Exercises and Cognition in Older Adults: A Review Guide to Work Out

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Abstract

Background: With aging, there are declines in various functions of the nervous system, including cognition. Exercise is well-known to produce positive multifaceted improvements in not only physical but also neurological functioning in aging population. Although current available results from potential studies are favorable, they are heterogeneous. Thus, there is still no consensus on which form, dosage, and duration of exercises are best for older people. Also, it is questionable how and to what extent can exercise effect specific form of cognitive functions. This review aims to summarize cognitive subdomain effects from particular types of exercise in the elderly.

Method: We perform computer searches of studies published in electronic databases MEDLINE, by pairing keywords and synonyms between *exercise types*-eg. 'exercise', 'aerobic', 'physical activity', 'flexibility', 'resistance training' and *cognitive domains and cognitive abnormality* in older adult such as 'cognition', 'memory, 'execution', 'attention', 'naming', 'word finding' and 'behavior', then we chose only the studies that included older adult cohorts. Target journals to be used include, but not limit to that of neurology, neuropsychology, aging and geriatrics, physiology, and rehabilitation medicine. This review will be focusing on the characterization of each exercise types and subtypes (i.e. aerobic exercise, resistance training, flexibility, mind and body exercise, weight training), with detailed reviews and discussions on their cognitive effects. The information could be a useful guide to work out for older individuals.

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Physical activity and neuroplasticity

In older adult, although normal aging may cause a decline in global cognition, brain plasticity may offer a room for adaptation. Brain plasticity, or neuroplasticity, is a self-change of microstructures and functions of human brains cells according to the external (in this context, this means extracranial) stimuli, which in turn would impact cognition and behavior.[1,2] In both human and animal studies, physical activities, in particular aerobic exercise, may function as an external stimulus for neuroplasticity, propelling neurogenesis[3,4], neural cell proliferation[5,6], and branching of neural dendrites.[6]

Changes in neural architecture could be better illustrated by the neuroimaging study. Flöel, Ruscheweyh[7] demonstrated the relationship between physical activity, neurotrophic factors and structural imaging changes. The author found that higher level of physical activity, regardless of type, was associated with higher serum neurotrophin granulocyte colony stimulating factor (G-CSF) level, and increased grey matter volume in prefrontal and cingulate gyri assessed by voxel-based MRI technique. The imaging findings of increase brain volume also concordant with several other studies.[8]

Aerobic exercise and cognition in older adult

Examples of aerobic exercise include walking, running and spinning. There are particular levels of aerobic exercise stratified by the intensity; high-intensity, moderate-intensity and low-intensity. In general, people who exercise may be able to estimate the level of exercise they are doing by observing shortness of breath, percentage of increased heart rate, or just how they feel.

The mechanisms underlying positive effect of aerobic exercise on cognition could start from physiologic changes during aerobic activity. Hillman, Erickson[9] reported that an increased heart rate produced positive effect on cognition. As a result, this would stimulate systemic intracellular cascades to proliferate neurotrophic factor[10] such as vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), granulocyte-colony stimulating factor (G-CSF), and brain-derived neurotrophic factor (BDNF).[7,11-15] Permeability property of these neurotrophic factors allowed them to cross the blood-brain barrier, nourishing the brain tissue.[11]

VO2max, a marker for aerobic fitness, and also cognition?

Objectively, the intensity of aerobic exercise and so-called cardiovascular or aerobic fitness can be measured by the parameter abbreviated as VO2max. The VO2max is the maximum amount of oxygen that a person can utilize during exercise. It is widely accepted marker for improved mortality.[16] Freudenberger, Petrovic[17] had performed a study in cognitively normal older adult. The author concluded that VO2max alone was associated with better global cognition and better performance in memory, executive function and perceptual-motor skill tasks.

VO2max is decline with aging because of loss of cardiovascular reserve and increases oxidative stress due to reactive oxygen species production.[18] However, at this time, it is presumable that aerobic exercise would improve VO2max, and so cognition[19], but the direct link between VO2max and cognitive function is not entirely known.[16]

In addition, aerobic fitness (as determined by VO2max), rather than an acute bout of aerobic

exercise, has greater influence on cognitive performance.[20,21]

Aerobic exercise, cerebrovascular function, and cognition

Aerobic exercise is well-documented that it facilitates cardiovascular fitness, which will also affect cerebrovascular 'fitness' as well. Human brain is the most blood-rich organ and do not know much how to be anaerobic (92% oxidative metabolism at resting state)[22], so it requires large amount of oxygen and glucose consumption. Although cerebral blood flow is fairly constant because of cerebral autoregulation[23], adequate amount of aerobic exercise may contribute to above-average blood circulation to the brain, together with facilitating adaptive response of the brain to an increased blood flow. Thus, more effective transferring of these nutrients has achieved. A study in older adult showed that participants who underwent moderate intensity walking had significantly increased middle cerebral artery blood flow velocity as determined by transcranial doppler ultrasound, comparing with non-exercise group.[24]

Moreover, positive effect of exercise to human intracranial blood circulation may proportionately be related to the degree of exercise intensity. Witte, Liu[25] had studied hemodynamics of human middle cerebral artery (MCA). The authors hypothesized that increasing exercise intensity, as determined by the aerobic fitness parameter VO2max, would increase MCA hemodynamic responses. The result showed that MCA amplitude in hemodynamic response observed in moderate intensity exercise, was significantly greater than that in low intensity exercise. Likewise, higher amplitude responses were negatively associated with age, but positively associated with higher VO2max. These findings could be implied that, with aging, aerobic exercise at which cardiovascular fitness or VO2max has been accomplished, would be beneficial to the cerebrovascular hemodynamic, which might possibly be a key important factor improving cognitive functions in older adults.

Long-term effect of aerobic exercise in older adults

Aerobic exercise does not only elicit immediate effect, but also being long term protective factor against age-related cognitive decline. Although this could occur in any type of exercise[26], aerobic exercise could be considered as the most promising one, since there are a growing body of literature that reported significant advantages of aerobic exercise in young adults, which were maintained throughout their ages. Brain volume maintenance was demonstrated in the 21-year in average longitudinal study reported by Rovio, Spulber.[27] In this study, participants were asked the question "How often do you participate in leisure time physical activity that lasts at least 20-30 min and causes breathlessness and sweating?", which reflected the aerobic outcome that involved breathlessness and sweating. Subjects who were routinely admitted to aerobic physical activity during their midlife, as determined by two or more aerobic activities a week, showed significant larger grey matter and total brain volume.

However, although preserved grey matter could be implied that its function in brain cognition should also be preserved, the author did not report objective cognitive tests of subject functional ability. These findings highlighted the importance of primary prevention of cognitive impairment should be encouraged since midlife or earlier, and be maintained throughout our lifetimes.

Executive function: the main effect

Improvement in executive function was well-established in many researches on aerobic exercise[28-30], compared to other cognitive domains. Executive function is a domain of cognition including planning, decision making, cognitive flexibility, coordinating and inhibitory control task.[31,32] Overall, these strategies are goal-directed behaviors.[33] The region of brain corresponding to executive function is frontal lobe and fronto-subcortical circuit.[32,34] This could be illustrated by the study of executive function measurement by Stroop test that evoked cortical activation at the dorsolateral prefrontal area in the Functional Near-Infrared Spectroscopy modality.[34] Aging has been reported to associated with decline in multiple executive function task[35-37], which might be due to alteration of micro and macro structure of brain connectivity among regions.[36]

Other cognitive domains benefit from aerobic exercise

Memory

Working memory is one of cognitive domains demonstrate advantages from aerobic exercise. Memory function is primarily stored in the hippocampus and also the adjacent structures in medial temporal lobe[32], along with the connection to the prefrontal area for processing inputs.[32,38]

As people age, hippocampus shrinks 1-2% per year in cognitively normal older individual[39], causing impaired memory function[37,40] as determined by word recall[41,42], visual span and spatial span short-term memory tasks.[43] Some individuals may have progressive memory impairment to the point that alteration in daily activities were observed, which may contribute to amnestic type mild cognitive impairment (MCI)[37] and so Alzheimer's dementia later on.[37,44]

Recent studies had shown the positive effect of aerobic activity on the memory. Erickson, Voss[45] reported that, in one-year period RCT done in normal older adult, aerobic exercise cohorts had increased hippocampal volume by 2%, which was accompanied by the improvement in memory function. This effect was not significant in the control group with stretching exercise. They also found the association between hippocampal volume and serum BDNF level. There was also a parallel study in older adults with cognitive impairment done by Morris, Vidoni.[46] Participants who were diagnosed as probable Alzheimer's disease were enrolled for 150 minutes per week aerobic exercise with target heart rate 60-75% reserve, and a set of cognitive test batteries was done at baseline, 13, and 26 weeks. The authors found that change in cardiorespiratory fitness was correlated with memory performance and bilateral hippocampal volume.

More objective evidences of positive effects of aerobic exercise on memory had been studied. One study using electroencephalography (EEG) recordings revealed that older adults with higher aerobic activity as determined by metabolic equivalent (METs) questionnaires, had shorter response time on the modified Sternberg's working memory tasks, and also higher amplitude in P3, N1, and shorter latency of P3 EEG electrodes.[47] Former studies had reported that augmentation in P3 amplitude corresponded to memory scanning and retrieval functions[48,49] Siette, Westbrook[50] using perfusion imaging, Maass, Düzel[51] reported that aerobic fitness improvement correlated with increased regional cerebral blood flow, blood volume, and hippocampal head volume in contrast-enhanced MRI.

However, there were some studies showed discordant result that no established significant relationship between aerobic fitness, as defined by standard indicators such as VO2max or metabolic equivalents (not the general terms as physical activity or aerobic exercise) and working memory ability.[7,52] This could possibly be due to heterogeneity in neuropsychological measuring tools and difference in the definition of aerobic fitness defined in each protocol.

Language

In healthy older adult, decreased verbal fluency or, in other words, word finding difficulty, appears to be the most common complaint of language deficit that has been reviewed extensively.[53-55] Verbal fluency is theoretically in part of executive function, memory and language domains.[32] We need (1) intact memory for adequate word storage, to serve as our internal dictionary, (2) proper executive function for searching, processing or create word outputs correctly, and finally, (3) we need language circuit, which primarily in the dominant fronto-temporal region, for managing language hierarchical components which include syntax (grammar), phoneme, grapheme, semantic (meaning) and pragmatics (use).[32,56] According to this statement, studying language function might be challenging to completely distinguish the result from other required cognitive domains.

There were several studies found that aerobic exercise elicited a positive outcome in language domain of cognition. Segaert, Lucas[57] investigated a relationship between aerobic physical activity and incidence of age-related language failures. Language failures were measured by giving the participant a definition of words on a screen, then the participant indicated that they knew the correct word of this definition or not, or if they could speak out the correct word. The author found that VO2max, an objective marker of aerobic fitness, were significantly correlated to lower incidence of 'tip-of-the-tongue' experiences in older adults. To further illustrate from their findings, in one constant age and vocabulary size, increasing one standard deviation of aerobic fitness would reduce the chance of word finding difficulty for 7.75 percent.

As mentioned above, studying language function by testing verbal skills from neuropsychological batteries may not be able to confidently indicate that the results are solely referred to language function. Therefore, concurrent structural and functional imaging study is one of solutions that we could selectively focus on the corresponding language areas. One imaging-based study was performed by Nocera, Crosson.[58] The authors had healthy older adult undergone a 12-week period of spin aerobic exercise to target 75% individual maximal heart rate reserves. Spin aerobic exercise allocated in this study included cadences, sprints and climbs. The control group were nonaerobic balancing exercise. Both cognitive test and imaging studies were done in this study.

In spin exercise group, there were better performance in semantic verbal fluency and Hopkins Verbal Learning Test (HVLT).[59] Also, post-exercise, real-time fMRI analysis during language tasks, the exercise groups showed significant lower level of blood-oxygen level dependent (BOLD) activity at Brodmann's area 44/45, inferior temporal gyrus, and angular gyrus, which were homologous areas to semantic verbal fluency, compared with control group.

Additionally, within the exercise group, there was a correlation between increased VO2, decrease in right inferior frontal BOLD activity, and increase in left lateralized activity. These findings were implied that, with an increase in VO2, there were less likely to recruit right brain and thus higher chance of left brain functioning in language tasks

Resistance exercise and cognition in older adult

Resistance training (RT) includes the type of exercise that generate voluntary activation of particular skeletal-muscle groups against external resistance.[60] Strength training is in similar definition to resistance training, with the use of word 'strength' instead to highlight the goal of resistance training which is 'muscle strength'. Variations of RT are classified by which the resistance is generated; body-weighted RT is tool-free technique such as planking and push-up; machine-weighted RT is by using machine; and free-weighted RT uses classic tools like dumbbell, sand bag, kettlebell; and suspension training as in TRX.

Resistance training was formerly thought to be of interest only for young body builder. However, more recently, benefit of resistance training has been considered to be encouraging across age groups. In older individuals, recent studies have shown that resistance training increases muscle mass, strengthens muscle power, and creates better body composition profile.[61,62]

Without considering purpose of resistance training in elderly is for cognitive strengthening or other physical benefit (such as improving sarcopenia), safety when performing resistance training in older adult is priority. Thus, following the standard guideline with individual adjustment is crucial. A consensus guideline of RT for older adults launched by American College of Sports Medicine (ACSM, 2010)[63] has recommended multiple-joint involved RT (such as squat) as primary approach, and single-joint for additional exercise, with moderate intensity load of 60-70 percent of one-repetition-maximum (1RM), for one or more sets of 10-15 repetitions with 2-3 minutes of rest in-between. The recommended RT tempo is at least twice per week and allow 48 hours or more separation between exercising in the same muscle group for muscle recovery.

In general, resistance training elicits improvement in functional ability in older adults.[64] Although this is fundamentally due to physical benefit, functional ability could also be considered as part of global cognitive function. Functional ability, together with global cognition are two major factors indicating cognitive impairment and dementia states. Current studies have been utilizing global cognitive measurement using standard neuropsychological batteries included MMSE, MoCa, and ADAS-Cog, with reliable outcome, albeit there was heterogeneity of testing protocols and interpretation of the result.[65-67]

Memory and executive functions

Regarding cognitive subdomains, there were studies that have shown positive outcomes in memory and executive function. A randomized-control trial performed by Best, Chiu[68] had revealed better memory performance in older adults with resistance training and also illustrated the effect of frequency of RT. The authors had cognitively normal older woman participated in 52-week, progressive, high-intensity RT program consisted of body weight and free weight approaches. Each RT session, 2 sets of 6-8 repetitions were administered, and were

increased if the participants could tolerate without discomfort. The control group was administered stretching exercise. The RT group was further divided into two frequencies; one subgroup had been assigned to RT session once a week, and the other subgroup being twice a week.

The Rey Auditory Verbal Learning test was used to assess immediate and delayed word recall. Stroop test, Trail Making Test, backward digit span and Digit symbol substitution test were used for executive function evaluation. The cognitive test results were compared among baseline, at 1-year completion of exercise intervention and 2-year follow up. The result indicated that RT had long-term positive effect on both executive and memory functions. Participants in both once and twice a week RT showed better executive performance compared with control group, while only biweekly groups had better memory performance.

Additionally, the findings from this study are a good illustration of an influence on cognition from dose-response relationship, in similar way to the physical performance.[69] Also, this study finding implied that RT might have unique mechanisms that run unevenly on specific cognitive domains. On the other hand, getting back to the aerobic exercise, aerobic effect seems generalizable to a majority of cognitive domains. Further study could be beneficial to explore other contributing factors determining cognitive outcome from resistance exercise; such as subtypes of RT, instruments to use, and different workout techniques used.

Attention and visuospatial functions

Spatial attention or awareness refers to the ability to perceive and understand the temporal and spatial stimuli of the surrounding (global attention) and also the focusing spot (focal attention).[32,70] Normal aging causes decline in spatial attention[71] which eventually would also decrease visuospatial motor skill[72], due to inseparable connection between spatial attention (served as 'input') and motor action-intention (served as 'output').[32] With comparison to aerobic exercise, resistance training requires more attention to target muscle action, correct posture, number of repetitions, and range of motion, thus to work out in this mode would consume a large capacity of awareness and visuomotor relationship. There were studies illustrated that these two corresponding cognitive domains might also be beneficial from resistance training. Fragala, Beyer[73] studied older adult with normal cognition by comparison between resistance training group versus control. The exercise group was assigned for structured, yet simple resistance training using body weight and machines such as leg extensions, leg curls, seated rows, lateral pull-downs, modified squats, modified split squats, modified stiff-legged dead-lifts, biceps curls, chest presses, shoulder presses, triceps extensions, abdominals, and calf raises. Load was administered individually at moderate intensity determined by OMNI scale.[74] The RT exercise protocol was set to 8-15 repetitions per session, 2 sessions per week. The total duration of program was six weeks. Both groups were assessed for spatial awareness by using NeuroTracker (CogniSens Athletic Inc.) - participants wore a virtual reality (VR) goggles and tracked designated objects as they moved in space. Visuomotor skill was assessed using reaction time by D2 Visuomotor Training Device (Dynavision LLC)-participants tapped the randomly illuminating buttons as fast as they could on the display which contained 64 buttons. Both cognitive domains together with serum BDNF, a marker for

neurogenesis, were evaluated in before-and-after fashion. The result from this study revealed that both groups had similar baseline cognitive score but RT exercise group showed significantly greater mean change after 6 weeks in all variables. They interpreted that spatial awareness had 85% improvement from resistance training.

Flexibility exercise and cognition in older adult

Flexibility exercise is originally categorized all variations in this types of exercise, for example, stretching exercise, mind and body exercise, balance exercise. To date, a trend in flexibility exercise has more likely been transformed to reflect 'mind and body' type, which combine simultaneous physical and mental concentration, rather than relate to only flexibility of body and muscle groups.

Some examples of mind and body exercise include Yoga, Tai Chi, Qigong and Pilates. Common characteristic of these mind and body exercises is performing physical movement while focusing on breathing, mindfulness (which also compatible to attention) and relaxation. They have become well-documented in recent researches for their cognitive effects, while other flexibility exercise, such as stretching exercise, have usually been used for control. Likewise, focusing on older individual, mind and body exercise is even more widely-accepted because of low impact and slow pace characteristics, which have been considered suitable for elderly.[75] In addition, since mind and body exercise requires high level of cognitive demand, apparently, this exercise method would theoretically play some positive effects to human cognitive function, which have been reported to slow down age-related cognitive decline.[76]

A meta-analysis of cognitive effect from mind-and body exercises[77] revealed that the majority of mind and body exercises improved global cognition in healthy older adult, and also older adult with cognitive impairment. Yoga has been found in a large body of literature as it improves executive function.[78-80] One example of these studies with clearly-structured, applicable protocol was done by Gothe, Kramer.[81] The author had healthy older individual age over 55, performed yoga three sessions per week for eight week, compared with stretching exercise as a control group. Cognitive measurements were done before and after the intervention, which included task-switching, digit backward and memory span. The result demonstrated that 8-week yoga intervention had significantly improved cognitive performance in executive function in the intervention group. Tai Chi and Qigong, a mind and body exercises originated from the other side of the world, also showed similar outcome. In addition, apart from executive function, memory was also found to be improved in mind and body exercise intervention in some studies.[78,82,83]

Summary

Exercise exerts benefit across age groups. With respect to older adults, not only physical but also cognitive effect that are vital, as cognition influences function in daily life. Because of current trend in health-consciousness, engaging in physical activity and exercise has become increasingly popular. Consequently, its popularity has created more and more variations in subtypes and techniques, which might be confusing for the beginner, especially the elderly. This review has discussed and exemplified particular studies with

practical exercise protocols with promising result in cognitive domains, in order to help health care workers approximately guide 'what type' and 'how' to start workout, for the best available outcome improving specific cognitive concerns in older adults.

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