

DIFFERENCES IN LONG- AND SHORT-TERM MEMORY PERFORMANCE AND BRAIN MATTER INTEGRITY IN SENIORS WITH DIFFERENT PHYSICAL ACTIVITY EXPERIENCE

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Due to increasing changes in demographics, maintaining cognitive functioning later in life has become both economic and social concerns, and thus finding a cost-effective solution is one of the priorities in research. Factors like physical and intellectual activities have been associated with better cognitive performance in later life. While several studies have considered the impact of short-term physical activity interventions on cognitive functioning, retrospective research focusing on life-time physical activity experience has been sparse. The aim of the study was to determine the relationship between memory performance and whole brain matter integrity in seniors with different regular life-long physical activity experience. Fifty-three Latvian seniors aged 65–85 ($M = 72.25$, $SD = 5.03$, 83% female) with no self-reported chronic disease participated in the study. Measures of memory, physical activity and whole brain matter integrity were obtained and analysed. The obtained results indicated no significant relationship between physical activity experience and short and long-term memory and whole brain matter integrity; however, brain matter integrity was significantly correlated with demographic factors like age and education. These results might be related to inadequate physical activity measures, as well as unequal physical activity experience in participants. In the future, more detailed assessment of physical activity experience should be considered.

Key words: *short-term memory, long-term memory, working memory, physical activity, diffuse tensor imaging.*

INTRODUCTION

Maintaining cognitive functions later in life has become one of the core topics in age-related research, due to demographical changes (e.g. the World Health Organization predicts that by year 2050 the population aged over 60 will contribute to 22% of the world population (Anonymous, 2015)) and the increasing diagnosis of neurodegenerative disease (Stern, 2012).

Ageing for a very long time has been associated with poorer memory performance, and memory decline is considered to be one of the main symptoms in Alzheimer's disease (Anonymous, 1992). Research indicates a relationship between ageing and decline in verbal working memory (e.g. Nittrouer *et al.*, 2016) and ability to encode new information (Hedden and Gabrieli, 2004). Several factors might contribute to neurodegeneration and more rapid cognitive decline, such as genetic factors (*APOE-4*, *GNG4*, *KCNQ2*)

(Bonham *et al.*, 2018), as well as life-style factors (e.g. smoking (Anstey *et al.*, 2007), alcohol consumption (Neafsey and Collins, 2011) and sedentary life-style (Siddarth *et al.*, 2018)). While decline in cognitive performance and brain volume is normally associated with neurodegeneration, it is also present in normal cognitive ageing. Studies have described age-related structural brain changes, e.g. ventricular dilatation up to 2.9% per year (Raz and Rodrigue, 2006), decline in white matter integrity (Bennett and Madden, 2014) and hippocampal volume (Bherer *et al.*, 2013). Changes in brain structure and integrity are directly related to changes in different cognitive domains, including decline in executive functions (Levin and Netz, 2015), associative memory performance (Reuter-Lorenz and Park, 2010) and ability to encode episodic and semantic memory (Hedden and Gabrieli, 2004).

Just as lifestyle factors might expedite the cognitive decline, they may contribute to maintaining cognitive processes and slowing the cognitive decline associated with ageing. There has been an extensive amount of studies that examined the relationship between aerobic activity and brain volume and integrity, and consequently, cognitive processes (e.g. see Young *et al.*, 2015 for systematic review); however, most of the studies have involved short-term physical activity interventions, not considering the overall physical activity during the life-span.

The number of studies conducted on the relationship between long-term aerobic activity involvement and cognitive performance and brain integrity has been sparse. A study conducted by Young *et al.* (2016) found no differences between professional athletes with at least 20 years high-endurance physical activity experience and age-related sedentary peers in cognitive performance, while identifying differences in white matter integrity (specifically axial diffusivity) (Young *et al.*, 2016). In contrast, preliminary results published by Sneider *et al.* (2017) found higher working memory scores in participants involved in competitive sports and regularly active (e.g. Nordic Walkers, cyclists, swimmers) compared to age-matched sedentary participants.

The aim of the study presented here was to investigate the relationship in cognitive performance and brain matter integrity in seniors with different regular life-long physical activity experience. Based on the results from short-term aerobic-physical activity intervention studies, we hypothesised that seniors with longer physical activity experience i.e. regular cycling, walking, athletics, would have higher performance in memory over time (i.e. long and short-term memory), as well as better brain matter integrity.

MATERIALS AND METHODS

Participants. Fifty-three participants, who were native Latvian speakers aged 65–85 ($M = 72.25$, $SD = 5.03$, 83% female), were recruited for the study. All participants reported no known cardiovascular, neurological, pulmonary or respi-

ratory diseases requiring inhalers, rheumatological diseases requiring pain medication, ongoing oncological diseases, psychiatric disorders or metallic implants that could cause injury during MRI procedure. Prior to aerobic capacity measures, all participants were screened for cardiovascular disease at Pauls Stradiņš Clinical University Hospital. Prior to data collection, participants were briefed on the aims and the structure of the study and provided written consent. All participation was voluntary, and participants retained rights to withdraw from the study at any stage. Ethical approval was obtained from the Rīga Stradiņš University Ethics Committee.

Cognitive assessment. Immediate and delayed recall was measured with a Memory ten-word test (Luria, 1976). This test involves memorisation of series of ten isolated (unrelated) words. The words were repeated twice and included a learning process. Participants were asked to remember and recall the words immediately, then once with cues and three times without cues. After 45 minutes participants were asked to recall the words without memory cues. In data analysis, sums of first (immediate recall) and last (delayed recall) trials were used. Working memory was measured using the Numbers Reversed test from the Woodcock-Johnson Test of Cognitive Abilities (Woodcock *et al.*, 2001). A list of numbers, increasing in length on each trial, was presented to the participants and they are asked to repeat the lists in reverse order. A total number of six trials was offered; however, the test was terminated after three incorrect answers in a row. A standardised score was used for data analysis.

Cardiovascular fitness assessment. Cardiovascular fitness was assessed by a measure of aerobic capacity (VO_2 max) acquired with a Monark839E stress testing bicycle ergometer. The participants were asked to cycle for 12 minutes, with the workload increasing every three minutes. The zero workload was based on clinical veloergometry results obtained at Rīga Pauls Stradiņš Clinical University Hospital by a certified specialist.

Life-style habits assessment. To assess life-style habits, the Social Determinants of Health Behaviours questionnaire (Anonymous, 2008) was used. The questionnaire measured physical activity over the past year and over the course of life, eating habits, and alcohol use and smoking. The length of physical activity over the course of life was identified with a response to three questions: “How many years have you been involved in aerobic exercise or dancing?”, “How many hours did you spend doing aerobic activities (past year)?” and “How many months for the past year have you spent doing aerobic activities or dancing?” Based on the mean results of replies, we drew a composite score, combining responses together, which were used in later data analysis. To ensure the validity of the score, it was correlated with the aerobic capacity measure (VO_2 max).

MRI measures. All images were acquired on a Siemens 1.5 Tesla Avanto MRI scanner (Siemens, Erlangen, Germany). High-resolution anatomical images were acquired using a

three-dimensional T1-weighted magnetisation prepared rapid acquisition gradient echo (MPRAGE) sequence [TR = 1160 ms; TE = 4.44 ms; inversion recovery time (TI) = 600 ms; field of view (FOV), 230 × 230 mm²; matrix size, 256 × 256; flip angle θ = 15 degrees; voxel dimensions, 0.9 × 0.9 × 0.9 mm³; acquisition time, 5 min].

Procedure. Data acquisition for each participant was conducted in three consecutive stages undertaken in a single visit. After general introduction regarding the aims and the structure of the research, participants were presented with the series of memory tasks mentioned above. Afterwards, MRI data were obtained in Pauls Stradiņš Clinical University Hospital. In the final stage, physical activity assessment was conducted.

DTI analysis. Diffusion tensor imaging (DTI) is a non-invasive method used for measuring water movements within brain tissues, based on the principle that water molecules diffuse differently along the tissues depending on its type, integrity, architecture, and presence of barriers. By using DTI, it is possible to infer the directional preference of diffusion or fractional anisotropy (FA) and molecular diffusion rate or mean diffusivity (MD). Diffusion in grey and white matter were calculated separately since anisotropy is more distinguished in white matter in comparison with grey matter or cerebrospinal fluid (Soares *et al.*, 2013; Acosta-Cabronero and Nestor, 2014).

For each participant Eddy correction using the eddy correct function FSL was used. Data were fitted to a diffusion tensor model using dtfit in FSL, thus obtaining maps for MD and FA. The $b = 0$ map was non-linearly warped into 2-mm MNI space using ANTS (version 2.1.) using symmetric diffeomorphic mapping. This process generates the diffeomorphic transformation required to warp each of the parameter maps to standard MNI space.

Statistical analysis. Statistical analysis was performed using IBM SPSS Statistics 21. Version X. To determine the relationship between the life-time physical activity, cognitive performance and brain matter integrity, the Pearson's r correlation was used. To exclude possible covariates, partial correlation analysis controlling for education, body mass index, alcohol use and smoking habits were conducted.

Table 1

MEAN INDICATORS OF DEMOGRAPHIC DATA, PHYSICAL ACTIVITY MEASURES, COGNITIVE TEST VALUES, AND DTI RESULTS

	M	SD
Age (years)	72.25	5.03
Education (years)	15.56	3.65
Physical activity composite score	33.91	24.03
Aerobic capacity (VO ₂)	25.41	8.19
Cognitive testing		
Immediate recall (max 10)	5.81	1.31
Delayed recall (max 10)	6.79	2.28
Working memory (max 592)	514.96	23.65
DTI results		
Grey matter FA	0.1410042830	0.0140641352
White matter FA	0.3650972830	0.0250328248
Grey matter MD	0.0011092453	0.0000657822
White matter MD	0.0007623019	0.0000287205

DTI, diffusion tensor imaging; M, mean; SD, standard deviation; FA, fractional anisotropy; MD, mean diffusivity

RESULTS

To examine the descriptive characteristics of variables, mean demographic properties (age, education), physical activity composite score and body composition measures (years of physical activity, aerobic capacity, BMI), cognitive testing results and DTI results were calculated (Table 1). 32% of participants reported using alcohol once or twice per year, 32% of participants indicated that they used alcohol two or three times per month, while 22% of participants noted, that they use alcohol weekly. 10% of participants denied using alcohol and 4% indicated that they use alcohol almost every day. None of participants reported that they were current smokers; however, 26% admitted to having smoked at some time in their lives. All data, apart from alcohol use and smoking, were normally distributed.

The responses regarding aerobic activity involvement, a physical activity composite score based on self-report questionnaire, were validated by positive significant correlation (Pearson's $r = 0.49$, $p < 0.01$) with aerobic capacity measures (VO₂) (Fig. 1).

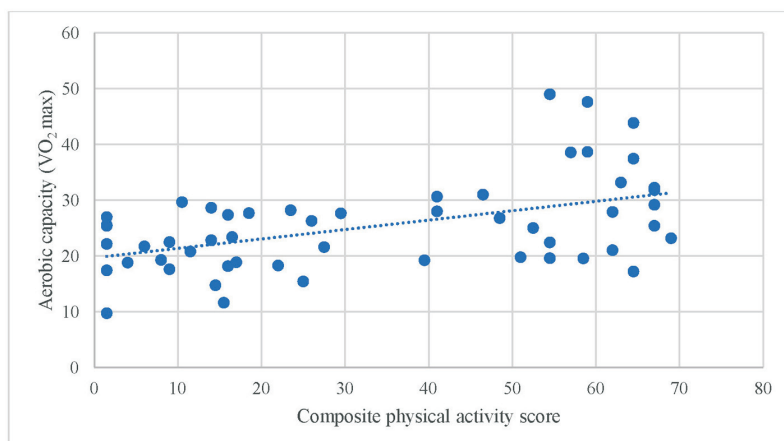


Fig. 1. Pearson's r correlation between VO₂ max as aerobic capacity measure and physical activity composite score.

RELATIONSHIP BETWEEN LIFE-TIME PHYSICAL ACTIVITY EXPERIENCE, MEMORY PERFORMANCE AND WHITE MATTER INTEGRITY (Pearson's r correlation coefficient)

Variables	1	2	3	4	5	6	8	9
1. PA composite score	–							
2. Immediate recall	–0.10	–						
3. Delayed recall	–0.13	0.50**	–					
4. Working memory	0.07	0.10	–0.08	–				
5. Grey matter FA	–0.23	–0.12	–0.07	0.12	–			
6. White matter FA	–0.12	–0.02	–0.11	0.14	0.73**	–		
8. Grey matter MD	0.09	0.07	–0.16	–0.21	–0.39**	–0.23	–	
9. While matter MD	0.03	–0.06	–0.11	–0.12	–0.28*	–0.63	0.55**	–

PA, physical activity, FA, fractional anisotropy, MD, mean diffusivity, * $p < 0.05$, ** $p < 0.01$

To identify whether there is a relationship between total life-time physical activity, memory performance and brain integrity in white and grey matter, Pearson r correlation analysis was conducted (see Table 2). The results indicated no significant relationship between any of these variables; however, we did find a negative, weak correlation between life-time physical activity and grey matter fractional anisotropy (accordingly, $r = -0.23$, $p = 0.10$).

To determine relationship between possible covariates — age and education, and brain matter integrity and cognitive performance, all combinations of variables were tested using Pearson's r correlation coefficient and multiple correlation analysis was conducted afterwards. For white matter, age was significantly correlated negatively with FA ($r = -0.33$, $p < 0.05$) and positively with MD ($r = 0.66$, $p < 0.01$). For grey matter, a non-significant negative correlation with FA ($r = -0.22$, $p = 0.12$) and a significant positive correlation with MD ($r = 0.70$, $p < 0.01$) were found. No significant relationships were found between age and cognitive performance. Education was positively correlated only with immediate memory results ($r = 0.27$, $p < 0.05$). Multiple correlation analysis, using age and education as demographic variables, showed significant relationships with grey and white matter diffusivity ($R = 0.72$, $F(2, 50) = 27.23$, $p < 0.001$ and $R = 0.66$, $F(2, 50) = 19.16$, $p < 0.001$) and grey matter FA ($R = 0.34$, $F(2, 50) = 3.22$, $p < 0.05$). No significant relationships were found between demographic variables and memory measures and white matter FA.

DISCUSSION

The aim of the study was to examine differences in long- and short-term memory performance and brain matter integrity in seniors with different physical activity experience. We hypothesised that participants with longer physical activity experience will have higher performance results in memory tasks and better brain matter integrity; however, our results did not support our hypotheses. The results were consistent with the results reported by Jeremy Young and colleagues (2016), where no significant differences were

found between professional athletes (i.e. long-term physical activity group) and socially active seniors (no-activity group), on either cognitive or brain structure indices. However, our results were in contrast to previous work (Tseng *et al.*, 2013) that reported a relationship between aerobic physical activity and white matter integrity. Results from the present study partially comply with results from preliminary analysis reported by Sneidere *et al.* (2017), in which participants with professional sports' experience were compared with active and sedentary seniors. Similarly, there were no significant relationships between long and short-term memory performance; however, significant correlation between athletic fitness and working memory performance was found.

While we found no relationship between brain matter integrity and physical activity, it should be taken into consideration that the analysis were based on whole brain white and grey matter indices. Previous studies have shown significant relationship between cognitive performance and brain regions, and thus the next step in this study will be to analyse regions of interest with the corresponding memory processes. Relationship between physical activity and brain matter integrity and volume has been associated with rather specific regions, such as hippocampus (Erickson, Voss, Shaurya, Basak, Szabo, 2011) and frontal and parietal brain regions (Kramer *et al.*, 2006), thus volumetric measures of brain structures should be considered in the future as well.

Brain matter integrity was closely related to demographic factors like age and education, which both have been considered as proxies in brain and cognitive ageing. Ageing especially has been associated with decline in hippocampus (Bherer *et al.*, 2013b) and increase in cerebral ventricles (Raz and Rodrigue, 2006). However, both demographic factors would be expected to be related to memory measures, which was not found in this study. The limited age range in the sample ($M = 72.25$, $SD = 5.03$), and the single index for short and long-term memory employed may have limited the sensitivity of the study regarding relationships with whole brain structure indices.

Even though there was a positive association between the composite physical activity score and cardiovascular fitness, the composite score can still lead to inaccurate representation of true aerobic activity involvement, which is a limitation to consider. It should also be noted that the results from our physical activity questionnaire take into account only physical exercise, while physical activity is actually any movement that results in energy expenditure (Avers, 2016). This aspect should be taken into consideration in later studies as many activities have aerobic activity elements (e.g. cycling to and from work, gardening etc.). Another question that remains unanswered is the impact of the amount, frequency and duration of physical activities on cognitive functioning (Anderson *et al.*, 2015). Recent studies indicate that even insignificant activities like daily low-level walking may affect the hippocampal volume in older women (Varma *et al.*, 2015). Currently work on a retrospective total life-span physical activity questionnaire has been started (Ulmane *et al.*, 2018). The questionnaire retrospectively measures the lifetime activity during several periods of life, and includes activities like house-work, occupational activity, transportation etc. The questionnaire is based on a similar measure developed by Friedenreich *et al.* (1998); however, the new measure involves more complex calculations of the final cumulative activity. Development and validation of such a questionnaire would allow researchers to identify the periods most sensitive to physical activity, as well as identify the type and regularity of the activity that might contribute to cognitive performance.

In the future, longitudinal study would be beneficial to examine the changes due ageing and the role of physical activity as a potentially protective factor. It should be noted that participants were not screened for Alzheimer's disease; thus, in the future, neurocognitive assessments and also APOE genotype should be considered as well.

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ATŠĶIRĪBAS ILGLAICĪGAJĀ UN ĪSLAICĪGAJĀ ATMIŅĀ UN SMADZEŅU VIELAS INTEGRITĀTĒ SENIORIEM AR DAŽĀDU FIZISKO AKTIVITĀŠU PIEREDZI

Līdz ar izmaiņām demogrāfiskajā situācijā, kognitīvo funkciju uzturēšana dzīves nogalē ir kļuvusi par ekonomisku un sociālu problēmu. Tādi dzīvesveida faktori kā fiziskās un intelektuālās aktivitātes tiek saistītas ar labāku kognitīvo funkcionēšanu vecumdienās. Daudzviet pētījumos tiek aplūkota tieši īstermiņa fizisko aktivitāšu saistība ar kognitīvo funkcionēšanu, taču retrospektīvu pētījumu skaits, kuros būtu aplūkota dzīves laika fiziskā aktivitāte, ir neliels. Pētījuma mērķis bija izpētīt saistību starp atmiņu, smadzeņu baltās un pelēkās vielas integritāti un fizisko aktivitāti senioriem ar dažādu dzīves laika fizisko aktivitāšu pieredzi. Pētījumā piedalījās 53 seniori vecumā no 65 līdz 85 gadiem ($M = 72,25$, $SD = 5,03$, 83% sievietes) bez pašu ziņotām būtiskām hroniskām saslimšanām. Pētījuma ietvaros tika veikti atmiņas, fizisko aktivitāšu un smadzeņu baltās un pelēkās vielas integritātes mērījumi ar DTI metodi. Netika atrasta statistiski nozīmīga saistība starp dzīves laika fiziskās aktivitātes mērījumiem un īstermiņa un ilgtermiņa atmiņas mērījumiem un smadzeņu baltās un pelēkās vielas integritāti, vienlaikus, smadzeņu vielas integritāte korelēja ar tādiem demogrāfiskajiem faktoriem kā vecums un izglītība. Šādi rezultāti varētu būt saistīti ar nepilnībām dzīves gājuma fizisko aktivitāšu mērījumos, kā arī dalībnieku līdzīgo fizisko aktivitāšu pieredzi. Nākotnē būtu vēlams izstrādāt precīzāku dzīves laika fizisko aktivitāšu izvērtēšanas instrumentu.