

ORIGINAL ARTICLE
EPIDEMIOLOGY AND CLINICAL MEDICINEPhysical capacities and leisure activities
are related with cognitive functions in older adultsFederica GONNELLI ^{1,2}*, Nicola GIOVANELLI ^{1,2}, Mirco FLOREANI ^{1,2},
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ABSTRACT

BACKGROUND: This study aimed to evaluate the relationship between physical activity habits, physical performance and cognitive capacity in older adults' population of Italy and Slovenia.**METHODS:** Anthropometric characteristics and body composition bioelectrical impedance analysis were evaluated in 892 older adults (60-80 y). Aerobic capacity was measured using the 2-km walk test and handgrip and flexibility tests were performed. Physical activity habits and cognitive functions were evaluated by the Global-Physical-Activity-Questionnaires (GPAQ) and by Montreal-Cognitive-Assessment (MoCA) questionnaires, respectively.**RESULTS:** GPAQ scores were associated with lower BMI ($r=-0.096$; $P=0.005$), lower percentage of fat-mass ($r=-0.138$; $P=0.001$), better results in the 2-km walk test ($r=-0.175$; $P=0.001$) and a higher percentage of fat-free mass ($r=0.138$; $P=0.001$). We also evaluated that a higher MoCA Score correlates with age ($r=-0.208$; $P=0.001$), 2-km walk test ($r=-0.166$; $P=0.001$), waist-hip ratio ($r=-0.200$; $P=0.001$), resting heart-rate ($r=-0.087$; $P=0.025$) and heart-rate at the end of 2-km walk test ($r=0.189$; $P=0.001$).**CONCLUSIONS:** Older adults with a higher level of daily physical activity showed reduction in fat-mass and BMI, and higher aerobic fitness; these characteristics have a protection effect on cognitive function.

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KEY WORDS: Aging; Exercise; Cognition; Habits.

In Europe, aging of population is settled into a well-defined trend of low birth rate and higher life expectancy. In 2016, 29.6% of the entire European population were older than 65 years, and between 2007 and 2017 in Italy and Slovenia people older than 65 years grown by 2.2% and 3%, respectively.¹ Data from 2016 reported that people over 65 were the 22% of the whole population in Italy and the 19% in Slovenia, but these numbers are expected to increase by 2070 reaching the 33% and 28% in Italy and Slovenia respectively.¹

During aging, the body presents numerous modifications including changes in body composition, increase in fat mass, decrease in lean mass, and consequently sarcopenia, reduction in bone density, but also greater risks of Alzheimer's disease (AD) and different types of dementia.²⁻⁵ Among these, decreased muscle mass in women,⁶ decreased strength level and sarcopenia^{7,8} were found to be correlated with an increased limitation in performing daily activities, increased risk of hospitalization and nurs-

ing home admission, and premature death.^{9, 10} It is worth mentioning that increasing sedentary behaviors as a consequence of limitation in daily activities or hospitalization, have been shown to negatively impact the general health status, as well as cognitive function.^{11, 12} In fact, physical activity is associated with lower risk for cognitive decline and improved cognitive function via different mechanisms like neurogenesis, angiogenesis and synaptic plasticity and can also reduce the age-related neural inflammation.^{13, 14} More specifically, cardiovascular fitness is positively correlated to hippocampal volume, which plays a crucial role in cognitive processing and memory function in women and episodic memory in men.¹⁵ Noteworthy, combining different types of trainings (*i.e.* aerobic, strength and coordination) may have a higher efficacy on driving positive brain changes and, consequently, cognitive function.¹⁶

Current literature includes a wide variety of studies evaluating physical fitness or physical habits and cognitive function in aging population. However, we believe that it is necessary to evaluate anthropometric measurements and multiple aspects of physical fitness, including strength, flexibility and aerobic capacity, and the connection with physical daily habits and cognitive function on a large representative population of Caucasian free-living older adults.

For this reason, in this study we performed a wide battery of tests within a large cohort of older people living in northeast Italy and Slovenia. We collected anthropometric measurements and assessed body composition, physical fitness level, daily physical activity habits and cognitive performance. We assessed physical daily habits and cognitive performance via the Global-Physical-Activity-Questionnaires (GPAQ) and Montreal-Cognitive-Assessment (MoCA) questionnaires respectively. MoCA questionnaire is widely used as a rapid screening tool to assess cognitive function in elderly population and has been validated in the Italian and Slovenian population.^{17, 18} We hypothesized that older adults who were more active (*i.e.* demonstrating a higher level of daily physical activity) would show better anthropometric characteristics, higher level of physical fitness and improved cognitive function compared to less active older adults.

Materials and methods

Ethical approval

The present study, PANGeA mass measurements study, was conducted according to the standards set by the latest revision of the Declaration of Helsinki and was approved

by the National Ethical Committee of the Slovenian Ministry of Health on April 17, 2012, under the acronym IR-aging 1200. The purposes and objectives of this study were carefully explained to the subjects and written informed consent was obtained from all of them.

Subjects

Subjects were contacted via local newspapers both in Italy and Slovenia. The first inclusion criteria to participate in the PANGeA mass measurements study, which was reported in the newspaper, was having between 60 and 80 years of age. A total of 924 subjects from the North-East of Italy and Central and West Slovenia were first enrolled in the study and participated in the measurements. Prior to the beginning of the study, all subjects completed a multidomain questionnaire. The subjects reported, among other information, socio-demographic data, information on health status and drug therapy, and completed a self-reported questionnaire on the usual physical activity (GPAQ).¹⁹ Subjects who were unable to walk independently and continuously for a distance of 2 km and/or subjects who had a severe cognitive decline defined as a MoCA Score less than 10 points (after correction for age and schooling) were excluded from the former analysis (N.=14). Moreover, subjects with acute illnesses or with a history of recent hospitalization (<6 months), diabetic subjects in insulin therapy or with drugs other than metformin were also excluded (N.=18). After the evaluation of inclusion criteria, the analysis was performed on a total of 892 free-living older adults (362 males and 530 females, age: 60-80 years).

Study protocol

Data were collected in six sport centers from Udine, Trieste, and Ferrara (Italy) as well as Koper, Ljubljana, and Kranj (Slovenia) in the summer of 2012. Subjects visited the sport center only once, the entire testing day took place in the same building and lasted approximately 2 hours for each subject. Priority was given to the accuracy of the measurements that were taken in a short period of time (three days for each center) and by the same sports scientists highly trained in running the physical test. At each center, cognitive tests (GPAQ and MoCA questionnaires) were administered individually and in a comfortable room by the same native scientists through the whole study period. Subjects were verbally instructed on how to complete the test by native speaker scientist. Physical capacity tests were administered in a gym set up to include multiple stations, one for each test.

Measurements

Anthropometric characteristics and body composition

Body mass (BM) was measured to the nearest 0.1 kg with a manual weighing scale (Seca 709, Hamburg, Germany) with the subject dressed only in light underwear and no shoes. Stature was measured to the nearest 0.5 cm on a standardized wall-mounted height board. Body mass index (BMI) was calculated as $\text{BM (kg)} \cdot \text{stature}^{-2} \text{ (m)}$. Waist and hip circumference (m) were measured using a tape to the nearest 0.1 centimeter and for each site, the average of three measurements was taken. The ratio between waist and hip circumference (WHR) was also calculated. Body composition was measured by using bioelectrical impedance analysis with a tetra-polar impedance-meter (BIA101, Akern, Florence, Italy), according to accepted method.²⁰ Body composition (fat-free mass [FFM] and fat mass [FM]) was obtained from the software provided by the manufacturer, which contains predictive equations and specific reference values for the pediatric, adult and geriatric population.

Physical capacities and physical daily habits

Physical capacities were assessed using 3 physical fitness tests suitable for the age group. A representative spectrum of the target group's physical abilities was thus obtained.

Aerobic capacity

The 2-km walk test (UKK Test)²¹ was used to evaluate aerobic capacity. The UKK Test was developed by the Urho Kaleva Kekkonen Institute for Health Promotion Research (UKK Institute), and serves as a measure of relative fitness, endurance and cardiorespiratory capacity. The test consists in completing the distance of two kilometers walking at the maximal steady velocity. The time to perform the test is expressed in minutes and is used to calculate the UKK Fitness Index (UKK-FI), considering age (yr), sex, Body Mass Index (BMI, kg/m^2) and the heart rate (HR) at the end of the test. The UKK-FI can be calculated as follow:

$$\text{Men: FI} = 420 - [(11.6 \times \text{min}) + (0.56 \times \text{HR}) + (2.6 \times \text{BMI}) + (0.2 \times \text{age})]$$

$$\text{Women: FI} = 304 - [(8.5 \times \text{min}) + (0.32 \times \text{HR}) + (1.1 \times \text{BMI}) + (0.4 \times \text{age})]$$

The equation results are the FI and can be inserted into 5 class domains that characterized the fitness level of the person.²¹ The FI classes are divided as follow: <70; 70-89; 90-110; 111-130; <130; where <70 is considerably below

the average and >130 is considerably above the average. Moreover, resting heart rate (HR_{pre}) and heart rate at the end of the UKK Test (HR_{post}) were measured using a heart rate monitor band (Polar, Kempele, Finland).

Handgrip strength

Strength was evaluated by the hand-grip test using a hand dynamometer (Jamar, Patterson Medical, Sutton-in-Ashfield, UK). The hand-grip test is considered a valid measure to evaluate strength in older adults.²² The subject performed the test in a seating position with the elbow flexed at 90 degrees and positioned on the side, but not against, of the body. The hand was positioned firmly on the dynamometer with the thumb pointing up. The average of three trials measured in Newton was considered for further analysis.

Flexibility

The flexibility of lower back and hamstring muscles was measured by the Sit and Reach Test. The test is considered a valid measure of flexibility in a population of older adults.^{23, 24} Each subject performed three trials, separated by at least 30 sec of rest, after a brief warm up. The test was performed using a box (Cartwright Fitness, Chester, UK) and the subject was asked to seat with both knees fully extended and pressed against the floor, with feet straight out. They were then asked to reach their toes or beyond. The maximum distance between the three measurements expressed in cm was then used for the analysis.

Physical daily habits

GPAQ^{19, 25} was used to evaluate physical daily habits of each subject and was conducted in a face-to-face interview fashion. It consists of 16 questions divided in three domains and a sedentary behavior. The three domains are the following: 1) activity at work; 2) travel to and from places; and 3) recreational activities. GPAQ analysis uses the Metabolic Equivalents (METs) and assigns a total of 4 METs and 8 METs respectively for moderate and vigorous activity per time spent in the specific activity. Finally, after correcting the answers as reported in the GPAQ Guidelines, each question was inserted in the following formula:

$$\text{Total Physical Activity MET-minutes} \cdot \text{Week}^{-1} = [(P2 \cdot P3 \cdot 8) + (P5 \cdot P6 \cdot 4) + (P8 \cdot P9 \cdot 4) + (P11 \cdot P12 \cdot 8) + (P14 \cdot P15 \cdot 4)]$$

In this formula P(n) is the answer to each question in the questionnaire.

World Health Organization recommendations give a cut-

off value for total physical activity MET-minutes·Week⁻¹ of 600 or 150 minutes of moderate to vigorous physical activity to be achieved in order to be considered healthy active.²⁶⁻²⁸

Cognitive performance

To assess the cognitive performance, we used the MoCA as it is a rapid validated screening test to detect mild cognitive impairment.^{18, 29-31} From the raw data we then calculated the MoCA value applying the correction for age and total years of education as suggested by previous authors.³⁰ The test consists of one page with multiple questions divided in the following domains: attention and concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculations, and orientation. Ten minutes are necessary to complete the test and the maximal score achievable is 30 points. A score of 26 or above is considered normal.

Statistical analysis

All anthropometric characteristics, physical capacities and cognitive functions are described using mean and standard deviation (SD) and median and interquartile range (IQR) values. The normality of the distribution was checked with the Kolmogorov-Smirnov Test and it was found that all variables were non-normally distributed.

The comparisons between male and female were carried out using the Wilcoxon-Mann Whitney Test; Spearman correlation coefficients were used to assess the strength and direction of association and multicollinearity between independent variables. Then, Generalized Linear Multivariate Analysis was performed to evaluate the impact of some variables on cognitive functions. All statistical analyses were performed by SAS, Release 9.4 (SAS Institute, Cary, NC, USA), with a significance set at $P < 0.05$.

Results

Anthropometric characteristics and body composition

When considering the whole population, mean age was 67.0 ± 5.1 (years), BM 73.7 ± 13.4 (kg), stature 1.65 ± 0.09 (m) and BMI 27.0 ± 3.9 ($\text{kg} \cdot \text{m}^{-2}$). Also, as described in Table I, males were older than females (+1.5%, $P = 0.004$) and had higher body mass, stature and BMI (+23.3%, +7.5% and +3.6%, respectively, $P < 0.001$) (Table I). At the same time, males showed higher waist circumference, WHR and FFM (+8.2%, +9.3% and +27.4%, respectively, $P < 0.001$) than females. However, males showed lower FM in absolute (-5.1%, $P = 0.011$) and relative (-27.1%, $P < 0.001$) values than females (Table I).

Physical capacities and physical daily habits

Males required less time to complete the 2-km walk test (-5.6%, $P < 0.001$), had lower HR_{pre} and HR_{post} test (-6.0 and -5.3%, respectively, $P < 0.001$) and UKK_FI (-18.1%, $P < 0.001$) than females, results are described in Table II.

Males showed (Table II) higher handgrip strength (+37.3%, $P < 0.001$) and lower flexibility (-31.4%, $P < 0.001$) than females. Finally, males spent more time in physical daily activities (+10.1%, $P < 0.05$) than females (Table II).

Cognitive performance

The cognitive performance, evaluated by the MoCA test, showed (Table II) that males had a higher education level (+3.9%, $P < 0.05$), but lower values of MoCA test expressed in absolute (-4.0%, $P < 0.001$) and adjusted (-4.3%, $P < 0.001$) score, than females.

Factors of PA habits and cognitive abilities

Physical daily habits were directly related with relative FFM ($r = 0.138$, $P = 0.001$) and UKK_FI ($r = 0.104$,

TABLE I.—Anthropometric characteristics and body composition of the subjects.

	Male (N.=362)		Female (N.=530)		P
Age (y)	67.6±5.3	66 (8)	66.6±4.9	66 (7)	0.004
Body mass (kg)	82.2±11.2	81.5 (14.5)	67.9±11.5	66 (15.1)	0.001
Stature (m)	1.73±0.06	1.73 (9)	1.60±0.06	1.6 (7.4)	0.001
BMI ($\text{kg} \cdot \text{m}^{-2}$)	27.6±3.4	27.2 (4.4)	26.6±4.1	26 (5)	0.001
Waist circumference (m)	0.98±0.10	0.98 (0.13)	0.90±0.11	0.89 (0.15)	0.001
Hip circumference (m)	1.01±0.07	1.01 (10)	1.02±0.09	1.02 (0.11)	0.054
Waist to hip ratio	0.97±0.06	1 (0.1)	0.88±0.07	1 (0.1)	0.001
FFM (kg)	56.9±6.2	56.9 (8.3)	41.3±4.7	40.7 (6.5)	0.001
FM (kg)	25.3±6.8	24.5 (8.7)	26.6±8.4	25.3 (9.3)	0.011
FM (%)	30.3±4.9	30.5 (6.4)	38.5±6.2	38.2 (7.2)	0.001

All values are mean±SD and median (IQR).
BMI: Body Mass Index; FFM: fat-free mass; FM: fat mass.

TABLE II.—Physical capacities and cognitive functions of the subjects.

	Male (N.=362)		Female (N.=530)		P
2-km walk test (min)	19.6±2.3	19.4 (3.1)	20.7±2.3	20.5 (3.1)	0.001
HR _{pre} 2-km walk test (bpm)	70.3±11.8	69 (17.4)	74.5±11.3	74.5 (16)	0.001
HR _{post} 2-km walk test (bpm)	110.7±20.8	111 (27)	116.6±19.2	117 (28)	0.001
UKK Fitness Index (u.a.)	74.7±26.2	73.1 (37.1)	88.2±20.9	90.3 (27.7)	0.001
Hand-grip force (N)	45.6±7.9	46 (11)	28.6±5.5	28.7 (7)	0.001
Sit & Reach test (cm)	33.4±10.8	34 (15.2)	43.9±9.3	44.3 (13)	0.001
GPAQ (MET·min ⁻¹ ·week ⁻¹)	5151±3760	4200 (4320)	4630±3374	3840 (3670)	0.047
Education (year)	12.7±3.5	13 (3)	12.2±3.7	13 (5.3)	0.035
MOCA test (u.a.)	24.7±2.9	25 (4)	25.7±2.9	26 (4)	0.001
MoCA test correct (u.a.)	23.3±2.7	23.6 (3.9)	24.3±2.5	24.6 (3.4)	0.001

All values are mean±SD and median (IQR).

HR: heart rate; GPAQ: Global Physical Activity Questionnaire; MoCA: Montreal Cognitive Assessment.

P=0.007), but inversely correlated with BMI ($r=-0.096$, $P=0.005$), relative ($r=-0.138$, $P=0.001$) and absolute FM ($r=-0.114$, $P=0.001$), and time spent in 2-km walk test ($r=-0.175$, $P=0.001$).

MoCA results were directly related with HR_{post} 2-km walk test ($r=0.189$, $P=0.001$), UKK_FI ($r=0.149$, $P=0.001$) and Education ($r=0.343$, $P=0.001$) but, inversely related with age ($r=-0.208$, $P=0.001$), waist circumference ($r=-0.080$, $P=0.024$), WHR ($r=-0.200$, $P=0.001$), HR_{pre} 2-km walk test ($r=-0.087$, $P=0.025$), time spent in 2-km walk test ($r=-0.166$, $P=0.001$).

Considering the adjusted MoCA for age and total year of education, HR_{post} 2-km walk test ($r=0.130$, $P=0.001$) and UKK_FI ($r=0.112$, $P=0.005$) were directly related with adjusted MoCA results. Conversely, WHR ($r=-0.167$, $P=0.001$) and HR_{pre} 2-km walk test ($r=-0.086$, $P=0.028$) were inversely related with results from the adjusted MoCA questionnaire.

In a multivariate analysis described in Table III, IV, the variables included into the equations provided a significant independent contribution to the model ($P<0.001$) for MoCA and adjusted MoCA test. When sex, age, time spent in 2-km walk test, WHR, HR_{pre} 2 km test and HR_{post} 2 km

TABLE IV.—Multiple linear regression analysis of adjusted MoCA.

Parameter	Estimate	Standard Error	t value	Pr> t
Intercept	28.75	1.81	15.89	<0.0001
Waist to hip ratio	-5.58	1.36	-4.10	<0.0001
HR _{pre} 2-km walk test	-0.02	0.01	-2.52	0.012
HR _{post} 2-km walk test	0.02	0.01	3.24	0.001
Root MSE	2.599			
Adj-R ²	0.047			
P	0.001			

test were entered in the model, R^2 was 0.117 for MoCA test (Table III). It is important to highlight that we interpreted the dichotomic variable “sex” as male. In other words, for the purpose of the analysis, being male is positively correlated with the MoCA Score. In fact, when inserted in a multiple regression analysis, being male and younger, performing the 2-km walk test with a better time, having lower WHR, HR_{pre} 2-km walk test and higher HR_{post} 2-km walk test correlate with the result of MoCA Score.

At the same time, when WHR, HR_{pre} 2 km test and HR_{post} 2 km test were entered in the model, R^2 was 0.047 for adjusted MoCA test (Table IV). When the adjusted MoCA Score was inserted in the multiple regression analysis, having lower WHR, lower HR_{pre} 2-km walk test and higher HR_{post} 2-km walk test showed a significant correlation.

Discussion

The main results of this study indicated that older adults who are more active in their daily life showed better anthropometric characteristics and physical capacities, and better results in cognitive function.

As we hypothesized, we found a positive correlation between the GPAQ Score and anthropometric characteristics, body composition and physical capacities. In fact, it was shown that general physical activity, or even a certain pe-

TABLE III.—Multiple linear regression analysis of MoCA.

Parameter	Estimate	Standard Error	t value	Pr> t
Intercept	36.20	2.60	13.93	<0.0001
Sex	0.75	0.29	2.55	0.011
Age	-0.09	0.02	-3.87	0.001
2-km walk test	-0.15	0.05	-2.94	0.003
Waist to hip ratio	-3.93	1.79	-2.20	0.028
HR _{pre} 2-km walk test	-0.03	0.01	-2.72	0.007
HR _{post} 2-km walk test	0.02	0.01	3.36	<0.001
Root MSE	2.763			
Adj-R ²	0.117			
P	0.001			

riod of exercise training, can positively impact body composition by decreasing BMI and fat-mass while increasing fat-free mass.³²⁻³⁴ At the same time, as shown in the present study, being generally more active is also affecting physical fitness as evaluated by the decrease time to perform the 2-km walk test and the increased UKK_FI which is in line with previous findings and recommendations.^{35,36}

In addition, as previously reported, gait speed, anthropometric characteristics, and other evaluations of fitness, which may reflect a good level of physical activity, were found to be inversely correlated with cognitive impairment or dementia.^{37,38} These studies have identified physical activity as a potent lifestyle factor that plays a critical role in predicting rates of cognitive decline^{39,40} and the subsequent development of age-related neurodegenerative diseases like AD.^{41,42} It is worth to notice that, in the present study, the MoCA Score was highly correlated with the measures of physical fitness and more specifically with the time to complete 2 km, the heart rate and the FI, as observed previously.⁵ In particular, decrease in brain volume and grey matter is a continuum during aging and associates with AD and dementia, but physical activity and higher cardiorespiratory fitness can lower this decline.⁴³ In addition, other physical activities like walking, can have a protective effect on AD, dementia and may also indirectly modify other potential risk factors (*i.e.* hypertension and obesity).^{44,45} Interestingly, during exercise the local blood flow to the brain increases as a direct response of the activity performed and such an increase indicates an enhanced neural activation.⁴⁶ Therefore, cerebral blood flow regulation can be considered of key importance when explaining the positive effects of exercise on cognitive function.^{47,48}

Other than aerobic activities, it was also demonstrated that a 6-month training period, including strength and flexibility, is enough to maintain cognitive function and general brain atrophy in people with mild cognitive impairment.⁴⁹ In fact, maintaining a higher muscle mass and lower body FM is associated with better cognitive performance.⁵⁰ However, in the present study, the MoCA Score was not directly correlated with strength or flexibility and this was also true when the adjusted value of MoCA was considered in the correlation analysis. In fact, when accounting for age and education year, the MoCA Score solely correlated with the WHR, HR and the FI. The reason for this may be found in the relative higher contribution of cardiorespiratory fitness rather than other physical factors in preserving cognitive function.

It was previously found that neurogenic factors like insulin-like growth factor-I (IGF-I), brain-derived neuro-

trophic factor and vascular endothelial growth factor are of key importance in mediating structural and functional changes particularly in the hippocampus region when triggered by an exercise stimulus.^{51,52} In older adults, these neurogenic factors are related with a reduced atrophy in hippocampal volume, vascularization and therefore cognitive decline but positive changes are linked to exercise.^{53,54} As reported by the multiple regressions, herein the MoCA Score strongly correlates with WHR and HR measures. It is possible that the higher cardiovascular fitness exhibited in the present population could be linked to increased blood flow supply to the prefrontal and hippocampus region that protects from cognitive decline. Even though a direct correlation between the MoCA and the GPAQ questionnaire was not appreciable, a more active daily habits involving aerobic activities may be responsible for the correlation between WHR and MoCA. In fact, engaging in aerobic activities can improve the WHR along with the reduction in fat mass.⁵⁵

Limitations of the study

Even though the present study was conducted on a relatively large population and on a wide variety of tests, it is important to take in consideration some limitations. In particular, we excluded from the former analysis subjects who scored less than 10 points in the MoCA test. This could be considered a confounding factor when evaluating extreme lower level of cognitive function. Moreover, we did not consider the time to perform the MoCA test which could give a deeper insight relative to the cognitive function in elderly population. At the same time, other domains of cognitive function (*i.e.* visual-constructional or memory) that are markedly declined during aging,⁵⁶ should be taken in consideration for further implications on cognitive function.

Conclusions

In conclusion, we collected data from a large population of older adults in Italy and Slovenia and demonstrated that, a higher level of physical activity habits can influence body composition by reducing FM, BMI and increasing FFM and the general aerobic fitness. Furthermore, it is also shown not only that these anthropometric measurements have a protection effect on cognitive impairment, but this can also be linked with daily physical activity. Finally, increased physical activity can directly improve cognitive performance but the opposite may also be true; that is, a high cognitive performance could lead to improved physical activity and better body composition. In an ag-

ing population with increasing incidence of dementia and cognitive impairment, physical activity intervention and strategies adapted for older adults are recommended to slow age-related decline and reduce disease-related cognitive impairment.

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