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Correlation of 6-minute walk test with cognitive function tests results. Preliminary results of Train Your Brain Study

Korelacja wyniku testu 6-minutowego marszu z wynikami testów funkcji poznawczych u osób starszych. Wstępne wyniki badań Trenuj Swój Mózg

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Abstract

Introduction. *Aging is related with, inter alia, cognitive functioning and aerobic capacity decline. Standardly designed Comprehensive Geriatric Assessment does not focus on inter-relationship between these two variables. However, recent studies indicate the concomitance between the level of aerobic and cognitive performance.* ***Aim.*** *The aim of this study is to assess the level of correlation between the results of 6-minute walk test (6MWT) with cognitive function tests results.* ***Material and methods.*** *In these preliminary studies 128 patients (21 men, mean age: 68.80, age range 58-88) were examined. Aerobic capacity was measured with 6MWT (6-minute walk test). Cognitive functioning was assessed with Mini-State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Trail Making Test Part B (TMT B). R-Pearson test was used to assess the level of correlation.* ***Results.*** *Results of 6MWT were significantly and positively correlated with MoCA score (r = 0.3365) and its two subtests – a word list delayed recall (r = 0.2842) and verbal fluency tests (r = 0.22). Moreover, results of the 6MWT were significantly was significantly and negatively correlated with TMT B results (r = -0.31). However, correlation with MMSE was not statistically significant.* ***Conclusions.*** *In these preliminary studies, results showed the coexistence between higher aerobic capacity and better scores in cognitive function tests in older adults, however, in case of MMSE tests results were not statistically significant. Longitudinal studies on larger samples are needed to estimate the level of influence of the aerobic capacity decline on cognitive functioning in aging process. (Gerontol Pol 2017; 25; 81-87)*

Key words: *6-minute walk test, cognitive function tests, older people, Trail Making Test part B, MoCA, MMSE*

Streszczenie

Wstęp. *Starzenie się jest związane między innymi z pogorszeniem się funkcji poznawczych i wydolności tlenowej. Standardowo, Całościowa Ocena Geriatryczna nie koncentruje się na wzajemnych relacjach pomiędzy powyższymi zmiennymi. Jednak ostatnie badania wskazują na wzajemne korelacje pomiędzy poziomem wydolności tlenowej i funkcjonowania poznawczego.* ***Cel.*** *Celem niniejszej pracy jest ocena poziomu korelacji między wynikiem testu 6-minutowego marszu (6MWT) z rezultatami testów funkcji poznawczych.* ***Materiał i metody.*** *W niniejszych, wstępnych badaniach 128 pacjentów zostało przebadanych (21 mężczyzn, średnia wieku: 68,80, przedział wiekowy 58-88). Wydolność tlenową mierzono za pomocą Testu 6-minutowego marszu). Funkcjonowanie poznawcze oceniano za pomocą testów: Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) i Test Łączenia Punktów Część B (TMT B). Poziom korelacji został zmierzony testem r-Pearsona* ***Wyniki.*** *Wyniki 6MWT były znacząco, pozytywnie skorelowane z wynikami testu MoCA (r = 0,3365) i z dwoma podestami tego testu: z przypominaniem odroczonymi (r = 0,2842) i fluencją werbalną (r = 0,2213). Ponadto rezultaty 6MWT były istotnie, negatywnie skorelowane z wynikami TMT B (r = -0,31). Jednakże korelacja z MMSE nie była statystycznie znacząca.* ***Wnioski.*** *W niniejszych, wstępnych badaniach wyniki pokazały współ-*

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istnienie lepszej wydolności tlenowej i lepszych wyników w testach funkcji poznawczych u osób starszych, jednak w przypadku testów MMSE wyniki nie były istotne statystycznie. Potrzebne są podłużne badania na większych grupach w celu oszacowania poziomu wpływu spadku wydolności tlenowej na stopień pogarszania się funkcji poznawczych w procesie starzenia. (Gerontol Pol 2017; 25; 81-87)

Słowa kluczowe: *test 6-minutowego marszu, testy funkcji poznawczych, starsze osoby, Test Łączenia Punktów Część B, MoCA, MMSE*

Introduction

Methodological issues in case of physical activity, physical exercise and cognitive functioning

Aerobic capacity decline and sarcopenia could be some of many factors, which have strong negative influence on quality of life in older people. Together with cognitive functioning decline, these factors could significantly contribute to deterioration of functioning in everyday life [1,2]. Systematic physical exercise is one of many non-pharmacological treatments to improve above mentioned health issues.

More than last 3 decades proved to be very fruitful in researches examining the interrelationship between the physical exercise and cognitive functioning. However, there are several methodological issues in this branch of science. First of all, there are two different methodological approaches: some studies, based on cross-sectional approach, showed positive correlation of cognitive function with fitness level [3-6]. Several studies are enriched by methods aimed at showing the biological background which could explain some aspects of observed correlation between aerobic capacity and cognitive functioning such as: more efficient white-matter functioning and improved structure [4], greater spontaneous brain activity [5], better hemodynamics in several areas: basal ganglia, thalamus, anterior cingulate cortex, supplementary motor cortex, right motor/somatosensory cortex, left somatosensory cortex, middle frontal gyrus [6] during executing dual-task. Moreover, advantageous brain geometry measured in several areas: hippocampus [3] frontal, parietal and temporal lobes [7] was also indicated in favor for participants with higher aerobic fitness. Noteworthy, cross-sectional studies are not able to give the information about the direction of influence in measured variables. For example, do better cognitive functioning is an effect of elevated level of physical activity, or do superior cognitive functioning in older people translates to fearless attitude relative to taking part in more demanding physical activities, such as long walks away from home or in fitness classes in larger groups? Above mentioned phenomenon called "reverse causation" could be the cause confounding conclusions drawn from cross-sectional studies; pre-existing cognitive impairment could potentially cause a reduction in physical activity.

Another approach are the longitudinal studies, which measure cognitive and aerobic performance in one point in a group of participants and compare these results in the same group after significant amount of time expire [8]. Noteworthy, accurate methods of fitness level measurement should be chosen: Burzyńska et al. [4] compared results of physical activity questionnaire and objective physical activity measurement done by accelerometer and showed, that results of physical activity questionnaire could be highly misleading. 83% of participants that took part in studies [4] subjectively admitted no participation in regular physical activity, defined in these studies as no more than two moderate bouts of physical activity per week in the past six months. In contrary, rest of participants reported taking part in some physical activities, however results from objective measurement by accelerometer showed that 40% of this group did not satisfy the requirements to be classified into group with minimum physical activity, defined by less than 150 min of moderate physical activity per week [4]. Likewise, 19% of the participants who admitted to be low-active were, in fact, more active than minimum physical activity criteria required [4]. Authors concluded that these results revealed inaccuracy in evaluating physical activity based on subjective questionnaires [4].

Another approach is to investigate the direct influence of physical exercise on cognitive functioning by using intervention-based study [9-15]. However, type of used exercise (aerobic, anaerobic) varies in studies. Most of them are based on aerobic exercise [9-11,14] however some showed that anaerobic resistance training [12,13] could also be effective in improving cognitive functioning. Additionally, time of interventions varies significantly; some measured acute effects of physical exercise [see 9 for a review], while other focused on chronic effects: after 12-weeks [11], four months [10], six months [12,14] and one year [13,15].

Secondly, in reviews of studies which describe above mentioned topics, inaccuracy of determining measured variables is conspicuous. The lack of distinction between physical activity and physical exercise could mislead the reader. In exercise science, physical activi-

ty refers to more broad term, which one of types is the physical exercise. Therefore every physical exercise is kind of physical activity, but not every physical activity must belong to the physical exercise category. Physical exercise refers to a relatively brief and intense bout of physical activity. During intervention-based studies protocols development, it seems to be very important to describe modality and intensity of training protocol very precisely, and yet best to compare the effects of different intensities [13]. Also, physical exercise interventions were directed to groups of healthy older people as well as older patients with Mild Cognitive Impairment [16], Parkinson [17] and other diseases, such as schizophrenia [18]. Therefore, results from groups of different specificity cannot be directly compared.

Last but not least, there is need to determine biological mechanism, which underlies influence of physical exercise on cognitive functioning. First, animal studies, and later, human-based studies showed increased release of trophic factors (brain-derived neurotrophic factor – BDNF, insulin-like growth factor-1 – IGF-1, vascular endothelial growth factor – VEGF) [19-22] in response to chronic and acute physical exercise. The increased expression of trophic factors was positively correlated with improved cognitive functioning. However, it rather does not explain why low-intense physical activity [23] such as walking [24,25] could be protective in cognitive functions deterioration. For example, some [25] report that walking at a leisurely pace for at least 1.5 hour per week in 2-years period was more effective in inhibition of cognitive decline compared to walking less than 40 minutes per week. Interestingly, observational studies, which measure correlation of trophic factors, for example BDNF, with the level of aerobic capacity and level of physical activity give contradictory results [26-29]. Some showed positive correlation between VO2max and BDNF [26], while others showed negative relationship [27] as well as between these two factors and habitual physical activity [28]. Moreover, negative correlation between BDNF level and total physical activity per month was estimated [29].

Train Your Brain study

Train Your Brain study aims to examine correlation between physical and mental activities as well as dietary and social factors and cognitive functioning in cross-sectional and longitudinal manners. Moreover, the direct influence of mental and physical exercise on cognitive functioning would be also examined in intervention-based studies.

In the present preliminary studies we would like to check is there any correlation between aerobic performance and cognitive functioning.

Material and methods

Patients were enrolled into studies through the regional radio and TV advertisements, during public health-promoting lectures, in Day Care Centers for the Elderly, and on various meeting-groups for older people. Assessment was conducted at Collegium Medicum University Hospital in Bydgoszcz, in Department and Clinic of Geriatrics and Department of Hygiene, Epidemiology and Ergonomics and was approved by the local ethics committee at the Collegium Medicum University (KB 340/2015). The first visit consisted of blood collection, neuropsychological, medical, social, economic, dietary and physiotherapy assessments, what together took three hours per one patient. Schedule of the examinations was arranged in a way to set blood collection, followed by neuropsychological assessment as first examinations.

In these preliminary studies 128 patients (21 men, mean age: 68.80, age range 58-88) were examined.

Cognitive functioning was assessed with Mini–Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Trail Making Test Part B (TMT B). MMSE is a well-known 30-points questionnaire used in neuropsychological assessment, it measures orientation to time and place, immediate recall and short-term verbal memory, calculation, language, and construct ability. The higher score indicates better cognitive performance. We assumed 24 point as cut-off score for Mild Cognitive Impairment diagnosis. MMSE is characterized by rather worse specificity and sensitivity than MoCA, however, plenty of similar researches are based on this test, therefore, MMSE has been incorporated into studies.

The MoCA assesses several cognitive domains. It measures all main cognitive domains; namely Visuospatial skills, short-term memory recall, executive functioning (examined by a mini-form of trail-making B task, phonemic fluency task and a two-item verbal abstraction task). Attention, concentration and working memory as well as naming and other language skills are evaluated. In MoCA test result of two subtests (Verbal Fluency subtest and delayed recall of five nouns) were taken into account separately during analysis. We assumed > 26 score for MoCA as a cut-off score for Mild Cognitive Impairment (MCI) diagnosis. However, if patient had score 25 and lower in MoCA, but MMSE score was 28-30 points, the cognitive functioning of patient was described as normal.

Trail Making Test part B is a fast-to-assess neuropsychological tool, which measures various skill from executive functioning domain: visuospatial skills, task switching and working memory to mention a few.

Aerobic capacity was estimated by 6-minute walk test (6MWT). The testing area was indoor and flat, as others [30] recommend. The corridor distance was 50 meters, to reduce patients' time spending on turning. However, because whole examinations took huge amount of time per one patient (approximately 3-hours) we did not provide any practice of walking before actual test started. We decided to ask patients to walk as fast as they are able to, and to maintain the same velocity during whole test. Moreover, we reminded patients two times about duration of test and ask to think about the walk velocity which he or she is able to maintain during this time. Most of patients were walking alone, if not, sufficient time interval between examination of the next patient have been maintained to exclude the competition factor. Some studies [31] showed that creating of competitive conditions can increase mean results of patients in this test up to 30%, comparing to group without such conditions.

Shapiro-Wilk test was used to test the normality of distribution. Correlation of above mentioned variables was measured with r-Pearson test. All statistical analyses were performed using statistical package (StatSoft, Inc. (2014). STATISTICA (data analysis software system), version 12. www.statsoft.com).

Results

Table I. Description of Participants (n = 128)

Characteristics (n1, n2)	Percentage/Mean (SD)
Age	68.80 (6.08)
BMI	26.94 (4.20)
Education years>14	41.40%
Worked/working as physical worker	18.75%
Still maintain a job position	17.96%
Hypertension diagnosis	45.31%
Current smokers	7.03%
SBP (n1 = 122)	140.94 (21.11)
DBP (n1 = 122)	83.77 (10.94)
TMT B (n1 = 116, n2 = 107	125.61 (57.74)
MoCA (n1 = 128, n2 = 128)	23.89 (3.20)
MoCA Verbal Fluency (n1 = 127, n2 = 124)	12.86 (4.22)
MoCA Delayed Recall (n1 = 128, n2 = 128)	2.21 (1.61)
MMSE (n1 = 128, n2 = 128)	27.46 (2.26)
MCI diagnosed	36.71 %
6MWT (n1 = 119, n2 = 116)	517.31 (81.86)

The *n* in circle brackets after tests name indicates number of participants before (n1) and after (n2) ignoring outliers.

Participants' age ranged from 58 to 88 years old. Mean Body Mass Index (BMI) in our study-group was calculated as 26.94. Our participants were well educated, their mean years of education is 14.12 (ranged 7-23 years). 24 of them were working in past, or still working as a physical employee, rest were white-collar workers or owner of a craft, service, entrepreneur or maintained/maintained

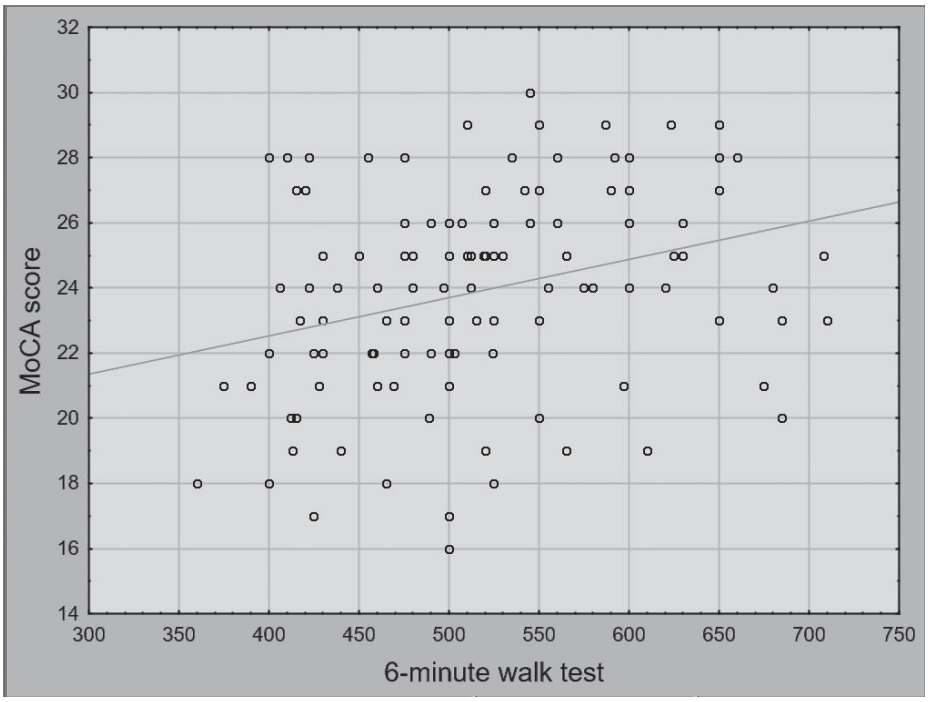

Chart 1. Scatter plot showing correlation between the MoCA and 6MWT scores

other jobs. 23 participants still maintain a job position. 58 participants were diagnosed with hypertension based on single-measurrment in our study (SBP > 140 and DBP > 90) mmHg. Moreover, there were 9 current smokers in this group only. Mild Cognitive Impairment was diagnosed in 47 participants. Results of 6MWT ranged from 360 to 710 meters.

Correlation results of cognitive tests and result of 6-minute walk test

Initial results of 6MWT ranged from 225 to 975 meters, after ignoring 3 outliers in analysis, final results ranged from 360 to 710 meters. Slight, statistically significant correlation between 6MWT with MoCA ($r = 0.3365$, $p = 0.001$) was noted (chart 1).

Additionally, correlation between Verbal Fluency subtest ($r = 0.2213$, $p = 0.028$) was noted. However, scatter plot (chart 1 and 2) shows that these correlations are rather non-linear.

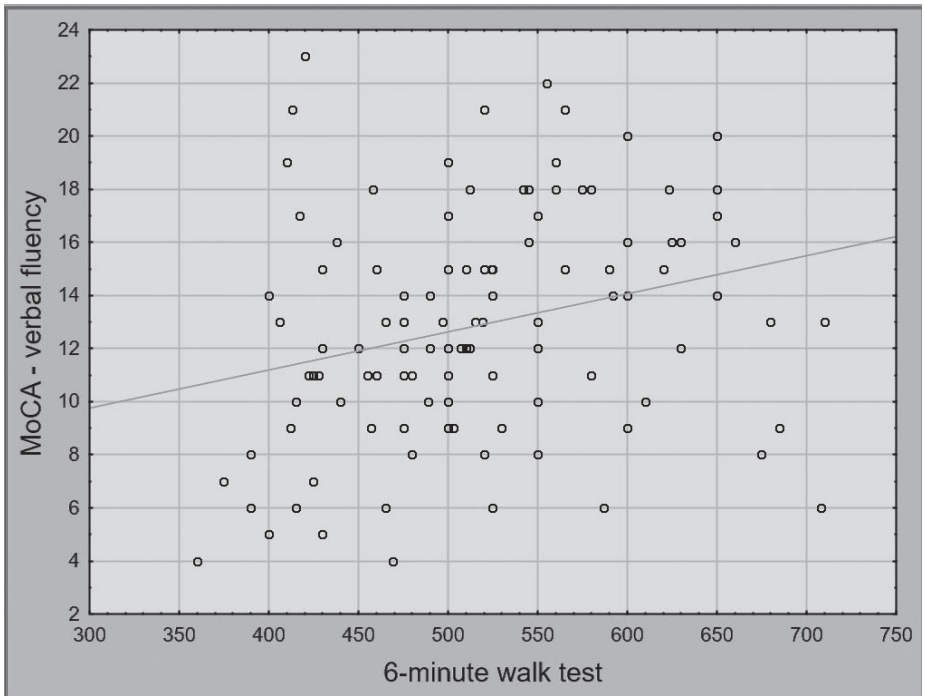

Chart 2. Scatter plot showing correlation between the Verbal Fluency subtest of MoCA and 6MWT scores

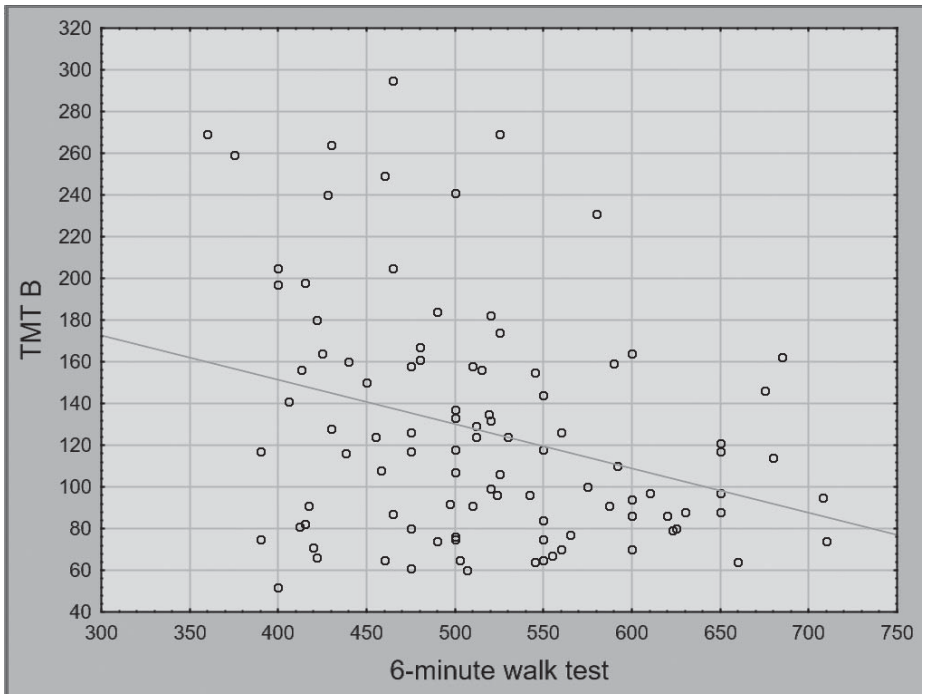

Chart 3. Scatter plot showing correlation between the TMT B and 6MWT scores

Correlation of TMT B with 6MWT tests results showed slightly negative correlation (r = -0.3111, p = 0.002). TMT B results higher than 300 seconds were treated as outliers and ignored during the analysis. The scatter plot shows that correlation is similar to linear.

Moreover, correlation of 6MWT with Delayed Recall subtest of MoCA test was also demonstrated (r = 0.2842, p = 0.004). Results of 6MWT was very slightly positively correlated with MMSE score, the results were not statistically significant (r = 0.0415, p = 0.683). Scatter plot shows that the correlation is nonlinear.

Discussion

Above studies showed positive correlations between all used cognitive functioning tests and 6MWT; all correlations were statistically significant, except of MMSE with 6MWT results. It could be probably because of limited value of MMSE [32] in Mild Cognitive Impairment diagnosis. However, scatter plots show that all, except for one, correlations are non-linear. The only linear correlation is a relationship between the TMT B and results of 6MWT. Interestingly, the mean result for 6MWT was reported to be 631 meters and was 84 meters greater in men compared to women, results were based on 51 healthy subjects aged 50-85 [30]. Mean results of this test were more than 100 meters lower in our sample group, however, our sample group was two times more numerous and slightly older (mean = 65 vs. 68,80 years old) [30]. According to our results, correlation between Trail Making Test part B with walking and other test of motor functioning was shown several times [33,34].

Conclusions

1. Significant correlations between all used cognitive functioning tests and 6MWT was observed; except of correlation with MMSE, which was not statistically significant.
2. Correlation of TMT B with 6MWT showed slightly negative, linear correlation: noteworthy, result of this test is measured in seconds needed to finish the test, therefore higher results indicates worse cognitive functioning.
3. All scatter plots revealed that correlations were non-linear, except one: showing correlation of 6MWT with TMT B.

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Conflict of interest

None

References

1. Farias ST, Mungas D, Jagust W. Degree of discrepancy between self and other reported everyday functioning by cognitive status: dementia, mild cognitive impairment, and healthy elders. Int J Geriatr Psychiatry. 2005;20(9):827-34.
2. Steffen TM, Hacker TA, Mollinger L. Age-and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. Phys Ther. 2002;82(2):128-37.
3. Erickson KI, Prakash RS, Voss MW, et al. Aerobic fitness is associated with hippocampal volume in elderly humans. Hippocampus. 2009;19(10):1030-9.
4. Burzynska AZ, Chaddock-Heyman L, Voss MW, et al. Physical activity and cardiorespiratory fitness are beneficial for white matter in low-fit older adults. PloS One. 2014;9(9):e107413.
5. Burzynska AZ, Wong CN, Voss M, et al. Physical activity is linked to greater Moment-to-Moment variability in spontaneous brain activity in older adults. PloS One. 2015;10(8):e0134819.
6. Wong CN, Chaddock-Heyman L, Voss MW, et al. Brain activation during dual-task processing is associated with cardiorespiratory fitness and performance in older adults. Front Aging Neurosci. 2015;7.
7. Colcombe SJ, Erickson KI, Raz N, et al. Aerobic fitness reduces brain tissue loss in aging humans. J Gerontol A Biol Sci Med Sci. 2003;58(2):M176-M180.
8. Van Gelder BM, Tijhuis MAR, Kalmijn S, et al. Physical activity in relation to cognitive decline in elderly men The FINE Study. Neurology. 2004;63(12):2316-21.
9. Brisswalter J, Collardeau M, René A. Effects of acute physical exercise characteristics on cognitive performance. Sports Med. 2002;32(9):555-66.

10. Dustman RE, Emmerson R, Shearer D. Physical activity, age, and cognitive- neuropsychological function. J Aging Phys Act. 1994;2(2).
11. Emery CF, Gatz M. Psychological and cognitive effects of an exercise program for community-residing older adults. Gerontologist. 1990;30(2):184-8.
12. Cassilhas RC, Viana VA, Grassmann V, et al. The impact of resistance exercise on the cognitive function of the elderly. Med Sci Sports Exerc. 2007;39(8):1401-1407.
13. Liu-Ambrose T, Nagamatsu LS, Graf P, et al. Resistance training and executive functions: a 12-month randomized controlled trial. Arch Intern Med. 2010;170(2):170-8.
14. Colcombe SJ, Erickson KI, Scalf PE, et al. Aerobic exercise training increases brain volume in aging humans. J Gerontol A Biol Sci Med Sci. 2006;61(11):1166-70.
15. Erickson KI, Voss MW, Prakash RS, et al. Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci U S A. 2011;108(7):3017-22.
16. Nascimento CM, Pereira JR, de Andrade LP, et al. Physical exercise in MCI elderly promotes reduction of pro-inflammatory cytokines and improvements on cognition and BDNF peripheral levels. Curr Alzheimer Res. 2014;11(8):799-805.
17. Tanaka K, de Quadros AC, Santos RF. Benefits of physical exercise on executive functions in older people with Parkinson's disease. Brain Cogn. 2009;69(2):435-41.
18. Pajonk FG, Wobrock T, Gruber O, et al. Hippocampal plasticity in response to exercise in schizophrenia. Arch Gen Psychiatry. 2010;67(2):133-43.
19. Ding Q, Vaynman S, Akhavan M, et al. Insulin-like growth factor I interfaces with brain-derived neurotrophic factor-mediated synaptic plasticity to modulate aspects of exercise-induced cognitive function. Neuroscience. 2006;140(3):823-33.
20. Ferris LT, Williams JS, Shen CL. The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. Med Sci Sports Exerc. 2007;39(4):728-34.
21. Voss MW, Vivar C, Kramer AF, et al. Bridging animal and human models of exercise-induced brain plasticity. Trends Cogn Sci. 2013;17(10):525-44.
22. Voss MW, Erickson KI, Prakash RS, et al. Neurobiological markers of exercise-related brain plasticity in older adults. Brain Behav Immun. 2013;28:90-9.
23. Sofi F, Valecchi D, Bacci D, et al. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. J Intern Med. 2011;269(1):107-17.
24. Abbott RD, White LR, Ross GW, et al. Walking and dementia in physically capable elderly men. Jama. 2004;292(12):1447-53.
25. Weuve J, Kang JH, Manson JE, et al. Physical activity, including walking, and cognitive function in older women. Jama 2004;292(12):1454-61.
26. Cho HC, Kim J, Kim S, et al. The concentrations of serum, plasma and platelet BDNF are all increased by treadmill VO 2max performance in healthy college men. Neurosci Lett. 2012;519(1):78-83.
27. Jung SH, Kim J, Davis JM, et al. Association among basal serum BDNF, cardiorespiratory fitness and cardiovascular disease risk factors in untrained healthy Korean men. Eur J Appl Physiol. 2011;111(2):303-11.
28. Currie J, Ramsbottom R, Ludlow H, et al. Cardio-respiratory fitness, habitual physical activity and serum brain derived neurotrophic factor (BDNF) in men and women. Neurosci Lett. 2009;451(2):152-5.
29. Chan KL, Tong KY, Yip SP. Relationship of serum brain-derived neurotrophic factor (BDNF) and health-related lifestyle in healthy human subjects. Neurosci Lett. 2008;447(2):124-8.
30. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. Eur Respir J. 1999;14(2):270-4.
31. Roomi J, Johnson MM, Waters K, et al. Respiratory rehabilitation, exercise capacity and quality of life in chronic airways disease in old age. Age Ageing. 1996;25(1):12-6.
32. Mitchell AJ. A meta-analysis of the accuracy of the mini-mental state examination in the detection of dementia and mild cognitive impairment. J Psychiatr Res. 2009;43(4):411-31.
33. Ble A, Volpato S, Zuliani G, et al. Executive function correlates with walking speed in older persons: the InCHIANTI study. J Am Geriatr Soc. 2005;53(3):410-15.
34. Mirelman A, Maidan I, Herman T, et al. Virtual reality for gait training: can it induce motor learning to enhance complex walking and reduce fall risk in patients with Parkinson's disease? J Gerontol A Biol Sci Med Sci. 2010;glq201.