Treadmill Exercise Prescriptions to Improve Fitness vs. Ambulatory Function after Stroke

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- Funding Agency: VA RR&D MERCE

Description:

Understanding optimal exercise formula(s) to produce specific physiological and functional effects is key to optimizing outcomes after stroke. In addition, delineating temporal profiles and durability of exercise outcomes, and impact of training strategy on these features, is requisite to defining the minimal and optimal training durations to improve long-term health outcomes. Our data shows TM training increases bold fMRI voxel area during P knee movement in bilateral motor cortex. We do not know whether these measures of neuroplasticity are differentially mediated by duration vs. velocity-based training, or optimized by 3 months training, a time when our data shows a relative plateau in ambulatory performance gains. Further, our studies reveal progressive gains in V02 peak across 6 months, but many patients did not gain in fitness until the 3rd to 6th month. This is a much longer training duration than conventional care, suggesting requirements for exercise training are different than conventional post-stroke rehabilitation. This study investigates the hypothesis that in chronic stroke patients a 6-month program of TM exercise progressed on the parameter of training velocity will optimize gains in CV fitness, compared to a duration-based training progression that will optimize gains in ambulatory function.

Figure 1: Participant undergoing treadmill exercise intervention

Objectives:

1. Determine the effects of velocity versus duration based training on CV fitness in stroke patients by measuring peak exercise capacity, cardiac output, and kinetics of oxygen consumption during treadmill exercise testing with open circuit spirometry.

2. Determine the effects of velocity vs. duration based training on ambulatory function measured by timed walks, gait biomechanics, and free-living ambulatory activity levels, and whether changes in ambulatory function are related to brain neuroplasticity measured by fMRI of paretic knee movement.

3. Determine the temporal profile of treatment according to training strategy by repeated measures of fitness and function after 3- and 6-months training.

Figure 2: Participant undergoing treadmill exercise

Research Plan & Methodology:

This randomized study compares effects of duration vs. velocity-based TM training regimens on fitness and ambulatory function in chronic stroke patients. Phase 1 - patients are screened (Mini

Mental Status, CESD for depression, alcohol intake survey) and undergo routine medical and CV evaluations and blood labs in VA RRDC Assessment Clinic to establish medical eligibility. Standard neurological evaluations (NIH Stroke Scale, Modified Asworth Spasticity Scale, range of motion and manual motor testing) and review of imaging records assess neurological eligibility, deficit profiles and stroke subtypes. Physician supervised treadmill tolerance test and peak effort constant velocity exercise stress test with vital signs monitoring determines treadmill safety, functional eligibility to participate (must walk 3 minutes at 0.2 MPH with handrail support), and cardiopulmonary safety in response to strenuous exertion. Eligible candidates undergo baseline testing (phase 2) including measures of fitness (VO_2 peak, gait economy), cardiac output during exercise, ambulatory function and BOLD fMRI of knee movement. Phase 3 - 6 months TM training with either velocity or duration based progression, followed by Phase 4 –repeat of fitness, ambulatory function and fMRI tests after 3 months, and Phase 5 – repeat of all baseline tests after 6 months training.

Preliminary Results:

Results of our study to date (Figure 3) show that increasing training intensity to 70-80% HRR using velocity progression across 6 months is well tolerated and produces a mean 39% increase in VO_2 peak. Clinical and demographic features of stroke subjects in this study have not been not different than in our prior studies. To put this in perspective, high velocity treadmill training (HI-TM) produces 2.3-fold greater gains than our moderate intensity TM protocols (Δ=2.27 ml/kg/min), and >4-fold gains compared to those we report across 6 months in a low intensity TM training cohort. To our knowledge, these fitness gains with HI-TM are the highest yet reported in stroke subjects. They restore 40% of the impaired fitness seen in stroke subjects toward that of non-stroke controls, and show no evidence of plateau across 6 months training. Therefore, even greater gains may be possible with longer training. A 1 Met higher (3.5 ml/kg/min) fitness level gain in men is reported to prospectively predict a 28-51% reduction in fatal cardiac events. Our preliminary data shows a +5.33 ml/kg/min absolute increase in VO_2 peak with HI-TM (~1.5 Mets). This fitness gain elevates the VO_2 peak level above the estimated threshold required for basic ADL activities. Thus, the magnitude of fitness gain with HI-TM would be expected to have significant functional and cardiometabolic health implications for these stroke subjects.

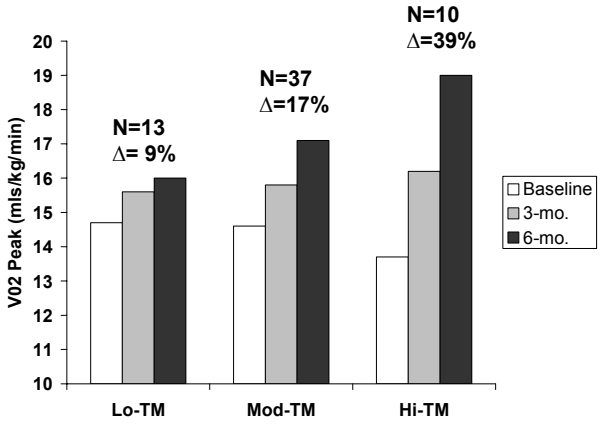

Figure 3

Figure 4: Participant undergoing treadmill exercise

Milestones:

Our results prospectively support our earlier cross sectional finding (Macko et al 2005) that velocity-based training progression, rather than heart rate based intensity progression is requisite to optimally improve fitness levels after stroke. The major finding is that HI-TM produces

approximately 2-fold greater gains in fitness than any other exercise program ever reported in stroke patients.

Future Grant & Publication Plans:

NIH R01 (Macko, Ivey, Co-PIs) Submitted February 2008- Awaiting Official Review

Exercise Models to Improve Cardiometabolic Health and Function after Stroke

This randomized study tests the hypothesis that higher intensity treadmill training (HI-TM) is more effective than a lower intensity lifestyle intervention (LILI) to improve fitness, insulin sensitivity and glucose tolerance by altering molecular regulation of HP leg muscle phenotype and metabolism. Alternatively, we propose that LILI will produce greater gains in balance and functional mobility, and that the combination of HI-TM + LILI will optimize long-term (12 month) cardiometabolic health and functional mobility outcomes in stroke survivors. Drs. Macko and Ivey submitted a 5 million dollar R01 grant to the NIH-NIA in February 2008 which greatly expands the scope of this arm of the Center of Excellence. The proposed project would have the added benefit of translating the study of different exercise models into the community, studying stroke survivors engaged in an exercise intervention over a full year, and developing a better understanding of the muscle molecular adaptations underlying improvements in fitness and function after stroke. Additionally, in March 2008 Drs. Ivey and Macko applied for supplemental funding from VA R&RD ($70,000) to expand this Center of Excellence project towards the study of the effects of differing treadmill training intensities on glucose metabolism and insulin sensitivity. We hypothesize that HI-TM will optimize adaptation in insulin sensitivity and glucose metabolism to improve cardiometabolic health in this high CVD risk population. This would be clinically significant based on a prevalence of abnormal glucose metabolism approaching 80% in chronic stroke, and findings that pre-diabetes and the pre-diabetic state equate to 2- and 3-fold higher risk for recurrent stroke, respectively.

Clinical Relevance:

Evidence-based consensus statements have emerged over the past decade recommending regular aerobic exercise to improve fitness and cardiovascular (CV) health for all Americans. The recommendations are structured on aerobic training intensity, the key determinant of CV-metabolic gains in able-bodied populations, as the cornerstone for designing exercise prescriptions. Based on emerging data that task-repetitive training can improve function by mediating neuroplasticity, we have investigated treadmill training (TM) to optimize locomotor learning, while providing aerobic conditioning in chronic stroke patients. Our initial non-controlled studies showed TM improves fitness, floor-walking function, and leg strength, while reducing paretic (P) hamstring spasticity. Yet, no guidelines exist for design of exercise after stroke and features of training needed to optimize gains in CV fitness versus function are unknown. This project is taking steps towards defining the optimal training strategy for chronically disabled stroke survivors.

Figure 5: Participants undergoing treadmill exercise