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Post-stroke exercise rehabilitation: What we know about retraining the motor system and how it may apply to retraining the heart

ABSTRACT

A plateau in recovery within the first few months of rehabilitative therapy was assumed to be the norm in stroke survivors. Recent studies in our laboratory examined the effect of 6 months of treadmill exercise training in chronically disabled stroke survivors. Treadmill exercise improves fitness and walking ability in patients when initiated 6 months or more following their index stroke. Functional imaging studies show that such exercise also induces subcortical reorganization in these patients. Future investigations will explore the relationship between these functional and structural effects and characterize the therapeutic mechanisms of post-stroke rehabilitation. Nonetheless, treadmill exercise appears to have motor, cardiac, and daily functional benefits in stroke survivors.

Ideally, rehabilitation following a stroke that leads to functional deficit will result in a rapid return to normal function. In the real world, however, a rapid improvement in function is rarely achieved. Between 80% and 90% of stroke survivors have a motor deficit, with impairments in walking being the most common motor deficits.[1] Most stroke survivors have a diminished fitness reserve that is stable and resistant to routine rehabilitative interventions. Recent research has begun to assess the value of exercise and other modalities of training during this period of stability to improve function long after cessation of other therapeutic interventions. This article will review this research and provide insight into those issues in post-stroke rehabilitation that remain to be addressed and may affect heart and brain physiology.

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STROKE REDUCES AEROBIC CAPACITY

At all ages, the fitness level of stroke survivors, as measured by maximum oxygen consumption, is reduced by approximately 50% below that of an age-matched normal population. In a study comparing peak oxygen consumption during treadmill walking between stroke survivors and age-matched sedentary controls, we found that the stroke participants had an approximately 50% lower level of peak fitness relative to the control subjects.[2] During treadmill walking at self-selected speeds, the stroke volunteers used 75% of their functional capacity, compared with 27% for the age-matched healthy controls. Furthermore, compared with the controls, the stroke subjects demonstrated a poorer economy of gait that required greater oxygen consumption to sustain their self-selected walking speeds.

CLINICAL TRIALS OF POST-STROKE EXERCISE REHABILITATION

In light of the efficacy of treadmill exercise in cardiac rehabilitation, we are evaluating whether treadmill exercise can similarly improve fitness, endurance, and walking velocity in stroke survivors. We have completed 6 months of treadmill training in two separate cohorts that show highly consistent results in terms of improved walking abilities in hemiparetic stroke subjects.[3,4] A third cohort is in progress to confirm these findings and examine the effects of intensity on the functional benefits[5] and mechanisms[6] underlying the effects of treadmill training.

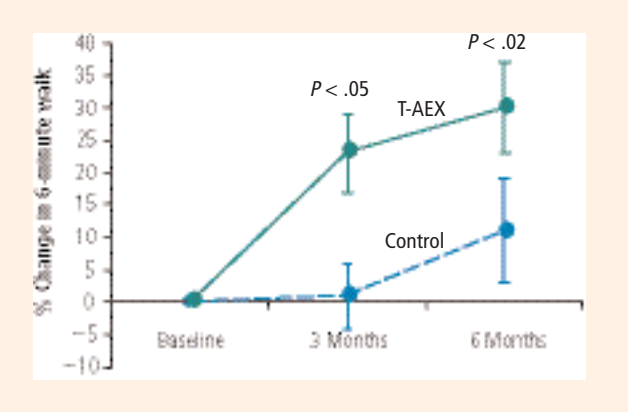

FIGURE 1. Mean change in distance during a 6-minute walk test after treadmill aerobic exercise training (T-AEX) and control therapy among ischemic stroke survivors with hemiparetic gait (25 T-AEX subjects, 20 controls). The between-group difference demonstrates the functional benefits provided by treadmill exercise therapy.[4]

Reprinted, with permission, from Macko RF, et al. Treadmill exercise rehabilitation improves ambulatory function and cardiovascular fitness in patients with chronic stroke. A randomized, controlled trial. Stroke 2005; 36:2206–2211.

Treadmill exercise results in functional benefits and improved glucose metabolism

The first cohort was a before-and-after comparison of stable stroke survivors who underwent a three-times-weekly treadmill exercise program for 6 months.[3] Peak exercise capacity testing (VO_2peak) revealed functional benefits with minimal cardiac and injury risk compared with baseline, demonstrating the feasibility and safety of treadmill exercise therapy in stroke-impaired adults.

The second cohort involved patients with chronic hemiparetic gait following ischemic stroke who were randomized to either treadmill aerobic training (three times weekly for 6 months) (n = 25) or a control rehabilitation program of stretching (n = 20).[4] The aerobic training group selected its own walking speed and increased its speed as tolerated; some participants in this group started with as little as 2 minutes on the treadmill. As shown in **Figure 1**, performance on the 6-minute walk test improved significantly in the aerobic training group, relative to the control group, over the 6-month study. Six-minute walk results paralleled the improved functional performance.

Potential mechanisms for the benefits

These findings raise the question of whether these beneficial effects of treadmill exercise are attributable to muscle training effects, cardiopulmonary circulatory training effects, or perhaps neural mechanisms involving economy of gait movements and neuroplasticity of the motor system.

This question is being examined in our third cohort, now under investigation. This cohort will evaluate the effects of treadmill exercise on 32 chronically disabled stroke survivors in a single-center study design that is randomizing 64 subjects to 6 months of three-times-weekly treadmill training or conventional physiotherapy.[6] Similar to our prior studies, subjects are randomized at least 6 months after their index stroke; this lengthy interval is deliberate because subjects are considered to be in a "plateau" phase of recovery, as they have previously completed rehabilitative therapy.

This group of 32 subjects will undergo both treadmill training and functional magnetic resonance imaging (fMRI) during unilateral knee movements to assess alterations in brain function during such movements over the 6-month study **(Figure 2)**. Previous fMRI studies of healthy controls and stroke patients identified activation of regions in the right side of the cerebral hemisphere with left knee movement.[7,8] In the new fMRI study, functional activation patterns of paretic and nonparetic knee movement will be compared between the exercise group and the control group, and the relationship between the activation pattern and the location of the brain-activation region will be characterized for the paretic and nonparetic knee movements.

Activation will be measured in five prespecified "regions of interest": the precentral gyrus, the postcentral gyrus, the supplementary motor area, the midbrain, and the cerebellum (anterior/posterior lobes). Difference activation maps of post-training minus pretraining fMRIs of paretic knee movement across all patients undergoing treadmill therapy will then be analyzed. The control group, which will receive dose-matched stretching activity from physical therapy, can be contrasted by comparing the patterns of pre/post differences in each region. This will allow for assessment of increased regional activation in the brain that should be specific to the treadmill training intervention. Furthermore, if a specifically localized regional activation difference is found, then individual fMRI and VO_2 training responses (VO_2peak, increase in walking speeds) can be correlated to further assess the relationship between regional activation and magnitude of functional response to the treadmill intervention.

DISCUSSION AND CONCLUSIONS

Central control of walking

Control of gait in animals is mediated by the cortex, brainstem/cerebellum,[9,10] and spinal cord—the so-called cervical gait and lumbar gait pattern-generating areas of the spinal cord. In humans, cortical and spinal gait pattern areas are thought to be major regulatory cen-

FIGURE 2. Brain activation before and after treadmill training is sampled in a stroke survivor using functional magnetic resonance imaging during unilateral knee movements. A plexiglass scaffold has been custom-designed to define range of motion and minimize concomitant head motion.

ters of ambulation. Whether the cortical areas influence ambulatory recovery mediated by exercise training or whether the recruitment of spinal gait areas is needed to improve motor control after stroke is not known in humans. We will test the hypothesis that the recruitment of cortical and/or subcortical areas is relevant to some or all of the exercise-induced neuroplasticity response to treadmill rehabilitation. If a consistent pattern of brain regional activation is associated with an improvement in walking ability, this finding will suggest potential brain targets for neurally directed rehabilitation interventions. If brain targets for rehabilitation produce viable therapeutic improvement in walking and cardiocirculatory performance (such as V_{O_2}), this will be further evidence of heart-brain interactions.

Future research directions

Studies to date demonstrate that long-term treadmill exercise affects both the brain and cardiac physiology. This has holistic implications for the function of the whole person as well. Yet several pressing issues continue to confront researchers in post-stroke rehabilitation. One is the optimal therapeutic target and the intensity of the rehabilitative effort. Is this improvement solely a response of muscle and cardiac tissue to exercise, or is it possible that improved neuromotor control is a critical component to a major recovery of walking function? Furthermore, the most efficacious elements of rehabilitative therapy are not known. Should treadmill training be high- or low-intensity, and should it be accompanied by strength training, agility and flexibility activities, or other elements directed at reacquisition of finer degrees of gait-related motor training and neuropsychological input, as achieved by tai-chi or yoga? Another issue is the proper dose of rehabilitative therapy, which has barely been explored, although recent preliminary work suggests that the response is dose-dependent. Finally, predictors of response have not been established because the mechanisms of therapy and surrogate markers for early response are not well understood.

Our future research plans are to assess whether a better understanding of neural targets for rehabilitative treatment will be a fruitful avenue to improve recovery. Additionally, this plan will assess whether fMRI can serve as a surrogate marker of recovery by offering a noninvasive means to measure response to rehabilitation.

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