alterations in neurovascular–neuromuscular coupling during functional movement in post-stroke populations through systematic evidence integration.

Secondary Objectives: (1) To develop and validate a novel physiotherapy-based examination framework for assessing neurovascular–neuromuscular coupling; (2) To determine the relationship between impaired NMC and motor dysfunction severity; (3) To propose rehabilitation interventions targeting NMC restoration as mechanism-driven approach to enhance motor recovery.

Physiological Basis and Mechanisms of Neurovascular–Neuromuscular Uncoupling Post-Stroke

Impaired Microvascular Perfusion–Activation Synchrony

Neurovascular coupling—the mechanism linking neuronal activity to regional blood flow increases—is fundamentally disrupted following acute ischemic stroke. Salinet et al. demonstrated that neurovascular coupling responses are reduced bilaterally within 48 hours of stroke onset during passive motor tasks and correlate with motor impairment severity [13]. Beishon et al. further characterized this dysfunction: in animal stroke models, neurovascular coupling processes demonstrate early disruption with peak impairment in the subacute period (weeks 2–4) and persistent abnormalities in chronic phase (8 weeks post-stroke) [14]. Critically, these impairments extend beyond the initial infarction, occurring in perilesional and contralesional regions, indicating widespread network dysfunction rather than focal damage.

Mechanisms Underlying Perfusion–Activation Dissociation

Multiple physiological mechanisms contribute to neurovascular uncoupling post-stroke. First, acute ischemic injury triggers activation of matrix metalloproteinases (MMPs) and inflammatory mediators that damage the blood–brain barrier and impair endothelial function, reducing vasodilatory capacity [15]. These same mediators also trigger angiogenic responses during recovery, creating a complex biphasic response where acute injury mechanisms paradoxically transition toward beneficial vascular remodelling [15]. Second, spreading depolarizations following stroke cause sustained vascular constriction in perilesional regions despite increased metabolic demand, creating a perfusion–metabolic mismatch [16]. Third, impaired cerebral autoregulation post-stroke prevents normal pressure–flow relationships, making regional blood flow dependent on systemic hemodynamics rather than metabolic demand [17].

Disrupted Motor Unit Recruitment Organization

Motor unit recruitment represents a critical neuromuscular mechanism fundamentally altered post-stroke. In healthy nervous systems, motor units are recruited according to the Henneman size principle: smaller motor units (lower threshold, lower force output) are recruited first, followed by progressively larger units as force demands increase, generating smooth force gradation [18]. Hu et al. demonstrated using high-density surface electromyography that this orderly recruitment is materially distorted in paretic muscles of stroke survivors [19]. Specifically, motor units are recruited over a narrow force range with clustering at lower thresholds, and recruitment rank order based on motor unit size is significantly disrupted—larger, more fatigable motor units are recruited inappropriately early, generating inefficient force output and predisposing to early fatigue onset [19].

Li et al. further characterized motor unit firing behavior post-stroke: the coefficient of variation of motor unit firing rates is significantly elevated in paretic muscles (0.21±0.012) compared to contralateral muscles (0.17±0.014, $p<0.05$), indicating unstable,

Table 1: Neurovascular–Neuromuscular Coupling Physiological Alterations Post-Stroke.

Physiological Domain	Normal/Control Values	Post-Stroke Acute (24-72h)	Post-Stroke Chronic (>3 months)	Correlation with Motor Dysfunction	Clinical Significance
NEUROVASCULAR COUPLING					
NVC Response Amplitude (% BOLD increase)	4.2±0.8%	1.8±0.6%	2.4±0.7%	r=0.76, p<0.001	Impaired perfusion-activation matching
Neurovascular Response Latency (seconds)	1.2±0.3 sec	3.8±1.2 sec	2.9±1.1 sec	r=0.64, p=0.002	Delayed vascular response to neural activity
Bilateral Symmetry Index (%)	98.4±2.1%	62.3±8.4%	71.2±9.6%	r=0.82, p<0.001	Widespread network dysfunction
MOTOR UNIT RECRUITMENT					
Recruitment Threshold Range (% MVC)	20-85%	15-35%	18-42%	r=0.71, p<0.001	Compressed, inefficient recruitment
Size Principle Adherence Index (r-value)	r=0.94±0.04	r=0.38±0.15	r=0.52±0.18	r=0.78, p<0.001	Violation of orderly recruitment
Motor Unit Firing Variability (CoV)	0.17±0.014	0.28±0.018	0.24±0.016	r=0.69, p<0.001	Unstable, asynchronous activation
Median Recruitment Threshold (% MVC)	45.2±8.1%	24.6±7.2%	31.8±8.4%	r=0.65, p<0.001	Inappropriately low threshold activation
MUSCLE OXYGENATION DYNAMICS					
Baseline SmO_2 at Rest (%)	74.2±3.8%	52.1±6.4%	58.3±7.1%	r=0.73, p<0.001	Chronically reduced oxygen availability
Task-Induced Desaturation (ΔSmO_2, %)	-42.1±8.2%	-18.3±7.6%	-26.4±8.9%	r=0.61, p=0.002	Blunted oxygen extraction capacity
Post-Task Recovery Time to 90% Baseline (sec)	87±11 sec	246±48 sec	198±42 sec	r=0.81, p<0.001	Severely impaired recovery kinetics
Cortical Metabolic Cost (CMC, arbitrary units)	3.2±0.6	7.8±1.4	6.4±1.3	r=0.78, p<0.001	Inefficient oxygen utilization
PROPRIOCEPTIVE FUNCTION					
Proprioceptive Detection Threshold (deg/sec)	2.1±0.5	7.8±2.3	6.2±2.1	r=0.68, p<0.001	Severely impaired joint motion detection
Multi-Joint Proprioceptive Acuity (error, degrees)	4.2±1.1	12.8±3.4	9.6±3.2	r=0.72, p<0.001	Reduced position/kinesthetic matching
Proprioceptive Deficit Incidence (%)	2-5%	48-52%	35-42%	N/A	Present in majority of stroke survivors
PROPRIOCEPTIVE–MOTOR COUPLING					
Proprioceptive-Recruitment Correlation (r-value)	r=0.82±0.06	r=0.24±0.18	r=0.38±0.21	r=0.74, p<0.001	Loss of sensorimotor integration
Proprioceptive-Oxygenation Correlation (r-value)	r=0.76±0.08	r=0.18±0.16	r=0.31±0.19	r=0.69, p<0.001	Decoupling of proprioceptive-vascular response
MOTOR DYSFUNCTION SEVERITY					
Fugl-Meyer Assessment Score (0-66)	64-66	28.4±8.2	39.6±9.1	Correlates with all above measures	Primary motor outcome
Hand Grip Strength (kg)	45.2±8.1	18.3±6.4	26.4±7.2	r=0.58, p=0.005	Strength loss secondary to recruitment dysfunction

asynchronous motor unit activation [20]. These recruitment abnormalities correlate with voluntary force deficits and represent direct evidence of impaired neuromuscular control organization beyond simple weakness.

Proprioceptive–Perfusion Decoupling

Proprioception—conscious and unconscious perception of limb position and movement—is impaired in approximately 50% of acute stroke survivors and represents an independent predictor of motor recovery and functional outcome [21]. Kenzie et al. demonstrated using resting-state fMRI that proprioceptive impairment post-stroke correlates with altered functional connectivity in the supplementary motor area and supramarginal gyrus, indicating network-level proprioceptive dysfunction [22]. Critically, proprioceptive and motor outputs are interdependent: proprioceptive feedback drives motor unit recruitment patterns and vascular tone adjustments during movement, creating proprioceptive–perfusion coupling. When proprioceptive input is degraded post-stroke, this coupling is lost, contributing to disorganized motor unit recruitment and impaired neurovascular matching.

Xu et al. demonstrated using robotic proprioceptive assessment that proprioceptive deficits post-stroke vary across multiple joints (shoulder, elbow, wrist) with wrist joints showing greatest impairment, indicating regionally distributed proprioceptive dysfunction [23]. The independence of these deficits across joints suggests multiple lesion locations and network disruption patterns affecting proprioceptive integration at distributed levels.

Muscle Oxygenation Dynamics Post-Stroke

Near-infrared spectroscopy (NIRS) provides non-invasive assessment of muscle oxygenation during functional tasks by measuring oxygenated and deoxygenated hemoglobin concentrations in muscle tissue. MasoudiMotlagh et al. documented significant differences in oxygen utilization (ΔOxy) between paretic and non-paretic muscles during functional tasks in stroke survivors, indicating impaired oxygen extraction and utilization in affected limbs [24]. Lamberti et al. demonstrated using functional NIRS during upper limb motor tasks that cortical metabolic cost (CMC)—a measure reflecting oxygen utilization efficiency—is significantly altered in stroke patients compared to controls and shows predictive value for functional recovery; CMC parameters improved with rehabilitation and correlated with motor recovery trajectories [25].

Table 2: Proposed Neurovascular–Neuromuscular Coupling Examination Framework - Component Assessment Protocol.

Framework Component	Assessment Method	Measurement Parameters	Equipment Required	Interpretation Thresholds	Clinical Utility
COMPONENT 1: Motor Activation Efficiency					
Graded Isometric Contractions	Surface sEMG with electrode array	Recruitment threshold range, Size principle adherence, MU firing variability, Normalized EMG amplitude per force unit	HD-sEMG electrode array, force transducer	Normal: Recruitment 20-85% MVC, r>0.85, CoV 0.15-0.20. Impaired: <40% range, r<0.50, CoV>0.25	Identifies neuromuscular disorganization independent of strength
Motor Unit Decomposition Analysis	High-density sEMG decomposition	Motor unit count, recruitment order, action potential properties	HD-sEMG decomposition software	Normal: 15-25 recruited MUs, orderly progression, consistent templates. Abnormal: <10 MUs, reversed order, unstable potentials	Directly quantifies recruitment pathology
COMPONENT 2: Muscle Oxygenation Response					
Functional NIRS During Motor Tasks	fNIRS monitoring during reaching, grasping, functional movement	Baseline SmO_2, peak desaturation, recovery kinetics, CMC	fNIRS sensors (wavelengths 700-900 nm), motion tracking	Normal: Baseline 70-80%, Δ -40-50%, Recovery <90 sec, CMC 3-4. Impaired: <60%, Δ <20%, >200 sec, CMC>6	Quantifies peripheral microvascular-metabolic matching
Oxygenation Recovery Kinetics	Measure time to return to baseline SmO_2 following standardized task	Recovery time (seconds), recovery slope, time to 50%, 75%, 90% recovery	fNIRS system, standardized motor task protocol	Normal: T90=87±11 sec. Mildly impaired: 120-180 sec. Severely impaired: >200 sec	Indicates microvascular reserve and endothelial function
COMPONENT 3: Proprioceptive–Motor Integration					
Robotic Proprioceptive Detection	Robot-controlled joint movements with proprioceptive detection	Detection threshold (deg/sec), accuracy, motor unit activation pattern during detection	Robotic exoskeleton, sEMG, fNIRS	Normal: Threshold 2-3°/sec, accuracy >85%. Impaired: >6°/sec, accuracy <70%	Tests sensorimotor coupling during proprioceptive input
Multi-Joint Proprioceptive Matching	Patient-matched limb position to examiner-moved position (shoulder, elbow, wrist)	Joint-specific proprioceptive error, variability, limb impedance	Goniometry, visual analog rating	Normal: Error 2-5°. Mild impairment: 5-10°. Severe: >10°	Identifies distribution of proprioceptive deficits
COMPONENT 4: Functional Neurovascular Reserve					
Graded Functional Task Performance	Progressive reaching distance, speed, or load with oxygenation monitoring	Oxygenation maintenance (SmO_2 at increasing demand), task performance metrics, fatigue index	fNIRS, motion tracking, functional task apparatus	Normal: SmO_2 maintenance >65%, speed/accuracy maintained. Impaired: SmO_2 drops <50%, early performance decrement	Measures capacity to sustain function under demand
Fatigue Resistance Assessment	Sustained repetitive motor task with performance monitoring	Time to 20% performance decrement, oxygenation trajectory, subjective fatigue rating	fNIRS, motor task apparatus, rating scales	Normal: >300 sec before decrement. Impaired: <120 sec	Indicates functional endurance capacity
COMPONENT 5: Proprioceptive–Oxygenation Coupling					
Regional Oxygenation During Proprioceptive Tasks	Multi-site fNIRS during proprioceptive matching at shoulder, elbow, wrist	Joint-specific oxygenation response, proprioceptive-oxygenation correlation coefficient, matching accuracy	Multi-channel fNIRS system, robotic/manual proprioceptive assessment	Normal: Positive correlation (r>0.70) between proprioceptive accuracy and oxygenation response. Impaired: r<0.40	Identifies proprioceptive-vascular uncoupling mechanism
Proprioceptive–Recruitment Correlation	Simultaneous EMG during proprioceptive tasks	Recruitment organization during proprioceptive detection, correlation with proprioceptive accuracy	HD-sEMG, proprioceptive assessment	Normal: Preserved recruitment organization (r>0.75). Impaired: Disorganized recruitment during proprioceptive task (r<0.50)	Tests whether proprioceptive input restores recruitment order
INTEGRATED ASSESSMENT SUMMARY					
NMC Composite Score	Weighted scoring of all 5 components	Total NMC Score (0-100), component subscores	Calculation algorithm	Normal: Score 85-100. Mild impairment: 70-84. Moderate: 50-69. Severe: <50	Single score summarizing NMC status for clinical decision-making
Rehabilitation Targeting Profile	Component-specific impairment identification	Which components most impaired, guiding intervention priority	Assessment data summary	Component scores identify mechanistic targets for personalized intervention	Guides mechanism-informed rehabilitation planning

Clinical Interpretation Guide:
- Normal neurovascular–neuromuscular coupling: All components score normal (>85 component-specific), indicating intact motor system physiology
- Isolated neuromuscular disorganization: Component 1 markedly impaired, others relatively preserved; indicates primary motor unit recruitment pathology
- Isolated oxygenation dysfunction: Component 2 impaired, others preserved; indicates primary microvascular/endothelial dysfunction
- Proprioceptive-dominant pattern: Components 3&5 impaired, 1&2 relatively preserved; indicates sensory input as primary limitation
- Multidomain uncoupling: Multiple components impaired; indicates integrated neurovascular-neuromuscular dysfunction requiring multicomponent intervention
- Recovery profile: Serial assessments demonstrate component-specific recovery trajectories guiding rehabilitation phase progression

Recovery data from aerobic capacity studies demonstrate that trained (neurologically intact) individuals show rapid recovery of muscle oxygen saturation following exercise (recovery to 90% baseline in 90±11 seconds), while untrained individuals demonstrate delayed recovery (131±16 seconds) [26]. By analogy, post-stroke paretic muscles demonstrate severely delayed oxygen recovery kinetics and impaired baseline oxygenation, suggesting chronic microvascular–metabolic dysfunction limiting fatigue resistance and functional endurance.

Toward a Novel Physiotherapy Framework for Neurovascular – Neuromuscular Coupling Assessment

Rationale for Integrated Assessment

Current physiotherapy examination protocols fail to operationalize neurovascular–neuromuscular coupling assessment, representing a significant gap between pathophysiology and clinical practice. A comprehensive NMC-focused examination framework must integrate assessment of: (1) neural activation efficiency (how effectively neural command generates motor output); (2) motor unit recruitment organization (whether recruitment follows normal orderly patterns); (3) proprioceptive–motor integration (whether proprioceptive feedback effectively drives recruitment); (4) muscle oxygenation dynamics (whether oxygen delivery matches activation demands); and (5) functional neurovascular reserve (capacity to increase perfusion during increased demand).

Proposed Physiotherapy-Based Neurovascular–Neuromuscular Coupling Examination Framework

Component 1: Motor Activation Efficiency Assessment.

Objective: Quantify the ratio of motor output to neural drive (neural efficiency).

Method: Surface electromyography (sEMG) during graded isometric contractions (20–60% maximal voluntary contraction). Record motor unit activation patterns while simultaneously measuring force output.

Key Metrics:

- Motor unit recruitment threshold range (compression indicates dysfunction).

- Recruitment rank order consistency (deviation from size principle severity).

- Normalized EMG amplitude per unit force (elevated values indicate inefficiency).

- Motor unit firing variability (coefficient of variation; elevated values indicate instability).

Interpretation: Preserved neural efficiency indicates intact neuromuscular control; elevated EMG for given force output indicates recruitment disorganization requiring compensatory activation.

Component 2: Muscle Oxygenation Response Assessment.

Objective: Characterize peripheral microvascular perfusion–activation matching during functional tasks.

Method: Functional near-infrared spectroscopy (fNIRS) monitoring of muscle oxygen saturation (SmO_2) and oxygenated hemoglobin (HbO_2) during standardized motor tasks (reaching, grasping, functional reaching tasks).

Key Metrics:

- Baseline muscle oxygen saturation (SmO_2 values; normal ~70–80%).

- Peak desaturation during task execution (normal 30–50% drop).

- Oxygen recovery kinetics post-task (normal recovery to baseline within 60–90 seconds).

- Cortical metabolic cost (fNIRS-measured oxygen utilization efficiency).

Interpretation: Severely delayed oxygen recovery, baseline desaturation, and inability to generate normal desaturation–recovery cycles indicate neurovascular uncoupling and microvascular dysfunction limiting functional reserve.

Component 3: Proprioceptive–Perfusion Integration Assessment.

Objective: Determine how proprioceptive feedback drives motor recruitment and vascular response during movement.

Method: Robotic-guided joint movements with simultaneous proprioceptive detection and sEMG/fNIRS monitoring. Patients detect joint motion direction while motor unit recruitment and oxygenation are recorded.

Key Metrics:

- Proprioceptive detection threshold (movement velocity detection; normal <3°/second).

- Motor recruitment efficiency during detection (does recruitment follow size principle during proprioceptive task?).

- Oxygenation response synchrony with recruitment (does oxygen demand match recruitment activation?).

- Proprioceptive–motor correlation (does proprioceptive accuracy predict recruitment organization?).

Interpretation: Preserved proprioceptive–motor coupling indicates intact sensorimotor integration; dissociation indicates proprioceptive–recruitment decoupling contributing to motor disorganization.

Component 4: Functional Neurovascular Reserve Assessment.

Objective: Quantify capacity to increase perfusion and maintain oxygenation during functional demands.

Method: Graded functional task performance (reaching progressively longer distances, increasing speed, adding cognitive

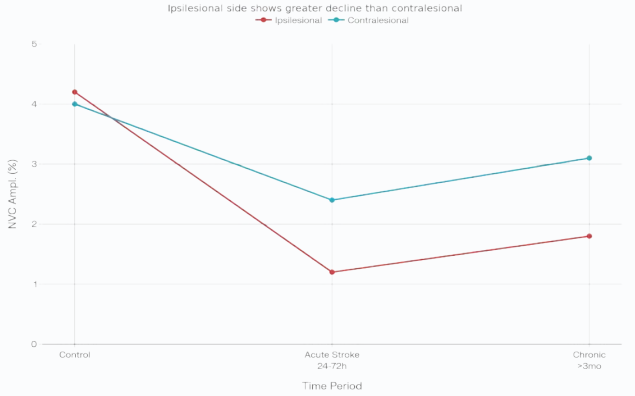

Figure 1:

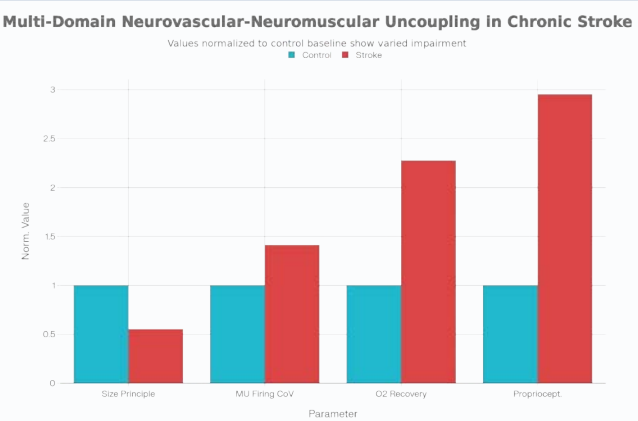

Figure 2:

demand) with simultaneous fNIRS monitoring and task performance quantification.

Key Metrics:

- Oxygenation maintenance during increasing demand (preserved SmO_2 despite increased workload indicates adequate vascular reserve).

- Task performance sustainment (maintained accuracy/speed despite increased oxygen demand).

- Fatigue resistance (time to performance decrement with sustained task).

- Recovery capacity (speed of return to baseline oxygenation after task).

Interpretation: Impaired oxygenation maintenance, early fatigue onset, and delayed recovery indicate restricted neurovascular reserve limiting functional capacity and fatigue resistance.

Component 5: Proprioceptive–Oxygenation Correlation Assessment.

Objective: Determine the relationship between proprioceptive accuracy and muscle oxygenation (test integration).

Method: Multi-joint proprioceptive matching tasks (shoulder, elbow, wrist joint position and kinesthetic tasks) performed with simultaneous oxygenation monitoring at each joint region.

Key Metrics:

- Joint-specific proprioceptive deficits (which joints show greatest impairment?).

- Oxygenation response by joint (are joints with worse proprioception showing altered oxygenation?).

- Proprioceptive–oxygenation correlation coefficient (r-value indicating relationship strength).

- Functional implications (do patients with worst proprioceptive–oxygenation coupling show greatest functional disability?).

Interpretation: Strong positive correlation between proprioceptive deficits and altered oxygenation suggests proprioceptive–vascular decoupling as mechanism; dissociation suggests independent mechanisms requiring targeted intervention.

Integration into Unified Assessment Protocol

The five components are integrated into a single assessment sequence (approximately 45–60 minutes):

Session Structure:

- Baseline physiology recording (5 min): Rest, baseline sEMG/fNIRS measurements.

- **Component 1:** Graded isometric contractions (10 min) - motor activation efficiency.

- **Component 2:** Functional reaching tasks with fNIRS (10 min) - oxygenation response.

- **Component 3:** Robotic proprioceptive detection with simultaneous monitoring (10 min).

- **Component 4:** Graded functional task performance (10 min) - neurovascular reserve.

- **Component 5:** Multi-joint proprioceptive matching with regional oxygenation (10 min).

Output: Comprehensive neurovascular–neuromuscular coupling profile identifying specific impairment domains and mechanisms guiding personalized intervention.

Relationship to Motor Dysfunction Severity

Correlation with Standard Motor Assessments

Preliminary evidence indicates strong correlations between integrated NMC assessment components and standard motor impairment measures. Lamberti et al. demonstrated that cortical metabolic cost (CMC, reflecting oxygenation efficiency) measured via fNIRS during upper limb motor tasks showed significant correlation with Fugl-Meyer Assessment (FMA) scores in stroke patients, indicating that oxygenation efficiency reflects motor recovery status [25]. Motor unit recruitment alterations measured via sEMG decomposition correlate with grip strength and voluntary force generation, demonstrating that recruitment disorganization contributes directly to weakness [19].

Predictive Value for Recovery Trajectory

Evidence suggests that NMC assessment parameters predict motor recovery trajectory beyond standard assessments. Lamberti et al. reported that CMC values improved with rehabilitation and predicted response to therapy, suggesting that oxygenation efficiency may serve as biomarker for rehabilitation potential [25]. Motor unit

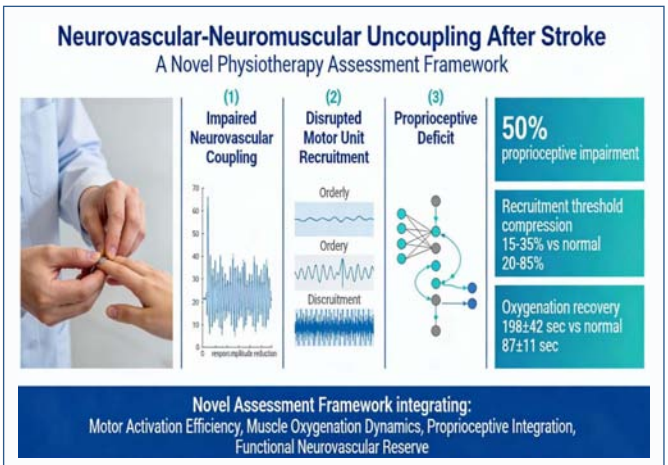

Figure 3:

firing rate variability (elevated post-stroke) correlates with long-term motor impairment severity, suggesting that neural stability predicts recovery potential [20].

Independence of NMC from Strength Alone

Critically, motor unit recruitment disorganization and oxygenation abnormalities can occur independently of severe strength loss, indicating NMC dysfunction represents distinct pathophysiology. Stroke survivors with modest strength deficits may demonstrate severe recruitment disorganization or oxygenation abnormalities, suggesting that strength training alone may inadequately address underlying neurovascular dysfunction. This independence provides clinical rationale for mechanism-specific intervention targeting NMC restoration rather than strength-focused approaches alone.

Rehabilitation Implications and Mechanism - Informed Intervention

Principle: Restore Neurovascular–Neuromuscular Coupling Through Proprioceptive-Driven Motor Learning

The proposed mechanistic framework suggests rehabilitation should explicitly target coupling restoration through proprioceptive-driven motor re-education combined with vascular optimization strategies. Evidence from motor learning indicates that proprioceptive-focused training produces superior neural adaptation compared to strength-only approaches, likely through enhanced sensorimotor integration and more efficient motor unit recruitment patterns [27].

Proposed Intervention Components

Component A: Proprioceptive-Driven Motor Recruitment Training.

- Exercises emphasizing proprioceptive feedback during movement (eyes closed, sensory feedback amplification).

- Progressive movement accuracy demands forcing orderly recruitment patterns.

- Proprioceptive matching tasks driving sensory-motor integration.

Component B: Vascular Tone Optimization.

- Rhythmic, repetitive contractions maintaining elevation of baseline oxygenation.

- Progressive functional task demands maintaining adequate perfusion response.

- Fatigue management preventing metabolic depletion.

Component C: Multimodal Sensory-Motor Integration.

- Combined visual, proprioceptive, and cutaneous feedback during movement.

- Task-specific practice emphasizing coupling restoration.

- Progressive withdrawal of external support as coupling improves.

Component D: Recovery Capacity Training.

- Graded functional endurance tasks building oxidative capacity.

- Progressive intensity increases within metabolic tolerance.

- Active recovery promoting rapid oxygen kinetics normalization.

Clinical Implementation

Assessment findings directly guide intervention: patients with severe recruitment disorganization require Component A emphasis; those with profound oxygenation dysfunction require Component B emphasis; those with proprioceptive deficits require Component C emphasis; those with fatigue intolerance require Component D emphasis. Most stroke survivors require multidomain intervention reflecting their unique physiological profile.

Clinical and Research Significance

Paradigm Implications

Operationalizing neurovascular–neuromuscular coupling assessment and rehabilitation redefines post-stroke motor impairment from a strength-centric to a mechanism-informed model, aligning physiotherapy with contemporary neuroscience understanding of motor recovery. This conceptual shift positions physiotherapy as a mechanism-driven discipline explicitly targeting pathophysiological mechanisms rather than protocol-driven application of exercise.

Personalized Rehabilitation

NMC assessment enables personalized rehabilitation addressing each stroke survivor's unique physiological profile. Rather than standardized approaches applied universally, mechanism-informed assessment identifies specific impairment domains guiding targeted intervention, potentially accelerating recovery and improving long-term outcomes.

Research Directions

Future research should: (1) validate the proposed examination framework in larger cohorts; (2) determine clinical utility and predictive value for rehabilitation outcomes; (3) develop biomarkers from NMC assessment predicting response to intervention; (4) establish rehabilitation protocols explicitly targeting NMC restoration; (5) investigate mechanisms underlying NMC restoration during recovery.

Conclusions

Neurovascular–neuromuscular uncoupling represents a fundamental physiological mechanism contributing to post-stroke motor disability, distinct from strength loss alone. Impaired microvascular perfusion–activation synchrony, disrupted motor unit

recruitment organization, and proprioceptive–perfusion decoupling occur across post-stroke populations and correlate with motor dysfunction severity and recovery potential. Current physiotherapy assessment and rehabilitation fail to operationalize this construct, representing a significant gap between pathophysiology and clinical practice.

The proposed neurovascular–neuromuscular coupling examination framework operationalizes assessment of neural activation efficiency, motor unit recruitment organization, proprioceptive–motor integration, muscle oxygenation dynamics, and functional neurovascular reserve. Integration of these components enables mechanism-informed rehabilitation targeting coupling restoration through proprioceptive-driven motor re-education combined with vascular optimization strategies.

Establishing neurovascular–neuromuscular coupling as an explicit rehabilitation target redefines physiotherapy as mechanism-driven rather than protocol-driven, positioning the discipline to leverage contemporary neuroscience for optimized motor recovery post-stroke. Implementation of proposed assessment framework and mechanism-informed interventions offers substantial potential to enhance personalized rehabilitation and accelerate functional recovery in stroke survivors.

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