



Does Intensive Aerobic Training Influences Cognition in Middle-Aged Men?

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Abstract

Purpose: The effect of chronic aerobic exercise on cognitive functions in middle-aged healthy adults.

Method: Thirty-three amateur runners (group of athletes) compared with thirty healthy adults with no previous involvement in sports (control group). Both groups were evaluated by means of comprehensive neuropsychological assessment for attention, processing speed, memory, visuospatial organization, executive functions and athletic test for aerobic capacity.

Results: The group of athletes had better performance in tests of scanning speed of visual information, in visuospatial-perceptual organization of new and complex information and shift and switching of attention.

Conclusion: Long-term aerobic exercise may be beneficial for cognitive functioning.

Keywords

Aerobic exercise, Cognitive function, Neuropsychological performance

functionality and especially on patient's quality of life [2].

Physical exercise and sports have beneficial effects on the human body. Recent studies support that physical exercise may be a protective factor against ischemic stroke [3], and many other degenerative neurological diseases including Parkinson's [4] and Alzheimer's disease [5]. It is argued that 30 minutes or more exercise (3-5 days/week, 60-75% VO₂) has a positive influence on cognitive function in healthy adults [6,7].

Aerobic exercise affects the density of cortical areas of the frontal and parietal lobes [8], which are highly involved in the speed of information processing and the effectiveness of executive functions [9]. Furthermore, the elderly with better aerobic capacity (compared to inactive but still normal elderly) have significantly less gray matter loss in the frontal, parietal and temporal lobes, less white matter loss in the anterior and posterior white matter tracts [10] and increased cerebral blood volume [11]. Additionally, they exhibit less decline with regards to verbal encoding and recall [12,13] and have increased volume of the anterior region of the hippocampus (including the dentate gyrus and area CA1) which is associated with improved spatial memory [14].

The beneficial effect of aerobic exercise has been demonstrated in animal studies as well. The structural changes in the brain of mice are associated with molecu-

Introduction

Normal aging is associated with thinning of both cortical and subcortical areas that lead to decline in cognitive process supported by these affected areas [1]. The effects of aging are especially pronounced within the domains of memory and executive functions [1], deficits of whose, particularly when they escalate to dementia, can have a dramatic impact on the independence,

lar and neurochemical changes, for example an increase of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) that is observed on both young and older subjects after exercise [15]. These changes include dendritic sprouting, angiogenesis and growth of new neurons from stem cells with subsequent reinforcing processes that support learning and memory [15]. It is suggested that exercise helps to increase cell survival, proliferation and neurogenesis in the hippocampus resulting in improved spatial learning ability and long-term potentiation (LTP) or synaptic plasticity [16].

Aerobic exercise has linked with beneficial effect on specific cognitive functions. Guiney and Machado [17] refer that there are strong evidence of exercise-linked benefits related to task switching, selective attention, inhibition and working memory. Erickson, et al. [14] showed that aerobic exercise associated with improvements in spatial memory. Further, according to Smith, et al. [18] aerobic exercise training is associated with modest improvements in attention and processing speed, executive function and memory. Also, studies in middle-aged subjects report that participation in physical activity, even light, can significantly slow the rate of cognitive decline during later adulthood [19-21] or reduce the risk of developing dementia or Alzheimer's disease [22-24]. Identification of risk factors associated with cognitive decline, particularly earlier in the life course, is crucial in developing prevention or intervention strategies.

Given that physical, and particularly aerobic, exercise improves specific cognitive processes and that poor cognitive performance in middle age may be clinically relevant since individuals with mild cognitive impairment may progress to clinically diagnosed dementia at an accelerated rate (10-17% & 4.5-10% transition rate per year for specialized diagnostic centers and community centers, respectively) [25,26], the aim of the present study was to examine the effect of physical exercise on specific cognitive functions in middle-aged adults. Specifically, we hypothesized that physically active individuals would have better cognitive performance compared to non-active controls. We also investigated whether the degree of aerobic capacity would be associated with the participant's neuropsychological performance.

Methods

Subjects

Sixty-three middle-aged male volunteers were recruited from the community (age range: 45-55 years, education range: 9-16 years). Thirty-three amateur middle distance runners formed the group of athletes (experimental group). The group of athletes, according to their training background, involved in regular aerobic training routines such as running, cycling and competitive sports, (3-5 sessions per week with average duration one hour) since their adulthood. All athletes, for at least the last five

years, involved in regular running trainings (3-5 intense sessions per week with average duration one hour).

The other thirty subjects, who were not involved in sports, formed the control group. The control group did not take part in recreational physical activities such as walking and biking and none of the subjects had any background in regular aerobic training or competitive sports of any kind since adulthood. Both groups were matched for age (age: 50.09 ± 2.95 vs. 50.20 ± 3.11 ($t_{29} = -0.17$) and education (education: 14.06 ± 2.00 vs. 14.00 ± 2.03 ($t_{29} = 0.22$)). All participants were screened to exclude individuals with health problems (stroke, cardiovascular disease, neurological and psychiatric diseases, metabolic diseases and those receiving specific medication), as well as smokers and obese participants. All participants gave their written informed consent after having been informed about the purpose and procedures of the study. To exclude the effect of depressive and anxiety status, both groups were assessed using Beck Depression (BDI) and Inventory Spielberger State-Trait Anxiety Inventory (SSTAI) [27,28].

Exercise and neuropsychological procedures

Exercise measures: All participants evaluated with Cooper 12 minute test [29-31] in order to define the fitness level. Subsequently, as the two groups differ significant in aerobic capacity level in Cooper 12 minutes test, in order to ensure that this difference is not due to exercise measuring procedure in which athletes are more familiar with, all participants ran or walked on a treadmill for forty minutes while their heart rate was monitored (training simulation). Participants were encouraged to run at the appropriate range heart rate for aerobic training (60-75%) [14]. Finally, anthropometric characteristics were measured before athletic test and compared across the two groups.

Neuropsychological testing: All participants were administered a series of neuropsychological tests to assess: a) attention and speed of information processing (Trail Making Test part A [TMT-A] [32], Symbol Digit Modalities Test [SDMT] [33]) b) visuospatial/perceptual ability (Rey's Complex Figure Test-copy form [RCFT-C]) [34]) c) verbal and visual episodic memory (Rey Auditory Verbal Learning Test [RAVLT] [35], Rey's Complex Figure Test -recall forms [RCFT] [34], Babcock Story Recall Test [BSRT] [36]), and d) the effectiveness of executive functions (Trail Making Test part B [TMT-B] [32], Stroop Neuropsychological Screening Test [SNST] [37]).

Neuropsychological procedures scoring: TMT-A score calculated in seconds by the completion of connection of a sequence of 25 consecutive targets on a sheet of paper. TMT-B score calculated in seconds by the completion of alternative connection between numbers and letters [32]. SDMT score, calculated by the number of correct symbols within the allowed time (90 sec) [33].

RCFT-C is scored for the accurate reproduction and placement of 18 specific design elements by copying. RCFT-IR and RCFT-DL are scored for the accurate reproduction and placement of 18 specific design elements from memory [34]. RAVLT-Tr 1-5 score calculated by the total number of words which are recalled in five presentations of a 15 word list. RAVLT-IR score calculated by the number of words which are immediately recalled after the intervention of a second word list. RAVLT-DL score calculated by the number of words which are recalled after a 20-30 minute delay [35]. BSRT-IR score calculated by elements of story which are recalled immediately. BSRT-DL score calculated by elements of story which are recalled after 20 minute delay [36]. SNST task score, calculated by subtracting the number of errors from the total number of items completed in 120 sec [37].

Statistical analysis

Before statistical analysis all variables were tested for normality using the Kolmogorov - Smirnov criterion. Numerical data are expressed as mean \pm SD. T tests were used to compare mean values between groups (athletes vs. non-athletes). Pearson correlation analysis was applied

to investigate any association between aerobic capacity and neuropsychological processes in both groups. SPSS 20.0 statistical package (SPSS, Chicago, IL) was used for statistical analysis. The level of statistical significance for the comparison of anthropometric characteristics as well as psychometric variables was Bonferoni corrected at $P < 0.016$ (0.05/3) and the level of statistical significance for the neuropsychological assessment was Bonferoni corrected at $P < 0.004$ (0.05/12).

Results

Table 1 presents the anthropometric characteristics for athlete and control groups. The athletes were taller than controls but this difference did not exceed the corrected level of significance for multiple comparisons. Also the athletes had a significantly smaller Body Mass Index (BMI) than controls.

Table 2 presents psychometric and neuropsychological performance measures of athletes and non-athletes. As seen in this table there were differences in specific neuropsychological performance measures between athletes and non-athletes while there was no difference in psychometric measures of depression and anxiety. More specifically

Table 1: Anthropometric characteristics of athletes and non-athletes.

	Athletes (N = 33)	Non-athletes (N = 30)	t	df	p
Height (m)	1.82 \pm 0.74	1.76 \pm 0.76	3.56	29	0.02**
Weight (kg)	75.7 \pm 5.33	78.3 \pm 7.62	-1.62	29	n.s
Body mass index (kg/m ²)	22.87 \pm 1.81	25.26 \pm 2.06	-4.20	29	0.001***
Age (years)	50.09 \pm 2.95	50.20 \pm 3.11	-0.17	29	n.s
Education (years)	14.06 \pm 2.00	14.00 \pm 2.03	0.22	29	n.s

Note: Values are expressed as mean and standard deviation (mean \pm SD).

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, n.s = non-significant.

Table 2: Between-group differences (athletes vs. non-athletes) on depression, anxiety and neuropsychological performance.

Psychometric measures	Athletes (N = 33)	Non-athletes (N = 30)	p	t	df	Normative data
BDI	3.45 \pm 2.73	3.63 \pm 3.28	n.s	-0.13	29	Depression \geq 10
SSTAI-X1	31.68 \pm 4.27	32.03 \pm 4.08	n.s	-0.49	29	State Anxiety \geq 43.21
Neuropsychological measures						
SDMT	49.13 \pm 9.50	45.07 \pm 8.10	n.s	1.69	29	52.27 \pm 8.48
TMT-A	33.49 \pm 17.00	43.37 \pm 12.23	0.007**	-2.84	29	44.98 \pm 15.85
RCFT-C	34.83 \pm 3.69	31.20 \pm 4.88	0.001***	4.89	29	35.15 \pm 1.26
RAVLT-Tr1-5	51.43 \pm 6.76	50.07 \pm 6.28	n.s	0.71	29	51.1 \pm 2.6
RAVLT-IR	9.70 \pm 2.19	10.57 \pm 2.01	n.s	-1.50	29	9.4 \pm 0.7
RAVLT-DL	9.16 \pm 2.27	9.23 \pm 2.82	n.s	-0.11	29	8.7 \pm 0.8
BSRT-IR	12.67 \pm 3.04	12.10 \pm 3.33	n.s	0.58	29	13.44 \pm 1.55
BSRT-DL	11.10 \pm 3.57	10.73 \pm 4.39	n.s	0.37	29	12.62 \pm 2.22
RCFT-IR	17.37 \pm 6.07	15.17 \pm 8.55	n.s	1.17	29	20.29 \pm 4.49
RCFT-DL	16.97 \pm 6.40	13.80 \pm 7.77	n.s	1.92	29	20.47 \pm 4.05
TMT-B	67.86 \pm 28.74	99.08 \pm 43.24	0.001***	-4.01	29	91.39 \pm 30.37
SNST	102.10 \pm 13.58	100.56 \pm 12.46	n.s	0.42	29	94.82 \pm 13.87

Note: BDI: Beck Depression Inventory; SSTAI: Spielberger State Trait Anxiety Inventory; X1: State form; X2: Trait form; SDMT: Symbol Digit Modalities Test; TMT-A: Trail Making Test part A; RCFT-C: Rey's Complex Figure Test copy form; RAVLT: Rey Auditory Verbal Learning Test; BSRT: Babcock Story Recall Test; RCFT: Rey Copy Figure Test; Tr1-5: Sum of Words Learned over Trials 1-5; IR: Immediate Recall; DR: Delayed Recall; TMT-B: Trail Making Test part B; SNST: Stroop Neuropsychological Screening Test. Values are expressed as mean and standard deviation (mean \pm SD).

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, n.s: non-significant.

athletes were faster than non-athletes both at TMT-A and TMT-B but the difference remained significant after correction for multiple comparisons only for TMT-B. Also, athletes performed significantly better than non-athletes at the RCFT copy neuropsychological test.

In addition, in Cooper 12 minutes test the group of athletes performed at excellent level $t(29) = 39.15$, $p = 0.001$, (2668 ± 149.19 m/12 min) whereas the group of non-athletes performed at below average level (1437 ± 86.07 m/12min). In training simulation we also found significant differences $t(29) = 34.52$, $p = 0.001$, on aerobic capacity between athletes (8.13 ± 0.47 km/40 min) and non-athletes (5.12 ± 0.40), as expected.

Discussion

The results of this study are in agreement with previous research concerning the effects of physical exercise on cognitive functions. The two groups differed in TMT-A with athletes performing better compared to non-athletes although this difference was not significant for multiple comparisons. This finding is suggestive of differences in attentional performance and especially in visuomotor tracking [10]. A 10 week regular exercise training in healthy participants improved performance on executive function tasks, including TMT [38]. Also, athletes showed significantly better performance in copying the complex shape of the Rey's CFT. Copying this complex shape besides perceptual processing, requires effective range of working memory, cognitive adoption strategy, planning, coordination and monitoring of operations until the completion of the project [39]. Brown, et al. [40] observed significant positive associations between physical exercise and the copy form of the RCFT. Furthermore, West [41] suggested that these tasks require constant mediation by a center executor because they do not become automatic and therefore the benefits of exercise would be reflected in these executive processes. It has been also suggested that physical exercise effects might be most readily observed on visuospatial tasks because visuospatial processes have been demonstrated to be more susceptible to aging than verbal skills [42,43].

Although it has been found that aerobic exercise has positive effects on memory function [21,44,45], in the present study we did not find any significant differences in neuropsychological measures of memory function between athletes and controls.

Also, our groups differed significantly in TMT-B with athletes performing better than non-athletes. These findings suggest differences in components of executive function, i.e. the switching and shift of attention and cognitive flexibility. Previous studies have confirmed the beneficial effects of aerobic exercise on cognitive functions supported by the frontal and prefrontal cortex [46]. Liu-Ambrose, et al. [47] refer that an exercise program can enhance the executive cognitive function of selective attention and conflict resolution in elderly. Moreover, acute exercise improves performance on executive

cognitive tasks such as planning, inhibition and working memory [10,48]. Our results are also in agreement with significantly improved cognitive flexibility in moderate and high exercise groups compared with control (non-exercise) group [49].

According to Singh-Manoux, et al. [19] physical activity moderates the decline in cognitive functioning typically associated with aging. The aspect of cognitive functioning that declines most with age is fluid intelligence [50], (e.g. visuomotor scanning-attention, visuo-perceptual organization skill, set shifting, cognitive flexibility) which seems to be intrinsically associated with information processing and involves short-term memory, abstract thinking, creativity, ability to solve novel problems, and reaction time. This aspect is also the one that benefits the most from long term exercise as shown in this study.

The observed differences between the two groups, although it does not indicate any pathology in anyway, however support the suggestion of the beneficial effect of long-term aerobic exercise on cognitive functions also in middle-aged healthy population and confirm its importance in successful aging.

Although several viable hypotheses have been proposed, the mechanisms underlying the association between physical activity and cognitive functioning are poorly understood. It is important to theorize possible explanations for our findings to further support future research in this field. It may be that physical exercise benefits cognitive function through disease reduction (e.g. Cardiovascular disease, Stroke, Diabetes, Hypertension) and/or enhance brain structure and function (e.g. Increase production and efficiency of neurotransmitters, Angiogenesis, Synaptogenesis, Neurogenesis) [41].

There were specific limitations in this study. First, the relatively small sample size is a limiting factor. Second, the group of athletes included only people with high aerobic capacity. The aerobic capacity depends on the training session frequency and intensity. In this study, athletes had a long and systematic sport engagement and for that reason it is likely that their aerobic capacity approached the upper limit of normal. This fact could result to an apparent ceiling effect, canceling the effect of correlation with any modulating variable. Also the use of various training programs, different time lags and reevaluation should be tested to better understand the residual effects of aerobic exercise. Furthermore, many of aging effects are first noted at 60 years of age or older, and therefore do not relate to this middle-aged cohort. Finally, the study subjects were only men and we cannot conclude whether our findings would apply to women.

In conclusion, the findings indicate that physical activity is an important factor in cognitive functioning in middle age and that its effects appear earlier than previously reported. It should be noted that the components of cognition which further deteriorate over the years are

those of attention and speed of information processing and the effectiveness of executive functions, and our results suggest that physical activity, specifically long-term aerobic exercise, may be beneficial for these same cognitive functions and reduce the risk of early cognitive decline in middle age.

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