

Aerobic, Resistance, and Cognitive Exercise Training Poststroke

Eduard Tiozzo, PhD; Mehdi Youbi, MD; Kunjan Dave, PhD; Miguel Perez-Pinzon, PhD; Tatjana Rundek, MD, PhD; Ralph L. Sacco, MD, MS; David Loewenstein, PhD; John E. Lewis, PhD; Clinton B. Wright, MD, MS

Stroke may cause physical or cognitive impairments. Approximately 50% to 75% of all stroke survivors have residual motor or cognitive disabilities that prevent them from living independently. Muscle weakness is considered a major cause of motor disability in stroke patients.¹ Impaired walking occurs in as many as 80% of individuals immediately after stroke,² with muscle weakness in the paretic limb explaining $\leq 50\%$ of the variance in gait among individuals with chronic mild-to-moderate poststroke hemiparesis.³ As a result, gait patterns become asymmetrical and gait speed reduced.⁴ Additionally, impaired walking is commonly observed beyond 6 months after stroke.⁵ This lack of walking competency can precipitate and exacerbate a sedentary lifestyle and cardiovascular deconditioning.

Previous work has shown that maximal oxygen consumption ($VO_2\text{max}$), as a measurement of cardiovascular fitness, is reduced to 10 to 17 mL/kg/min within the first month after stroke⁶ and remains below 20 mL/kg/min beyond 6 months.⁷ The same values can be 45% lower than in age-matched and healthy individuals.⁸ The implication of low $VO_2\text{max}$ becomes even more important knowing that a minimum of 20 mL/kg/min is needed for performing daily activities⁹ and for independent living among older stroke patients.¹⁰ In addition to stroke-related decline in cardiovascular fitness, a natural decline in $VO_2\text{max}$ occurs after the age of 50, averaging a 5% to 10% (or ≈ 5 mL/kg/min) loss per decade. Therefore, elderly stroke patients may face disease- and age-related declines in cardiorespiratory fitness.

In a meta-analysis of 11 studies ($n=1105$), low physical activity (PA) levels, for example, 4355 daily steps taken, have been observed among stroke patients.¹¹ People with other chronic diseases, such as chronic pulmonary obstructive disease, have reported as few as 2237 steps a day.¹² The medical establishment, including the American Heart Association, recommends 10000 steps a day, which is not easily achievable through routine daily activities, and requires additional effort even by healthy individuals. Observational data from America on the Move reported that over 1000 healthy adults took an average of 5117 steps per day.¹³ Thus, reduced physical

inactivity in stroke patients, compared with healthy individuals, can further compromise their cardiorespiratory fitness and walking ability.

Impaired cognitive processes in perception, attention, executive function, memory, and language affect almost two-thirds of stroke patients.¹⁴ It is also estimated that $\leq 32\%$ of patients can have persistent cognitive impairment ≤ 3 years after the first stroke.¹⁵ Such impairments can reduce a person's independence in performing basic (eg, eating and dressing) and instrumental (eg, housework and social interaction) activities of daily living (ADLs)¹⁶ and increase risk of mortality¹⁷ and dementia.¹⁸

As a vulnerable patient population that is at risk for accelerated functional decline, stroke survivors may benefit from cognitive training and increased PA. However, the extent of those benefits and the ability of stroke patients to tolerate physical exercise programs of varying intensity after stroke are less understood, as is the optimal timing after the event. Similarly, the potential benefits of cognitive training after stroke need further study regarding timing, key cognitive domains to be emphasized, and duration of therapy. In this review, we summarize the effects of increased PA and exercise or cognitive training poststroke.

Exercise Modalities

The effectiveness of increased PA and exercise in the primary and secondary prevention of a variety of conditions and diseases is evident. More specifically, these benefits include lower body weight, better control of hypertension, glucose tolerance, improved lipid profiles, and an overall reduction in the risk of cardiovascular disease, diabetes mellitus, colon and breast cancer, osteoporosis, osteoarthritis, depression, and anxiety.¹⁹ The benefits of increased PA have also been observed in stroke prevention, with highly active individuals exhibiting a 21% lower risk of ischemic strokes and a 34% lower risk of hemorrhagic stroke.²⁰ Despite a considerable effect of increased PA on stroke, the overall evidence of its therapeutic effect on morbidity and mortality after stroke is still surprisingly weak.²¹

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From the Evelyn F. McKnight Brain Institute (E.T., M.Y., K.D., M.P.-P., T.R., R.L.S., C.B.W.) and the Departments of Neurology (E.T., M.Y., K.D., M.P.-P., T.R., R.L.S., C.B.W.) and Psychiatry and Behavioral Sciences (E.T., D.L., J.E.L.), University of Miami Miller School of Medicine, Miami, FL.

Correspondence to Clinton Wright, MD, MS, 1120 NW 14th St, CRB 1349, Miami, FL 33136. E-mail c.wright21@med.miami.edu

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Exercise training programs are classified as aerobic exercise (AE) for improving cardiovascular fitness, resistance exercise (RE) for improving muscular strength and power, and combined AE and RE training (CARET). Based on epidemiological studies, it is clear that AE and RE independently have distinct clinical and public health implications. For example, mechanical loading forces on the bones are essential for osteogenic responses that can lead to improved bone mineral density and reduced risk of osteoporosis. Although mechanical loading with RE results in enhanced bone metabolism, the same benefits of AE are often absent or modest.²² Conversely, a meta-analysis of the effect of different types of exercise on visceral adipose tissue, responsible for a cascade of metabolic disturbances, reported effective lowering of visceral adipose tissue with AE, whereas RE failed to induce significant reduction.²³ Moreover, CARET results in greater reduction of glycosylated hemoglobin and risk of diabetes mellitus, compared with AE or RE alone.²⁴ For that reason, public health guidelines recommend that adults engage in both exercise modalities.

Regardless of the proven benefits of RE, most exercise interventions primarily implement AE training protocols. However, it is still unclear whether CARET or AE or RE alone demonstrate better improvements among stroke patient populations.

Exercise and Cognitive Function

Exercise may have physiological effects capable of reducing the risk of cognitive decline, but data on stroke survivors are limited. Several beneficial mechanisms have been hypothesized in the relatively small number of human clinical trials, including a reduction of stress-related damage and attenuation of vascular risk. The social interaction of exercise may also have a positive impact on cognition.²⁵ Finally, it has been suggested that exercise training enhances brain plasticity through increased cerebral perfusion and upregulation of brain-derived neurotrophic factor, a protein strongly linked to neurogenesis and dendritic expansion. Elevated levels of brain-derived neurotrophic factor have also been associated with larger hippocampal volumes and enhanced learning and memory function.²⁶ A positive association between aerobic fitness and hippocampal volumes has been observed predominantly in animal models with less evidence from human studies.²⁷ However, one randomized controlled trial (n=120)²⁸ and one observational study (n=165)²⁹ demonstrated AE-induced increases in hippocampal volumes as well as improved memory among older adults (>55 years) without dementia. The literature on the specific pathways through which RE may influence cognition is limited, and one meta-analysis found greater improvements in cognition from CARET over AE training alone.³⁰ Despite the well-known benefits of exercise on multiple organ systems, our knowledge about the link between exercise and the brain is limited with some evidence that increased PA enhances cognitive performance poststroke.³¹

Large well-designed clinical trials are needed to address the extent of potential benefits from different exercise programs and their parameters (ie, intensity, frequency, and duration) for cognition after stroke.

Aerobic Exercise

Most exercise interventions in stroke survivors still predominantly implement AE protocols with a cycle ergometer as the preferred mode. Evidence shows that many stroke patients do not walk well enough to achieve sufficient improvements in cardiovascular function.³² Lower values of both VO_2max and maximum heart rate (HRmax) have been consistently observed during cycle ergometer versus treadmill exercise.³³ For that reason, the training intensities implemented in AE have been lowered for the cycle ergometer, compared with treadmill protocols (50% to 70% HRmax versus 50% to 85% HRmax), and the same finding should be translated into the clinical setting. Overall, cardiorespiratory fitness improves after AE training protocols of at least 8 to 12 weeks (intensity 50% to 80% of HRmax; 3–5 days/week; 20–40 minutes) in patients with mild to moderate stroke.^{9,34} The magnitude of changes in VO_2max among stroke patients is similar to healthy sedentary adults or participants in cardiac rehabilitation (12.5% versus 10% to 30% versus 13% to 15%, respectively).³⁵ Even if the observed improvements are small in absolute terms (eg, ≈ 1 mL/kg/min),³⁶ considering low baseline fitness levels, the same improvements can have significant functional carryover for stroke survivors. In addition to improved cardiorespiratory capacity, one systematic review³⁶ supported the idea that AE improves gait velocity and capacity in randomized trials involving ≤ 133 mildly to moderately affected stroke patients. This benefit may be even more evident with task-oriented therapy (ie, strengthening the lower extremities, enhancing walking balance and speed, or treadmill walking at higher intensity) reported in 2 randomized controlled trials with exercise sessions performed for 6 weeks (n=91; >1 year poststroke)³⁷ and 6 months (n=91; >6 months poststroke).³⁸ Although AE seems to lead to improvements in functional capacity, the effect of the same training modality on cognition is still unclear and insufficiently investigated.

Safety is an important concern in exercise studies involving stroke patients. A 6% recurrent stroke rate has been reported in an AE intervention group,³⁹ with the same rate being comparable to the recurrent stroke risk in the general population.⁴⁰ The fact that major adverse events in stroke studies have not been directly attributed to AE training is encouraging and raises the possibility of starting exercise training (and testing) in the early period after stroke (<7 days poststroke).

Future stroke studies involving AE training should determine optimal protocols for individuals with different physical limitations and cardiovascular risk. The research should focus on feasibility and the long-term effects of AE on cardiorespiratory fitness and functional capacity, as well as on cognitive functioning and health-related quality of life.

Resistance Exercise

Roughly twice as many AE training studies, compared with RE protocols, have been performed in stroke patients.⁹ Even though RE has been included in national guidelines and recommended for general health promotion, it remains an understudied and underappreciated exercise modality in stroke. Exercise frequency in RE studies of stroke has varied from 2

to 5 weekly sessions and from 4 to 12 weeks in length. These studies incorporated progressive RE, a method that increases the overload of resistance, thus demanding additional muscle force production. RE training in stroke has been shown to improve muscle strength in the lower extremities in 24 stroke participants (mean age 61 years; ≈20 months poststroke) after 10 weeks and in 42 stroke participants (mean age 66 years; 6 months to 6 years poststroke) after 12 weeks.^{41,42} Increased weight-bearing (on the affected leg) and gait speed were demonstrated in subacute poststroke after only 4 weeks of RE. The same improvements were greater in individuals (n=8) undergoing functional strength training that focused on power, balance, and weight-bearing exercises compared with a traditional RE protocol (n=10) that focused on improving muscle tone and avoiding excessive muscle power.¹ However, the increase in muscle strength does not always translate into significant improvements in walking and health-related quality of life.⁴³

In a 1-year randomized controlled trial involving over 100 healthy individuals, RE compensated for the equivalent age-related strength losses over 3 to 5 years. Interestingly, the training-induced benefits of the same RE training extended to 7 years after cessation of the study.⁴⁴ In addition to being understudied, RE interventions involving stroke patients have been shorter in duration and smaller in sample size compared with AE intervention studies. Because no adverse effects have been reported from this training modality,⁹ safety concerns should be minimal in conducting large-scale trials involving RE training among stroke patients.

The same future trials should focus on their feasibility and their immediate and residual health-related effects.

Combined Exercise and Stroke

The beneficial relationship between RE and health and chronic disease was recognized only recently.⁴⁵ The American College of Sports Medicine first introduced RE into its guidelines in 1990 as a beneficial component of comprehensive fitness programs for healthy adults of all ages. However, RE should serve as a complement to AE, rather than as a replacement, for therapeutic exercise.

A combined exercise program seems to be well-tolerated by stroke patients. In a randomized controlled trial involving multiple healthcare sites, 92 stroke survivors (mean age 69 years; <28 days poststroke) completed 36 CARET sessions, each in duration of 90 minutes and over 12 weeks. The benefits of the program extended beyond spontaneous recovery and usual care in strength, endurance, and balance.³⁹ Similar findings have been reported by Pang et al⁴⁶ in a community-based controlled intervention trial, implementing CARET among 63 stroke survivors (mean age 65 years; >1 year poststroke). A more recent study by Marzolini et al⁴⁷ consisted of a 6-month CARET program (60 minutes sessions, 3 times/week, for 19 weeks) in 41 patients with motor impairments (mean age 63 years; ≥10 weeks poststroke) showed significant gains on the Montreal Cognitive Assessment and in cognitive subdomains of attention/concentration and visuospatial/executive function. The number of individuals meeting criteria for mild cognitive impairment also decreased. Thus, it is conceivable that CARET in stroke patients could affect multiple domains of disabilities compared with more isolated gains achieved from AE or RE alone.

Future stroke studies involving CARET should focus on examining their additive and synergistic effects on multiple health outcomes compared with AE or RE alone.

Cognitive Training After Stroke

The cognitive effects of stroke are as varied as their topography might suggest with any cognitive domain potentially affected.⁴⁸ However, dysphasia, slowed information processing, and executive dysfunction are arguably the most common.³¹ In a 10-year prospective study involving close to 100 young patients with ischemic stroke (median age 43 years), mental slowness was present even ≤10 years after stroke.⁴⁹ A recent large trial also demonstrated that even small infarcts are commonly associated with cognitive impairment.⁵⁰ Any form of cognitive decline after stroke places a burden on stroke patients and their caregivers, and strategies for cognitive rehabilitation, or training, with a

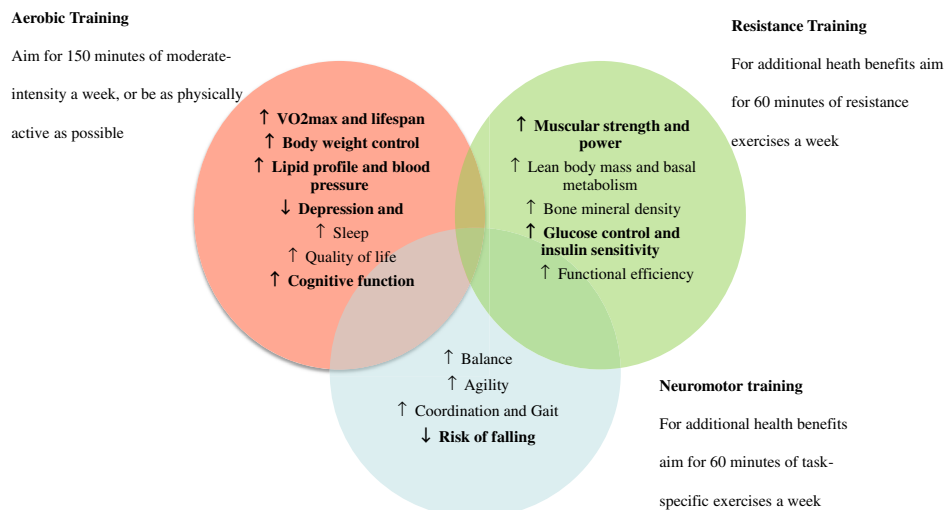


Figure. General recommendations and complementary health benefits of combined exercise training. ↑ indicates values increase; ↓ indicates values decrease; Bold indicates strong evidence, considering causality and dose response, in adults and older adults (US Department of Health and Human Services, 2008 Physical Activity Guidelines for Americans).

goal to improve function and ameliorate disability are critical. A recent systematic review⁵¹ of a limited number of studies did not report extended benefits of cognitive training to function and basic and instrumental ADLs. However, positive transfer effects of cognitive training in performing ADLs were observed in 29 stroke patients with apraxia (duration 8 weeks; <4 weeks and >2 years poststroke).⁵² Another review⁵³ identified only 2 small randomized trials (n=<15), with isolated improvements in trained memory task and immediate and delayed recalls.

Combining motor and cognitive training in a performance-based and problem-solving approach is an increasingly promising treatment for enhancing functional outcomes on trained and untrained tasks.⁵⁴ Furthermore, combined exercise and cognitive training interventions could theoretically enhance neural plasticity. In a recent multicenter randomized control trial,⁵⁵ 83 stroke patients (>4 months poststroke) underwent combined cognitive and exercise training over 12 weeks. The primary objective of the study was to evaluate the effect of cognitive training alone and combined training on psychological and physical variables associated with stroke, such as fatigue, depression, and sleep. The greatest improvements were seen in poststroke fatigue when cognitive training was combined with exercise.

The amount of literature on the isolated effects of cognitive therapies on specific impairments in stroke patients is limited, involves small sample sizes, and has methodological limitations and inconclusive results. Although cognitive training/rehabilitation may result in improvements in specific cognitive domains, the data are insufficient relating such interventions to real world cognitive processes and proficiency in everyday functional ADLs.

Further work with sufficiently large samples is required to allow exploration of these issues and to reach reliable conclusions. A greater emphasis should involve the examination of transfer effects to ADLs that improve function and quality of life after stroke. Finally, potential additive or synergistic effects of cognitive training, combined with therapeutic exercise, should be explored.

Conclusion and Future Directions

Overall, studies demonstrate that stroke-related impairments can be improved from properly designed and supervised therapeutic exercise programs. A most recent review confirmed the beneficial role of exercise on multiple effects on life after stroke, such as improved cognition, arm function, and balance and gait.⁵⁶ However, more research is needed to quantify optimal intensities, frequencies, and durations in different exercise modalities. Additionally, a paucity of research has investigated the effect of exercise alone, or combined with cognitive training, on restorative cognitive rehabilitation after stroke. After effective exercise and cognitive modalities are clearly identified, perceived barriers to adherence and the sustainability of interventions need to be better understood before widespread implementation can be attempted.

It is important to note that even if therapeutic exercise fails to restore physical and cognitive impairments to prestroke levels, increased PA and exercise can enhance overall well-being

and reduce multiple risk factors (Figure) responsible for recurrent strokes and coronary events among stroke patients.

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