Proposal for construction of a dynamic multi-dimensional integrated assessment system for exercise and brain health

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- Research Background
- Research Significance
- Roadmap
- Innovative Highlights
- Anticipated Outcomes
- Project Advantages

Research Background

Physical inactivity is a critical modifiable risk factor for chronic diseases. Exercise intervention is one of the cornerstones for prevention and therapeutic strategies.

Since 1975, American College of Sports Medicine (ACSM) has advocated for the use of evidence-based exercise prescriptions through its seminal work "ACSM's guidelines for exercise testing and prescription" for the management of chronic diseases.

However, the ACSM framework remains predominantly anchored in cardiopulmonary exercise testing paradigms, there are no standards yet in terms of exercise testing for brain health.

Background——Critical scientific phenomena and questions

- The limited associations between cardiorespiratory fitness and cerebral hemodynamics, challenging the traditional view "strong CRF, strong brain"
- Intensive aerobic training, particularly HIIT, may induce impairment in hippocampal volume
- Cerebral pulsatility, central arterial stiffness are independent and critical risk factors for brain structure

A separate set of exercise testing, and physical performance for brain health, independent of CRF, is critical

Framework for exercise workload and cerebral hemodynamics

Framework for real-time dynamics of CBF during exercise

Research Significance

- Overcoming the limitations in American College of Sports Medicine Guidelines: exercise testing and prescription
- Leading criteria establishment for exercise and brain health
- Leading the establishment of a dynamic multi-dimensional integrated assessment framework for exercise-induced neurovascular health

Research Roadmap

Discovery of Clinically Actionable Biomarkers Linking Physical Performance metrics to Neurovascular Health Outcomes

Investigating the intrinsic relationships between physical performance and neurovascular signatures- including cerebral integrity (structure and function), cognitive performance, mental health, neurodegenerative disorders- through the lens of dynamic motor-brain health coupling mechanisms, with the goal of identifying and validating clinically translatable biomarkers.

Discovery of Clinically Actionable Biomarkers Linking Physical Performance metrics to Neurovascular Health Outcomes

By constructing a multidimensional brain health assessment framework encompassing the “exercise-hemodynamics cerebral” axis, and integrating technologies such as wearables, neuroimaging, this initiative aims to:

(1) Implement brain health risk stratification: establish quantitative predictive models linking physical performance and neurological diseases susceptibility, enabling identification of high-risk cohorts;

(2) Optimize precision intervention targets: develop biomarker-guided exercise prescription algorithms

(3) Enable dynamic monitoring

Potential biomarkers

- Left ventricular ejection fraction
- Cardiac output
- Cardiac index

- Aortic stiffness
- Carotid stiffness
- Cerebral pulsatility index
- Blood pressure variability
- Heart rate variability

- Neuroinflammation factors
- Brain-derived neurotrophic factors
- amyloid-β (Aβ),Tau protein,…

- Life’s essential 8

- Cerebral oxygen extraction fraction
- Cerebral blood flow
- Cerebral metabolic rate of oxygen consumption

- Dynamic cerebral autoregulation, cerebrovascular reactivity

- Brain volume, gray matter volume, white matter lesion, white matter hyperintensities, microstructure integrity, hippocampal volume

- Cognitive performance
- Mental health

Potential biomarkers

Health-related metrics

- Aerobic fitness: VO_2peak,
- Muscle strength: handgrip strength, knee-extension strength
- Flexibility: sit-to-reach test
- Body composition

Skill-related metrics

- Agility/coordination: shuttle run
- Balance: single leg stance
- Muscle power: 300-m shuttle run, jump test, bench squats
- Speed/reaction time test

Physical functional performance metrics

- Gait speed
- Walking test: 6-minute walking distance
- Gait performance
- Lower-extremity functional test: timed-up-and-go (TUG), Sit-to-Stand test
- Short physical performance battery

Development of a hemodynamic Response Assessment and Testing Platform for Exercise intervention in the Brain-Heart dual-system

Exercise workload-cerebral perfusion dynamic coupling model:

(1) By establishing a central arterial stiffness-medicated CBF oscillation model to evaluate cerebrovascular regulatory efficiency, this framework develops multimodal dose-response models for gray/white matter microstructure injury gradients. It quantifies the time-delayed effects and spatial heterogeneity of exercise interventions (modality, intensity, dosage) on regional (e.g., hippocampus) cerebral perfusion pressure through advanced neuroimaging.

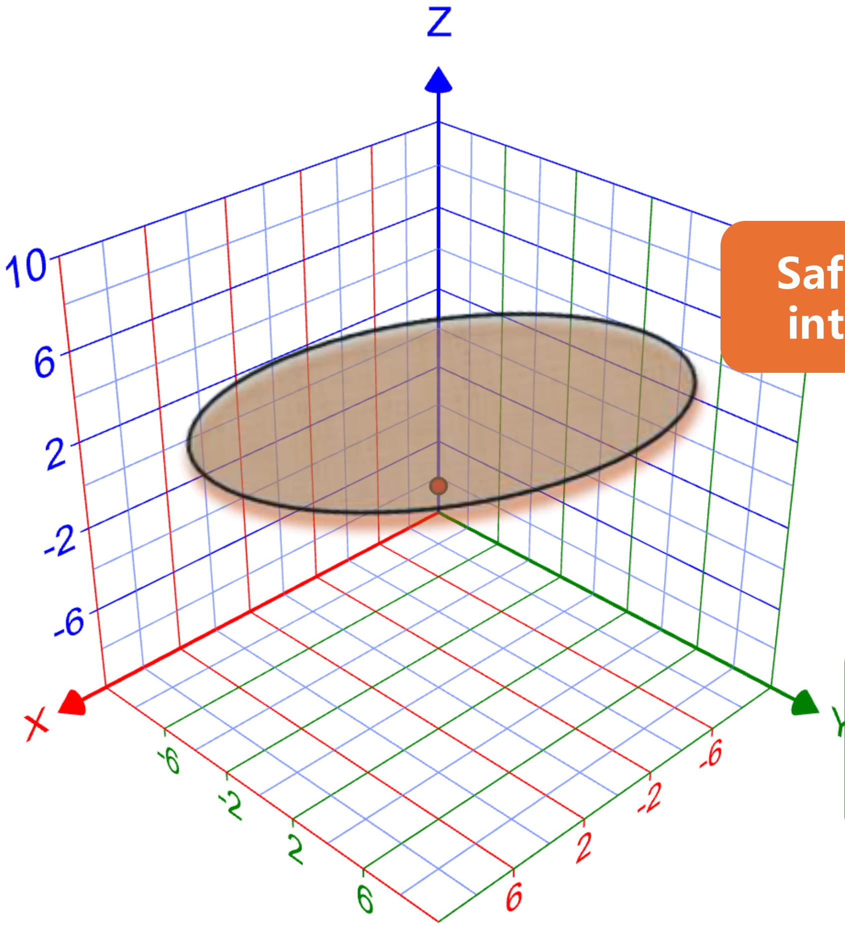
(2) Integrating deep learning-driven risk stratification algorithms, the model identifies hemodynamic optimization windows under neurovascular unit, thereby establishing evidence-based thresholds for neuroprotective exercise prescription design.

Development of a hemodynamic Response Assessment and Testing Platform for Exercise intervention in the Brain-Heart dual-system

Brain health metrics

Dynamic monitoring Mapping for

- Risk Stratification
- Optimize precision intervention targets



Safe zone for exercise intensity and dosage

Cardiac health metrics

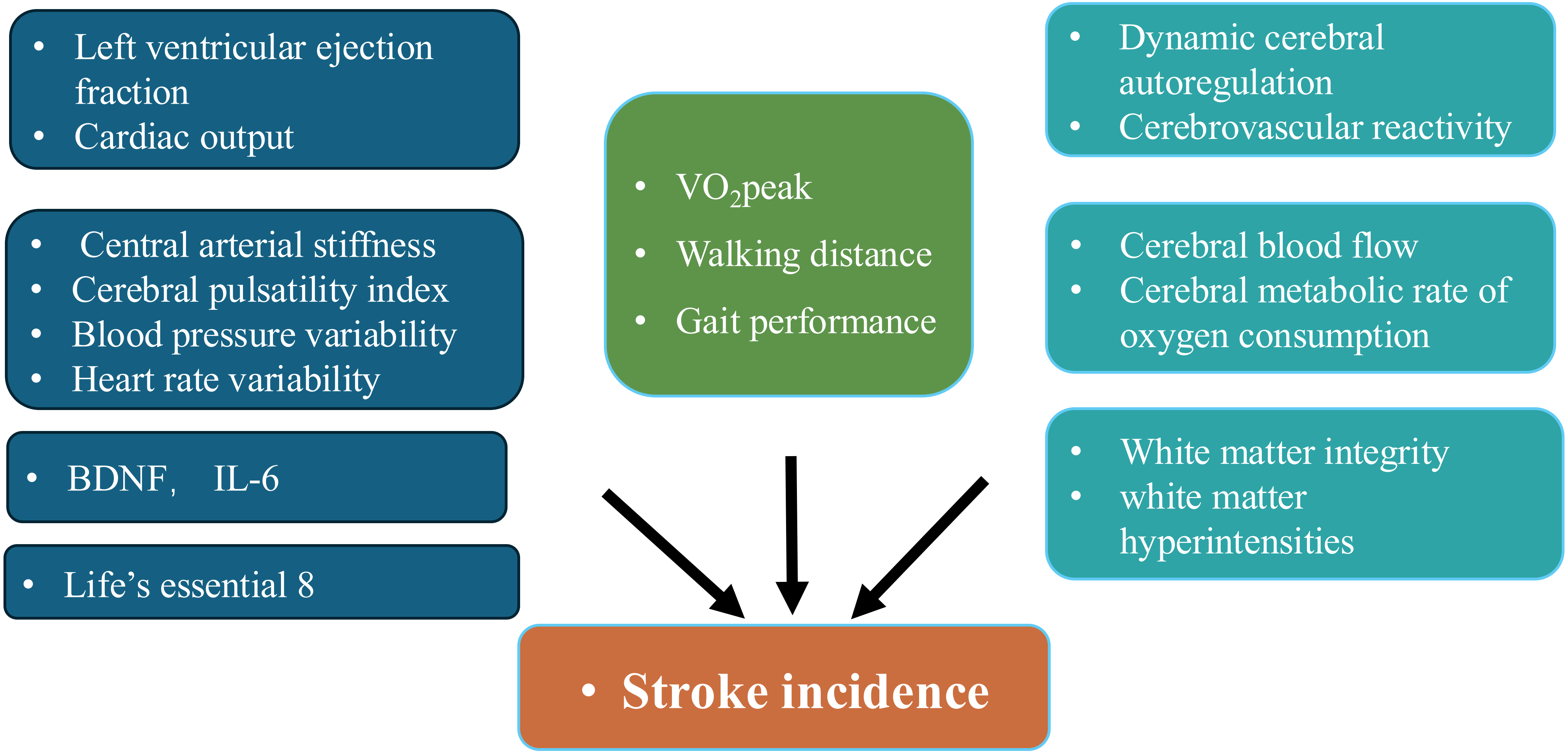
Physical performance metrics

Multidimensional Early-Warning System for Stroke Prevention and Prognosis

Integrating cardiac metrics, central arterial stiffness, cerebrovascular hemodynamics parameters, cerebral integrity, physical performance, this system identifies critical pathological pathways through a multimodal risk stratification model.

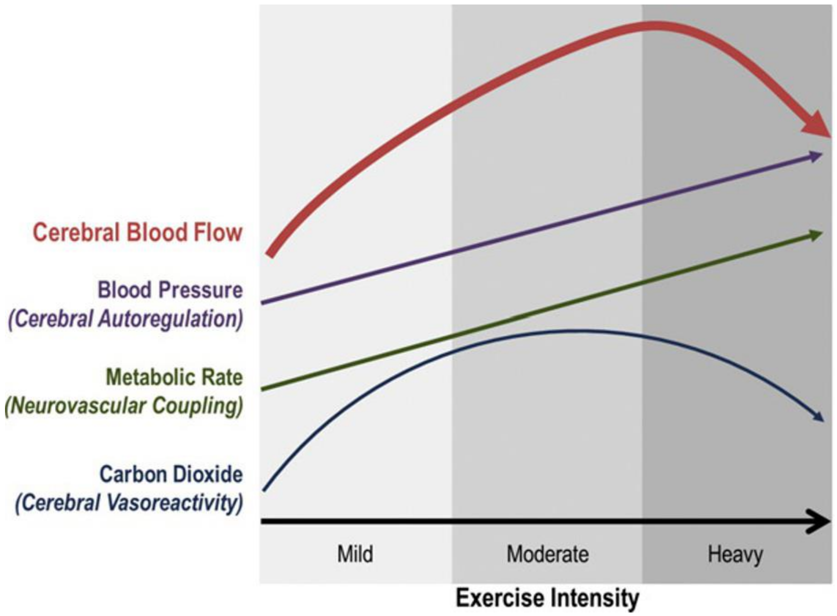
For instance, low LV ejection fraction, aortic stiffness, increased pulsatile index in MCA, and reduced VO_2peak and walking distance are associated with high stroke risk.

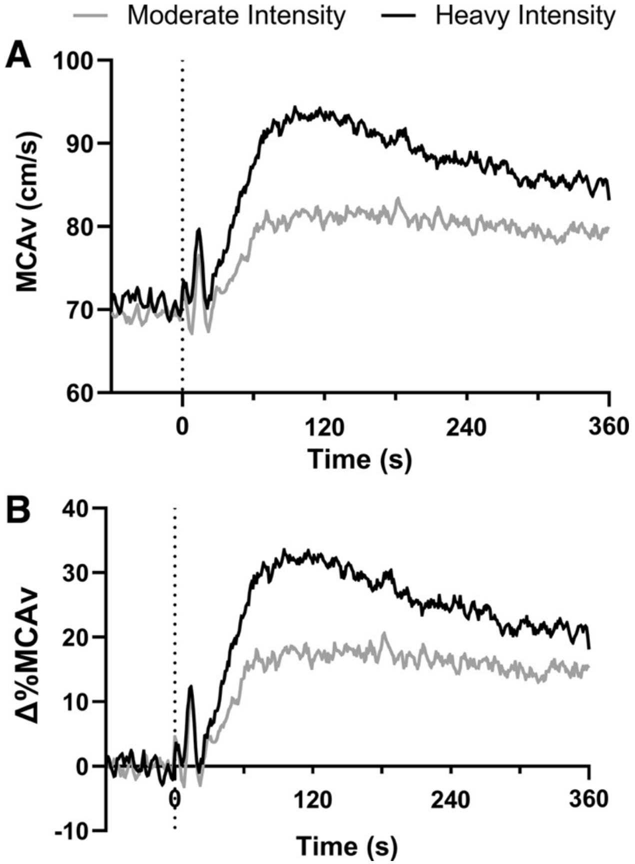
Potential biomarkers along the pathways



Establishing a novel paradigm in stroke recovery and rehabilitation:

Transitioning from Exercise-driven physical function enhancement to cerebral hemodynamic stability optimization strategies





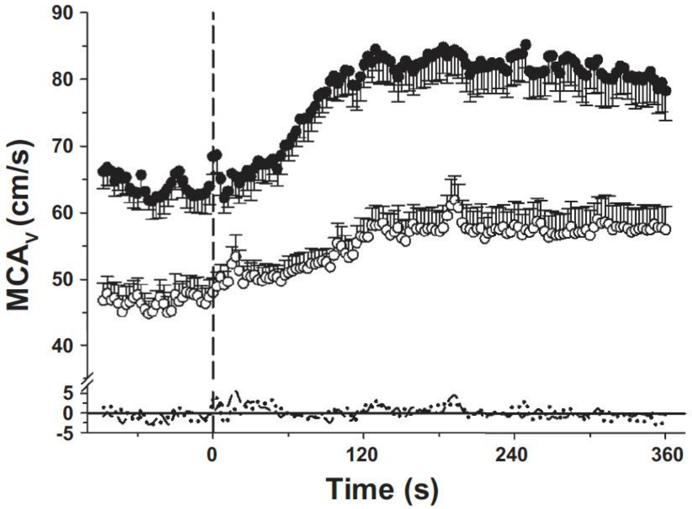
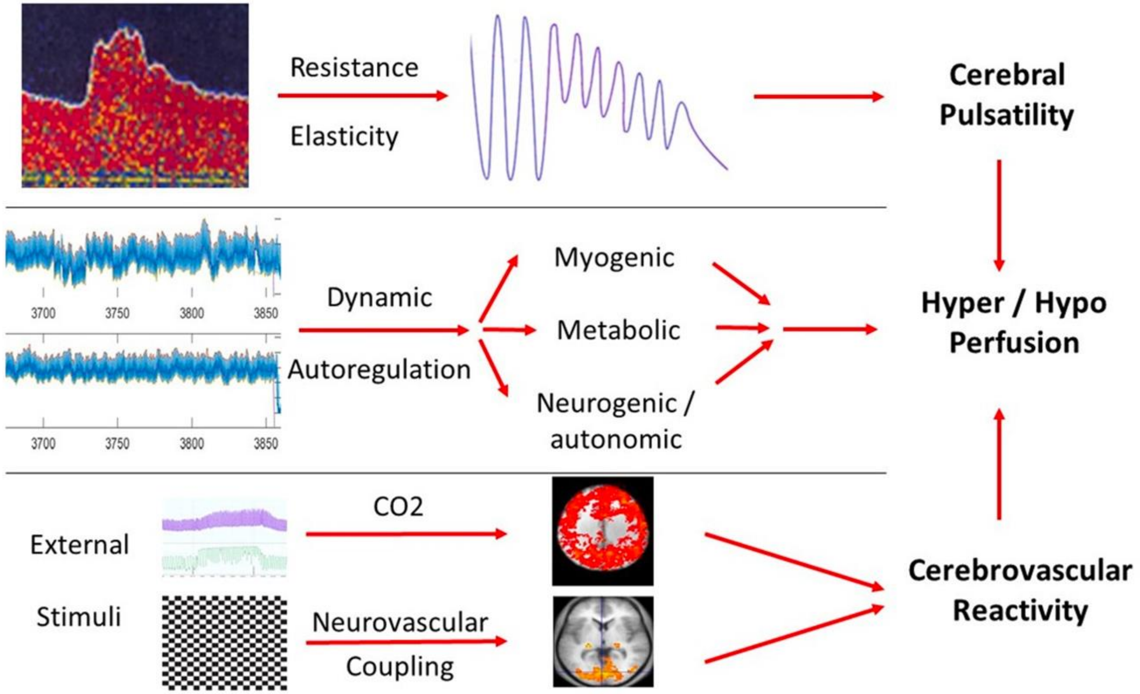
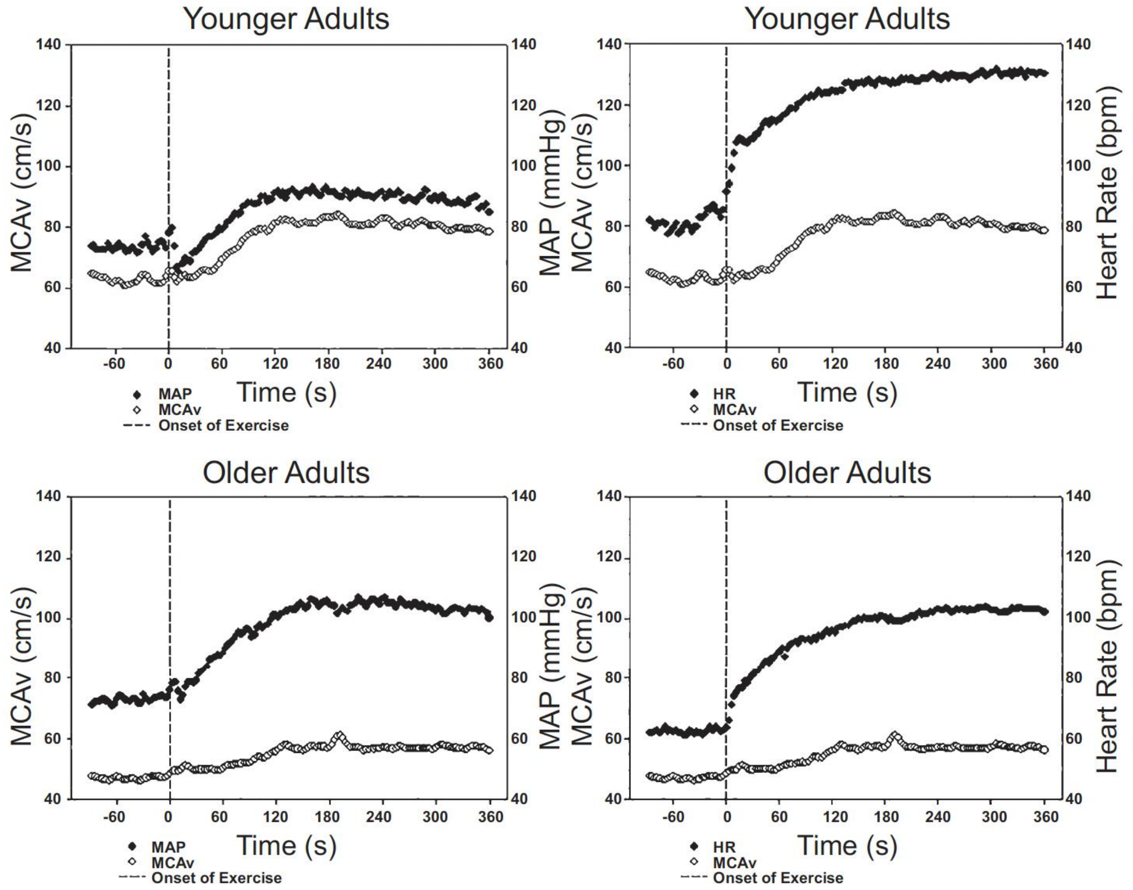


Fig. 3. Group mean blood velocity measured in the middle cerebral artery (MCA_V) before and after the onset of moderate-intensity exercise in subjects matched for work rate. Onset of exercise is represented by dashed vertical line (*time 0*). Filled symbols represent young group, and open symbols represent older group. Residuals are presented just above the horizontal axis for young (dotted line) and older (dashed line) subjects. Analysis included 11 young and 11 older subjects. Values are means ± SE.

Re-defining exercise intensity metrics (non heart rate or VO_2peak dependent): Establishing a "cerebrovascular stability-safe intensity zone"





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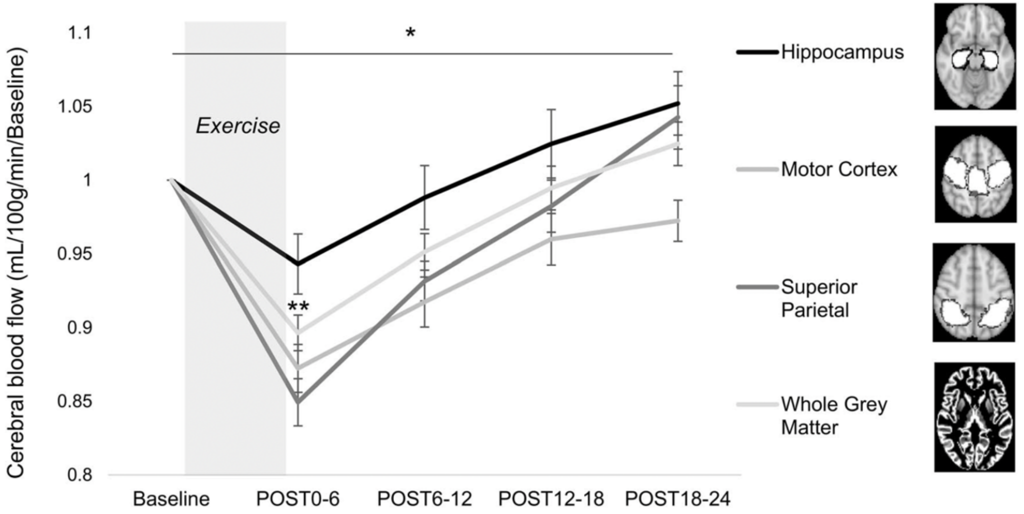


Fig. 2. Regional CBF at baseline and over an acute time course following a bout of moderate-intensity aerobic exercise in older adults. ROIs included hippocampus, motor cortex, superior parietal cortex, and whole brain gray matter. Standard Montreal Neurological Institute masks for each ROI are included for reference (right panels). All brain regions showed change in CBF over time after exercise, characterized by an immediate CBF reduction followed by a gradual CBF increase over the course of the 24-min assessment period. There was a time-by-region interaction effect in which the hippocampus demonstrated an attenuated immediate CBF reduction compared to other brain regions ($X^2 = 6.1$, $^{**}P = 0.048$) and a more robust rebound effect. At the final assessment 18–24 min postexercise (POST18-24), only hippocampal CBF exceeded baseline levels ($^{*}P = 0.037$).

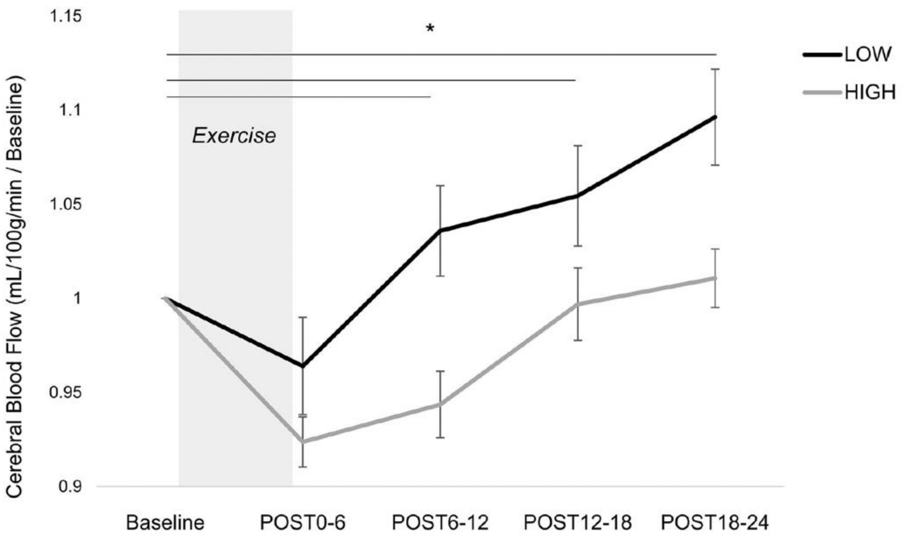
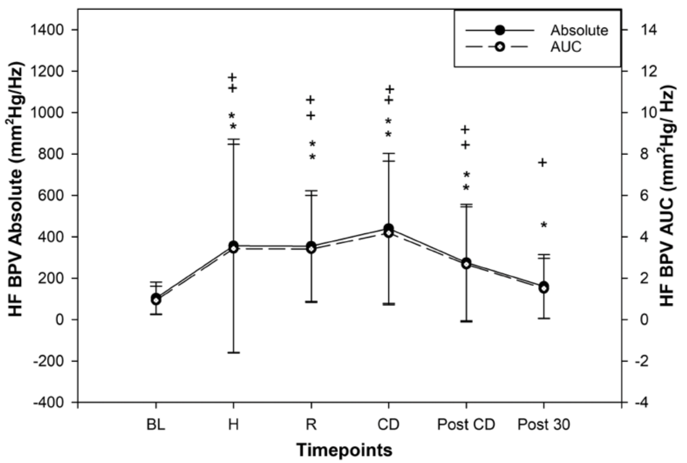
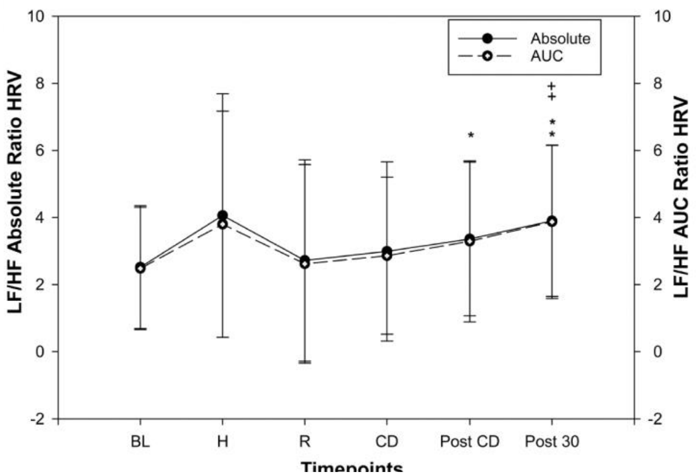
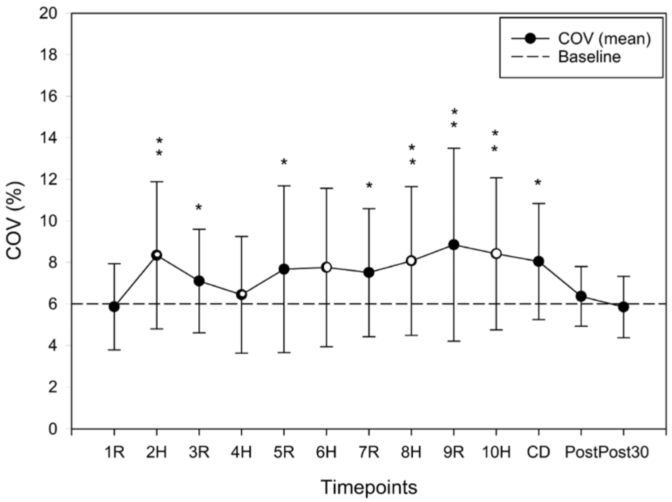


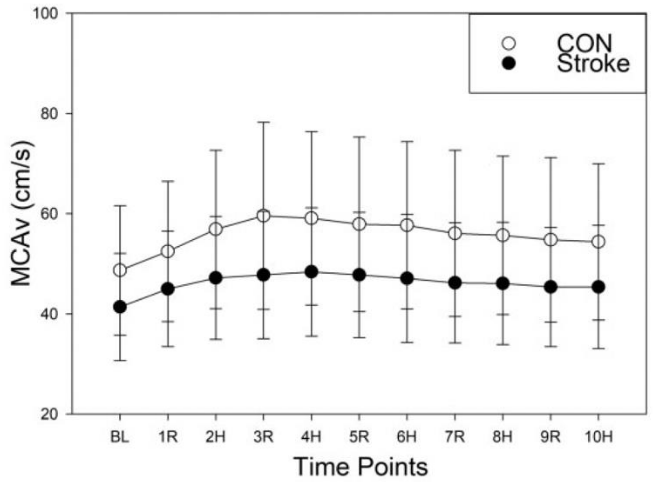
Fig. 3. Hippocampal blood flow response to a bout of moderate-intensity aerobic exercise in older adults with low (<26.13 mL/100 g tissue/min) and high (≥26.13 mL/100 g tissue/min) baseline hippocampal perfusion levels. Older adults with low baseline perfusion showed an attenuated immediate drop in the hippocampal blood flow at 0–6 min postexercise (POST0-6) followed by a more rapid and robust hyperemic rebound effect over the 24-min assessment time course following exercise cessation, exceeding baseline levels at 6–12 (POST6-12) and 18–24 min (POST18-24) postexercise ($^{*}P < 0.03$). Older adults with high baseline perfusion showed no increase in hippocampal blood flow above baseline levels at any timepoint assessed.

HIIT for improving VO_2peak: Potential impairment in cerebral autoregulation mechanisms in healthy population and stroke patients (research in cerebral hemodynamics)

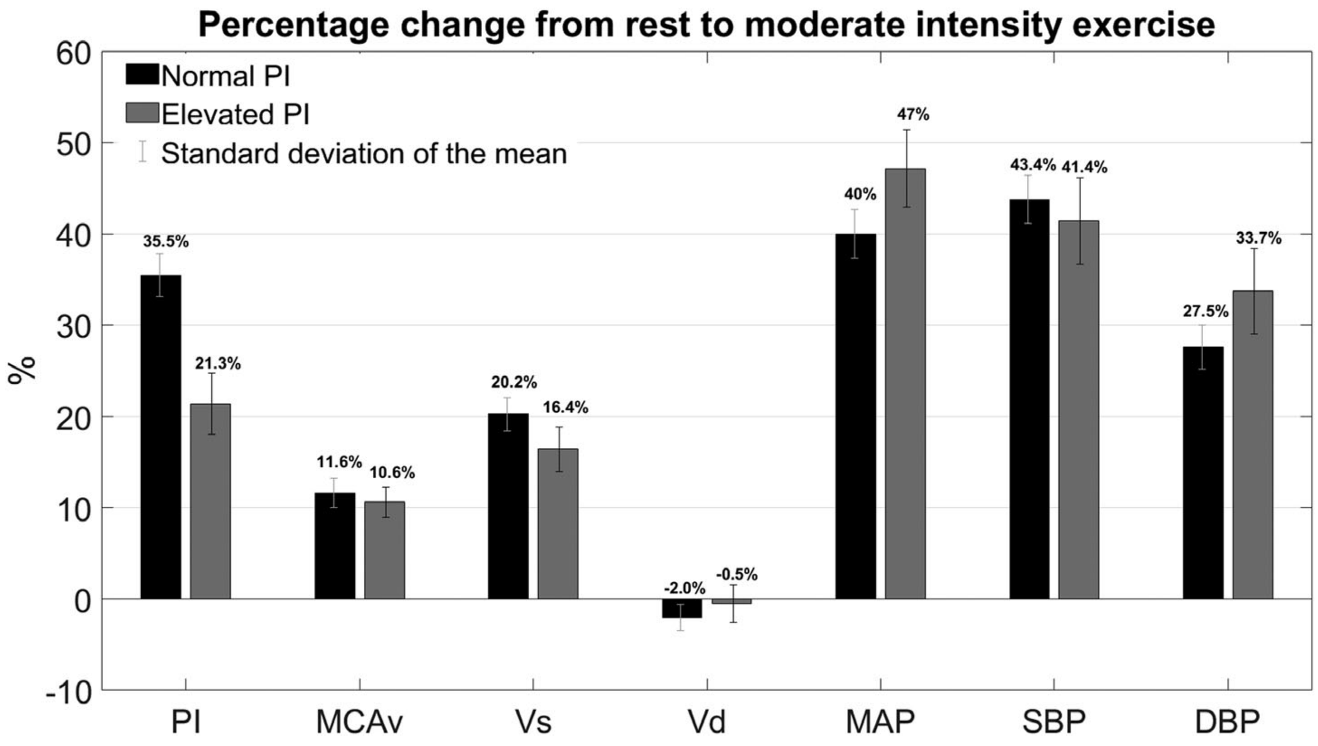








Standards establishment: models for exercise training and cerebral hemodynamics for healthy population and stroke patients (TCD)



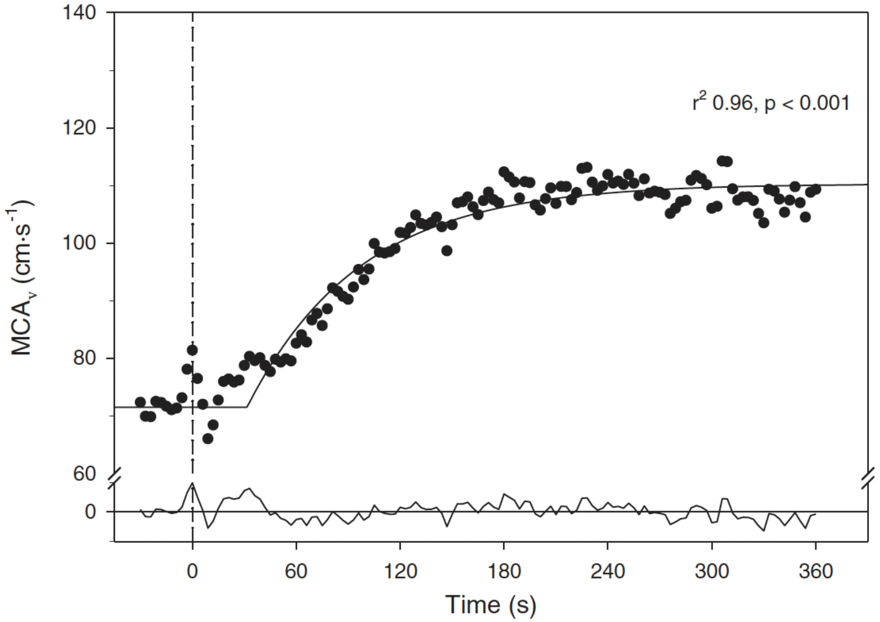


Fig. 1. Typical middle cerebral artery velocity (MCAv) at rest and response following the onset of moderate-intensity exercise (dashed vertical line, *time 0*). Notice the close fit (solid curve at *top*) to the time delay + exponential model as supported by the high correlation coefficient and residuals profile (solid line at *bottom*). Results from *subject 2*.

Innovative highlights for the Project

Multi-dimensional integrated assessment systems for exercise and brain health

The first exercise testing for Brain-heart health-oriented dual-system dynamic evaluation and testing platform

Promotion of the novel paradigm (cerebral hemodynamic as an integral part) of stroke recovery and rehabilitation

Anticipated outcomes for the project

- Establishment of a dynamic multi-dimensional integrated assessment framework for exercise-induced neurovascular health
- Establishment of the Brain-heart health-oriented dual-system dynamic evaluation and testing platform

- **The multidimensional early-warning system for stroke prevention and prognosis**

- **Models of aerobic training and cerebral hemodynamics for stroke recovery and rehabilitation**

Thanks