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## **Exercise after stroke and spinal cord injury: Common biological mechanisms and physiological targets of training**

### **INTRODUCTION**

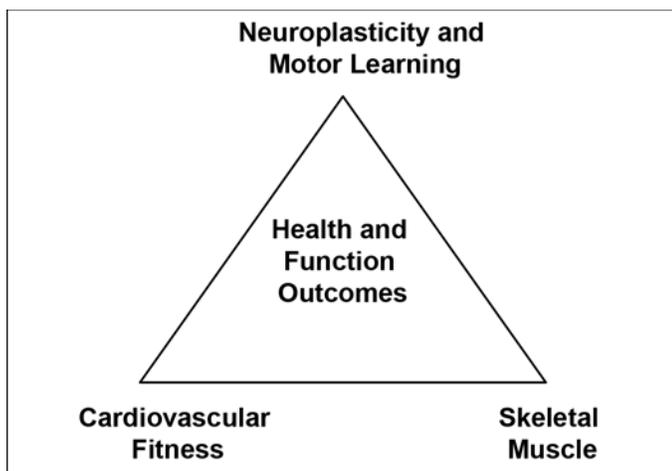
Over the past decade, various novel exercise therapies have emerged as a unifying approach to improving physiological fitness and physical function for individuals with neurological mobility impairments. Inspired initially by seminal studies in spinalized cats, models of locomotor relearning have advanced from bench to bedside in human spinal cord injury (SCI) and been applied to the study of exercise rehabilitation for individuals with hemiparetic stroke. Hence, a new and rapidly evolving science of clinical exercise physiology is now being established in neurological disability, with stroke and SCI constituting the leading edge in clinical and translational research. Out of this research, several common themes in conceptual training strategies and mechanisms of exercise-mediated adaptations are emerging that appear mutually informative to stroke and SCI investigators. This special issue of the *Journal of Rehabilitation Research and Development* is dedicated to veterans disabled by stroke and SCI and aims to advance our understanding of the biological mechanisms by which exercise may improve health and function following central nervous system (CNS) injury.

The general message is that exercise models can be targeted to affect multiple physiological systems that determine long-term health and functional outcomes in both stroke and SCI. Exercise therapy can be considered a multisystem model that includes the key domains of adaptations in CNS sensorimotor control; cardiovascular-metabolic health; and body composition, including bone health (**Figure**).

This issue highlights the multisystem model of exercise-mediated adaptations by examining selected, promising exercise intervention models for stroke and SCI, which are outlined in the remainder of this editorial.

### **EXERCISE-MEDIATED NEUROPLASTICITY IN STROKE AND SPINAL CORD INJURY**

The model of task-oriented exercise training is based on advances in our understanding that task-repetitive training can potentially alter CNS plasticity at multiple levels, even years after a disabling neurological event. While brain plasticity and motor learning during upper-limb stroke rehabilitation have received the most study, convincing evidence now exists that lower-limb



**Figure.**

Exercise therapy as multisystem model that encompasses adaptations in central nervous system sensorimotor control; cardiovascular-metabolic health; and body composition, including bone health.

motor control and locomotion are modifiable by exercise training. Forrester et al. (p. 205) review new evidence for neural plasticity, through which ankle and knee motor control are modifiable with task practice in patients with chronic hemiparetic stroke. Patterson et al. (p. 221) underscore the clinical relevance by providing the first report of the long-term effects (6 months) of progressive treadmill training on gait temporal-distance parameters in 39 patients with chronic stroke. Their data show that treadmill training improves selected gait temporal-distance parameters (but not symmetry) and ambulation across a number of different gait demand conditions, consistent with locomotor learning. Lynskey et al. (p. 229) provide a translational research overview of animal and human data on neuroplasticity after SCI, the potential for exercise-mediated neuroplasticity, and molecular mechanisms that may help bridge the gap between animal research and human intervention. Their promising conclusions are that activity-dependent plasticity is possible across multiple levels of the neuroaxis—spinal, cortical, and subcortical—and that multiple strategies, including electrophysiological stimulation and pharmacological and/or gene therapy can potentially enhance plasticity processes, defining directions for future mechanistic research.

## CARDIOVASCULAR HEALTH BENEFITS OF EXERCISE

Based on animal studies in spinalized cats, variants of treadmill training have emerged as models for locomotor relearning in SCI and stroke rehabilitation. These training models are also targeted at improving other outcomes, including cardiometabolic health. Hicks and Martin Ginis (p. 241) provide a comprehensive overview of studies showing that exercise training improves lipid profiles, glucose tolerance, and psychological well-being. Similarly, Ivey et al. (p. 249) provide evidence that treadmill training in patients with chronic stroke improves not only ambulatory function but also fitness and cardiometabolic health even decades after stroke. Collectively, these findings support a rationale for regular exercise to reduce insulin resistance and improve cardiovascular health and fitness for individuals with SCI- and stroke-related disabilities.

## STRUCTURAL-METABOLIC CHARACTERISTICS OF MUSCLE AND BONE HEALTH AFTER STROKE AND SPINAL CORD INJURY

After SCI, major structural and metabolic abnormalities exist in skeletal muscle, including gross muscular atrophy and a major shift to a fast, myosin heavy-chain muscle molecular phenotype that fosters insulin resistance. In patients with stroke, Hafer-Macko et al. (p. 261) report remarkably similar abnormalities in hemiparetic muscle linked to increased expression of tumor necrosis factor- $\alpha$  in the inflammatory pathway, a common denominator for atrophy and insulin resistance. McKenzie et al. (p. 273) report results of the first human genome survey in skeletal muscle of stroke patients that profiled families and included 116 genes that differ in expression between hemiparetic and nonparetic leg muscle. These findings suggest that a fundamental metabolic shift toward anaerobic metabolism in hemiparetic skeletal muscle is accompanied by abnormalities in gene expression for muscle contractile proteins, inflammatory mediators, cell cycling, and signal transduction.

Dudley-Javoroski and Shields (p. 283) provide an overview of the major skeletal muscle and bone abnormalities and their rapid time course after SCI. They report the promising finding that early functional electrical stimulation elicits appropriate mechanical load, preserving muscle mass and trabecular bone integrity, which is important for preventing fractures in this population. Unfortunately, bone health has received much less attention in the stroke population. Eng et al. (p. 297) clearly define stroke as a model of disuse osteoporosis with an alarmingly high fall rate and fracture risk. These investigators outline the evidence that structured exercise potentially improves indexes of balance, preserves femoral neck bone density, and improves trabecular bone content. In addition, this novel community-based exercise intervention holds promise for community translation.

### **INNOVATIVE EXERCISE MODELS**

So that implementation of exercise programs that improve care for individuals with disabilities can be expanded, models must be customized across a broad range of deficit severities and be extended to the community. As Rimmer et al. (p. 315) outline, individuals with stroke have numerous environmental and personal barriers to exercise, including cost, access, and a lack of confidence that expertise or appropriate programs are available in their community. Macko et al. (p. 323) report a pilot study of adaptive physical activity conducted in Italy to improve basic mobility

function for older individuals with chronic stroke. Stuart et al. (p. 329) propose exercise models designed for community translation that may have public policy implications as we consider how to better address the long-term health and wellness of individuals with chronic neurological disability.

### **ADVANCED TECHNOLOGIES FOR DELIVERING ACTIVITY-BASED EXERCISE**

Throughout this issue, the underlying theme is that activity-based interventions have widespread health benefits ranging from changes in neural behavior to enhanced muscle and bone function. Unfortunately, delivering such interventions to individuals after stroke and SCI is difficult because of the severity of their motor impairments. Hidler et al. (p. 337) discuss the introduction of robotics into rehabilitation and how these devices can deliver mass-practice therapies. Preliminary evidence is also provided demonstrating the cardiovascular benefits of robotics-based gait training in individuals after SCI.

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