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Aerobic fitness and multidomain cognitive function in advanced age

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ABSTRACT

Background: Studies generally describe the relationship between physical fitness and cognitive function by measuring only one or two specific cognitive tasks. In addition, in spite of the significant increase in life expectancy, the age of participants in these studies does not extend beyond a mean age of 70 years. This study was thus designed to examine the relationship between physical fitness and function in multiple cognitive domains in subjects older than those previously reported.

Methods: Thirty-eight individuals, aged 65.3 to 85.3 years, performed a graded, progressive, maximal exercise test. Based on a median score of peak VO_2, participants were divided into low-fitness and moderately-fit groups. Cognitive function was assessed by means of a computerized neuropsychological battery.

Results: The moderately-fit group achieved significantly better scores on the global cognitive score ($U = 97$, $p = 0.04$), and a significant correlation was found between peak VO_2 and attention, executive function, and global cognitive score ($r_s = .37, .39, .38$ respectively). The trend for superior cognitive scores in the moderate-fitness compared to the low-fitness groups was unequivocal, both in terms of accuracy and reaction time.

Conclusion: Maintenance of higher levels of cardiovascular fitness may help protect against cognitive deterioration, even at an advanced age. An adequately powered randomized controlled trial should be performed to further evaluate this hypothesis.

Key words: predicted peak VO_2, neuropsychological testing, physical activity, global cognitive function, old age

Introduction

Aerobic activity appears to moderate the decline of cognitive function associated with aging (Angevaren *et al.*, 2008). Moderately intense aerobic activity results in an increase in the ability of the heart to deliver oxygen to the working muscles, and this is indicative of an increase in cardiovascular fitness (American College of Sports Medicine – ACSM, 2006a). These gains in cardiovascular fitness are thought to be associated with other physiological changes influencing cognitive performance. These include improved cerebral blood flow and energy metabolism (Rogers *et al.*, 1990), changes in cerebral structure (Colcombe *et al.*, 2003), and alteration in neurotransmitter activity (Neeper *et al.*, 1995). Thus, improvement in cardiovascular fitness has potentially beneficial effects on cognitive capacity (Colcombe *et al.*, 2004).

Large-scale studies based in the community support this assumption, indicating that physical activity (Yaffe *et al.*, 2001; Weuve *et al.*, 2004) or physical fitness (Barnes *et al.*, 2003) are related to the preservation of cognitive health in older adults. While these studies utilized the Mini-mental State Examination (MMSE) (Folstein *et al.*, 1985) as a cognitive outcome measure to determine the risk for developing dementia, this screening tool is not sensitive enough to reveal subtle changes in specific cognitive functions.

Recent cross-sectional studies have described the association between age and physical activity on the one hand, and various aspects of executive function on the other (Hillman *et al.*, 2006; Themanson *et al.*, 2006). These studies generally evaluated the frequency, duration and intensity of physical activity by means of self-reported questionnaires. However, such questionnaires may also reflect other factors, such as the level of social engagement or a

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generally healthy lifestyle, which in turn may protect against cognitive decline. In addition, even though cardiovascular fitness is largely a product of aerobic activity, the ability of subjective questionnaires to reflect cardiovascular fitness is limited. Previous studies have in fact indicated that it is physical fitness and not physical activity that is related to cognitive function (Etnier *et al.*, 2003; Netz *et al.*, 2009). Therefore, aerobic fitness (as reflected by the predicted peak VO_2) and maximal heart rate (HRmax), which are based on objective physiological measurements, may better depict the relationship between physical fitness and cognitive function.

Some studies have assessed aerobic fitness in relation to cognitive function in older adults. However, although many of the age-related decrements in cognition are not observed until after 60 years of age (Schaie, 2004), the age of participants in those studies did not go beyond a mean age of 70 years (Etnier and Landers, 1997; Barnes *et al.*, 2003; Netz *et al.*, 2009). This is in spite of the significant increase in life expectancy, with those older than 85 years representing the fastest growing segment of the population (National Center for Health Statistics, 2004). Unfortunately, although people are living longer, they are not necessarily living healthier lives (National Center for Health Statistics, 2004).

Most studies examining the relationship between physical activity or fitness and cognitive function usually assess only one or two specific cognitive tasks, most often an executive control task such as the flanker task (Hillman *et al.*, 2006), task switching (Themanson, *et al.*, 2006), or the alternate uses test (Netz, *et al.* 2009). Quantitative reviews exploring a wider range of cognitive tasks, however, failed to find consistent results – possibly due to the application of different approaches to classifying cognitive tasks. While Colcombe and Kramer (2003) reported that physical activity improved all cognitive categories, they emphasized the benefit on executive functions. In contrast, although a recent review (Angevaren *et al.*, 2008) found a positive relationship between cardiorespiratory fitness and cognitive capacity, the greatest benefits were rather on motor function and auditory attention. The authors recommend that clinicians and scientists in the field of neuropsychology seek mutual agreement on the use of a standard battery of cognitive tests, in order to make research on cognition more clinically relevant and results more reproducible. We thus decided to use a standardized computerized cognitive assessment battery (Mindstreams, NeuroTrax Corp., NJ, U.S.A.) in the present study.

We aimed to assess whether physical activity and fitness, as determined by the completion of a self-reported questionnaire and by measuring predicted peak VO_2, was associated with cognitive function comprising multiple cognitive domains in older community-dwelling subjects.

Methods

Participants

Subjects were residents of a retirement village who expressed their willingness to participate in the study. Exclusion criteria included a score of <24 on the MMSE (Folstein *et al.*, 1985), active ischemic heart disease, congestive heart failure (functional capacity level 2 or more according to the American Heart Association), uncontrolled hypertension (systolic blood pressure of over 160 mmHg and diastolic 90 mmHg), neurological deficit due to previous stroke, depression (>8 on the short version of the Geriatric Depression Scale (GDS), Brink *et al.*, 1982), dementia (according to DSM-IV criteria; American Psychiatric Association, 1994), cancer treated by chemotherapy, anemia (Hb < 12g%), renal failure (creatinine > 1.5mg/dL), poorly controlled diabetes mellitus (HBA1C > 8%), change in medications in the two weeks prior to the study, inability to use a computer (due to difficulties in vision or motor function) and smoking.

The study was approved by the Ethics Committee of the Meir Medical Center (Kfar Saba, Israel). All subjects provided written informed consent for participation in the study.

Clinical assessment

Demographic information, including education level, marital status, country of origin, handedness, prior computer experience, occupation and employment status was provided by the participants. Medical history was obtained by interview. Cognitive screening was performed using the MMSE, screening for depression utilized the 15-item GDS, and functional status for instrumental activities of daily living (IADL) was assessed using the Lawton and Brody Scale (Lawton and Brody, 1969). Medications were coded according to therapeutic categories (for example, antihypertensives, anticoagulants, etc.). Diseases were categorized according to systems (such as cardiovascular, gastrointestinal, musculoskeletal and others). For the purpose of the study, a score of 0–2 on the GDS was considered to be "no depression'" and 3–6 partial depression, and a score of 1 on the Lawton IADL was considered high functioning, 1.1–1.66 average and 2 low functioning.

Physical activity assessment

The Habitual Physical Activity Questionnaire (HPAQ; Baecke *et al.*, 1982) was used for assessing

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the level of physical activity. This questionnaire provides four indices of habitual physical activity: an occupation activity index, a sport activity index, a leisure activity index; and a total score. The sport activity index is composed of the multiplication of three scores: level of intensity, time and proportion (activity per month). The range of possible scores on the full questionnaire is 3 to 15. This questionnaire has been shown to be reliable and valid in previous studies with older adults (Pols *et al.*, 1996; Netz *et al.*, 2009). Because participants in this study were retirees and did not have a score on occupation activity, this part was excluded. Therefore, the total score included the sport index and the leisure activity index only.

Assessment of aerobic fitness

In order to assess the level of aerobic fitness level (predicted peak VO_2) and maximal heart rate (HRmax), participants performed a graded, progressive, maximal exercise test on a motorized treadmill (Woodway, Germany). For the duration of the test, the electrocardiogram (ECG), heart rate (HR), blood pressure, and rating of perceived exertion were monitored continuously, using a 12-lead ECG, a sphygmomanometer, and the Borg scale (Borg, 1986), respectively. Subjects with abnormal cardiac signs or symptoms were excluded from the study. The test commenced with a 2–5-minute practicing and adaptation. Based on the modified Balke protocol (ACSM, 2006a), an initial speed of 3.2 km/hr with a gradient of zero was determined. The gradient was increased by 2.5% every 2 minutes until a symptom (dizziness, breathlessness, changes in ECG, etc), limited max was reached or until the subject reached exhaustion. The test continued for 6–13 minutes (mean 9.75 ± 1.6).

Prediction of peak VO_2: Peak VO_2 was estimated from the last stage of the graded maximal treadmill exercise challenge. The following equation was used to estimate peak VO_2 for each subject: VO_2 ($ml^{*}kg^{-1*}min^{-1}$) = 0.1 (final speed) + 1.8 (final speed) (final fractional grade) + 3.5 $ml^{*}kg^{-1*}min^{-1}$ (ACSM, 2006a).

Cognitive assessment

Cognitive function was assessed using the Mindstreams (NeuroTrax Corp., NJ, U.S.A.,) computerized battery that utilizes novel adaptations of traditional neuropsychological tests to provide an overall measure of cognitive function as well as an evaluation of specific cognitive domains. The battery comprised the following tests: Go-NoGo Response Inhibition, Verbal Memory, Stroop Interference, Nonverbal Memory, Catch Game and Visual Spatial Imagery. Previous research has shown that these tests have good concurrent validity and reliability and are highly correlated with performance on traditional neuropsychological batteries (Dwolatzky *et al.*, 2003; Schweiger *et al.*, 2003). The battery is simple to use, requires no previous computer experience and is web-based with a central database. All tests are run in the same fixed order, and all responses are made using either the computer mouse or the number pad on the keyboard. Outcome parameters include accuracy, reaction time (RT) and standard deviation (SD) of RT, as appropriate for each test. Given the speed-accuracy tradeoff (Cauraugh, 1990), a performance index (computed as [accuracy/response time] $\times$ 100) is computed for timed tests in an attempt to capture performance both in terms of accuracy and response time.

Outcome parameters are calculated using custom software blind to group membership (VO_2 scores). To permit summarizing the performance in each cognitive domain across different types of outcome parameters (e.g. accuracy, RT), each outcome parameter is normalized and applied to a standard score scale (mean 100; SD 15) in an age- and education-specific fashion. Normalized subsets of outcome parameters are averaged to produce four summary scores, each indexing a different cognitive domain:

Memory: mean accuracies for learning and delayed recognition phases of the Verbal and Nonverbal Memory tests.

Attention: mean response times for the Go-NoGo test and the no interference (meaning) phase of the Stroop test and mean standard deviation of response time for the Go-NoGo test.

Visual-spatial: mean accuracy for the Visual-Spatial processing test.

Executive function: performance indices for the Stroop test and Go-NoGo test mean weighted accuracy for Catch Game.

These index scores (cognitive domains), and a *Global Cognitive Score*, computed as the average of these index scores, provided a measure of cognitive function (Dwolatzky *et al.*, 2003).

Procedure

Following a lecture at the retirement village on cognitive functioning and physical activity in advanced age, residents were invited to participate in the study. Possible candidates were interviewed by trained research assistants to provide general demographic and medical data, and received an outline of the proposed study. Those who expressed an interest in participating in the study were interviewed by a physician (TD) and provided

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written informed consent following a detailed explanation of the study. The physician then performed a complete medical chart review to gain a more complete medical history and the subject underwent a physical examination. Questionnaires were administered and Mindstreams testing was performed. All these procedures were carried out at the retirement village. Within two weeks of the final interview, suitable participants underwent exercise testing at the physiology laboratory of the Wingate Institute.

Data analysis

The small number of participants who were eligible to complete the exercise test, and the fact that tests of normality (Kolmogorov-Smirnov) indicated that three cognitive domains (Memory, Attention and Global Cognitive Score) were not normally distributed (also medications and diseases are nominal variables that cannot be analyzed by parametric tests) have led us to use non-parametric tests – i.e. Mann Whitney and Spearman correlation.

Initially, our plan was to divide participants into fitness categories based on the ACSM (2006a) norms. However, all participants in the present study had very poor scores relative to the ACSM norms, thus limiting the possibility of using these norms. More specifically, while age norms for peak VO_2 are provided by the ACSM (2006a) for each decade for men and women, the highest decade specified is that of 60 years and older. For this age group the average (50th percentile) peak VO_2 for men is 34.6 ml*kg-1*min-1 and for women 26.7 ml*kg-1*min-1. In our study the median score for men was 23.95 (range 7.0–34.8) and for women 18.0 (range 5.4–31.5), both representing poor scores (below the 10th percentile) relative to the ACSM norms for those older than 60 years (ACSM, 2006a). Since no specific values were provided by the ACSM for age groups 70–80 or 80–90, participants in the present study were divided into two groups somewhat arbitrarily – namely above and below the 50th percentile.

A median score (50th percentile) of 18.5 $ml*kg^{-1}*min^{-1}$ was determined for both genders combined, for the following reasons: (i) group differences on gender distribution were not significant; (ii) no gender differences were detected on any variable including all cognitive tests; and (iii) only one male was misplaced relative to the median score for men in this study (although he had a score of 22.4, which is less than the median score for men, he was placed in the moderate VO_2 group). Thus, those with predicted peak $VO_2 \leq 18.5$ $ml*kg^{-1}*min^{-1}$ were defined as the low fitness group and those with $VO_2 > 18.5$ $ml*kg^{-1}*min^{-1}$ as the moderately fit group.

Results

Figure 1 describes the selection of subjects for participation in the study. Prior to the exercise test, 31 subjects (out of the 101 elderly residents who expressed interest in participating in the study) were excluded based on the criteria noted previously, and 14 withdrew consent. During the exercise test, 18 more subjects were excluded due to abnormal exercise test, including ST segment changes, atrial fibrillation, or multiple ventricular premature beats. Thirty-eight individuals, 26 women and 12 men, aged 65.30 to 85.31 years old, mean age 77.54 ($\pm$5.28) years, were found to be eligible to complete the maximal exercise test, and thus participated in the study.

Demographic and physical characteristics of the two groups are presented in Table 1. As beta-blockers (antihypertensive medication) affect heart rate, HRmax scores are presented separately for those who were on beta-blockers and those who are not. Apart from predicted peak VO_2, the groups differed with respect to physical activity level (HPAQ). No differences were found on any other demographic variables and no relationship was found between age and any of the cognitive tests or categories. The two groups had similar clinical characteristics (see Table 2); however, significantly (Fisher's Exact Test) more subjects in the low fitness group used antihypertensive medications ($p = 0.02$) and were more limited in IADL ($p = 0.04$) than those in the moderately fit group.

Table 3 presents all outcome parameters. A clear trend for better scores among participants with a moderate peak VO_2 compared to those with low peak VO_2 emerged in all scores, both in terms of accuracy as well as reaction time. Although in most cases differences were not significant, the trend of scores consistently favored the group with moderate VO_2. Generally, the standard deviation of the reaction time scores in the low VO_2 group was greater than that of the moderate VO_2 group.

Results for each cognitive domain are reported in Table 4. A clear trend for better scores (in absolute values) in the moderately fit compared to the low fitness group was present for all scores. Significantly better scores for the moderate VO_2 group were observed for the Attention and the Global Cognitive Score. Spearman correlations assessing the relationship between the scores on each cognitive domain and the predicted peak VO_2 scores were significant for Executive Function, in addition to Attention and Global Cognitive Score.

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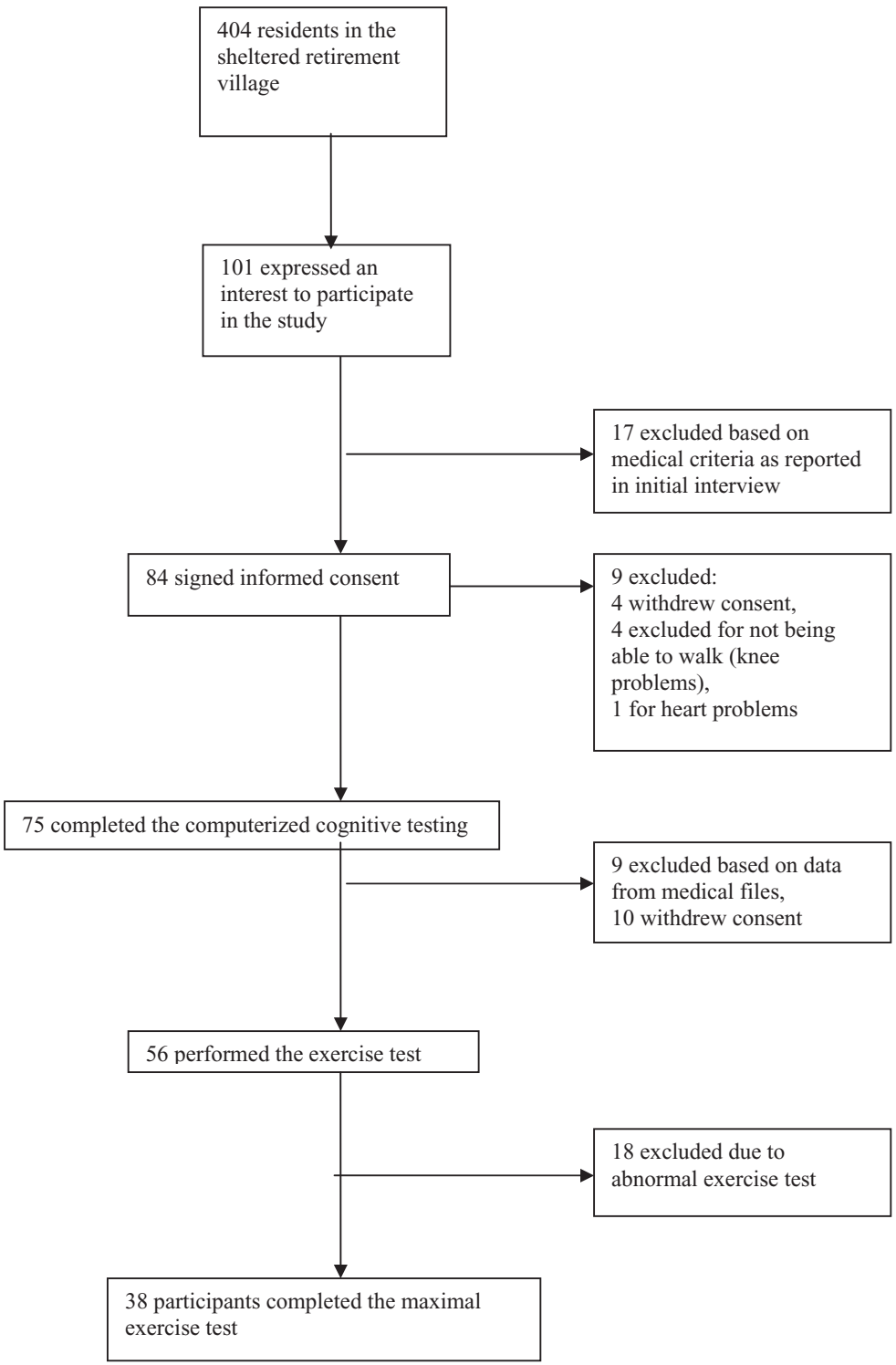


Figure 1. Selection of participants.

None of the correlations assessing the relationship between the scores on the cognitive domains and the HPAQ scores was significant (range −0.2 to 0.2).

Since the predicted peak VO_2 groups differed with regard to the use of antihypertensive medications and Lawton IADL scores (more subjects in the low VO_2 were taking antihypertensive medications and had lower Lawton IADL scores than those in the moderate VO_2 group), the Mann-Whitney test was performed assessing differences in the Global Cognitive Score between participants taking antihypertensive medications and those not taking these medications, and between high and low Lawton scores, for both VO_2 groups. No

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Table 1. Participants' demographic and physical characteristics

VARIABLES	LOW FITNESS, PREDICTED PEAK VO_2 ≤ 18.5 $ml^{*}kg^{-1*}min^{-1}$ (N = 20)	MODERATE FITNESS, PREDICTED PEAK VO_2 > 18.5 $ml^{*}kg^{-1*}min^{-1}$ (N = 18)
Age, mean years (SD)	77.77 (4.35)	77.29 (6.3)
Gender (N)		
Women	15	11
Men	5	7
Height, mean cm (SD)	158.71 (7.6)	163.67 (10.3)
Weight, mean kg (SD)	69.3 (7.2)	68.2 (9.4)
BMI, mean (SD)	28.05 (3.1)	26.18 (3.7)
Education, mean years (SD)	13.15 (2.74)	13.61 (3.6)
Handedness, left-handed (N)	1	3
Computer experience (N)		
Frequently	13	13
Seldom	7	5
Predicted peak VO_2 $ml^{*}kg^{-1*}min^{-1}$ (SD)	13.42 (4.4)	25. 26 (4.3)*
HRmax (SD)		
No beta-blockers	133.1 (8.0)	127.12 (15.4)
Taking beta-blockers	102.45 (17.08)	109.5 (10.61)
All	115.37 (20.71)	125.17 (15.8)
Habitual physical activity		
Total score (SD)	5.35 (0.55)	5.81 (0.58)*
Sport activity index (SD)	2.81 (0.44)	3.12 (0.38)*
Leisure activity index (SD)	2.54 (0.48)	2.7 (0.44)

BMI = Body Mass Index.
HRmax = maximal heart rate.
*t test $p \leq 0.03$.

Table 2. Participants' clinical characteristics

VARIABLES	LOW FITNESS, PREDICTED PEAK VO_2 ≤ 18.5 $ml^{*}kg^{-1*}min^{-1}$ (N = 20)	MODERATE FITNESS, PREDICTED PEAK VO_2 >18.5 $ml^{*}kg^{-1*}min^{-1}$ (N = 18)
MMSE, mean score (SD)	28.45 (1.6)	28.39 (1.6)
Geriatric Depression Scale (N)		
No depression (score 0–2)	18	16
Possible depression (score 3–6)	2	2
Lawton (IADL) (N)		
Normal (score 1)	10	15†
Below normal (score >1)	10	3
Medication Groups (N)*		
Antihypertensives	15	6†
Anticoagulants	6	8
Lipid lowering	9	8
Other	11	10
Disease Groups (N)*		
Cardiovascular	10	7
Gastrointestinal	0	3
Musculoskeletal	1	0
Other	8	3

MMSE = Mini-mental State Examination.
IADL = Instrumental Activities of Daily Living.
† Fisher's Exact Test $p<0.05$.
* Participants may belong to more than one group.

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Table 3. Summary score performance for low- and moderate fitness groups*

MINDSTREAMS TEST		OUTCOME PARAMETER	LOW FITNESS, PREDICTED PEAK VO_2 ≤ 18.5 $ml^{*}kg^{-1*}min^{-1}$ (N = 20)	MODERATE FITNESS, PREDICTED PEAK VO_2 >18.5 $ml^{*}kg^{-1*}min^{-1}$ (N = 18)	MANN WHITNEY P VALUE
Go-NoGo		Accuracy	87.72 (15.33)	91.89 (9.65)	0.66
		Reaction time	558.59 (291.03)	454.56 (44.30)	0.37
		Performance Index	18.59 (6.10)	28.38 (2.85)	0.35
Verbal Memory		Accuracy, 1st repetition	42.00 (28.58)	55.56 (25.95)	0.2
		Accuracy, 2nd repetition	59.50 (31.70)	73.89 (31.46)	0.11
		Accuracy, 3rd repetition	65.00 (33.17)	76.67 (32.72)	0.18
		Accuracy, 4th repetition	65.00 (34.26)	78.89 (32.34)	0.15
		Accuracy, all repetitions	58.30 (30.23)	71.67 (29.32)	0.13
Stroop Test					
	No interference letter color	Accuracy	87.89 (14.37)	95.29 (12.31)	0.05
		Reaction time	1019.47 (666.86)	650.88 (163.07)	0.23
		Performance Index	12.06 (6.32)	15.57 (4.00)	0.14
	No interference word meaning (choice reaction time test)	Accuracy	91.95 (12.17)	98.82 (4.85)	0.004
		Reaction time	838.47 (423.32)	593 (99.65)	0.22
		Performance Index	13.96 (6.96)	17.15 (3.15)	0.22
	Interference color vs meaning	Accuracy	65.56 (36.47)	68.75 (42.50)	0.43
		Reaction time	1097.5 (581.58)	872.57 (590.89)	0.08
		Performance Index	8.63 (6.87)	11.33 (7.21)	0.3
Non Verbal Memory		Accuracy, 1st repetition	42.85 (22.03)	52.33 (21.07)	0.26
		Accuracy, 2nd repetition	43.95 (24.22)	53.06 (27.33)	0.41
		Accuracy, 3rd repetition	44.65 (26.79)	57.28 (30.68)	0.28
		Accuracy, all repetitions	45.65 (22.84)	55.61 (26.66)	0.27
		Accuracy after 10 min	45.33 (29.67)	58.00 (32.90)	0.29
		Time to make first move	881.18 (229.04)	729.64 (235.79)	0.09
Catch Game		Average number of direction changes per trial	0.40 (0.251)	0.36 (0.23)	0.67
		Total Score	439.87 (204.77)	551.52 (208.08)	0.12
		Summed accuracy across sublevels weighted by difficulty (range 0–1000)			

*Note: All Accuracy parameters are in % correct; all timed parameters are in milliseconds; performance index is (accuracy/response time) × 10.

differences were detected between those taking and those not taking antihypertensive medications in the moderate ($U = 35$, $p = 0.96$) or in the low ($U = 25$, $p = 0.39$) peak VO_2 groups. On the other hand, differences were found in the low VO_2 group, with those with a higher level of function on the Lawton IADL scoring higher on the Global Cognitive Score than those with a lower functional level ($U = 17$, $p = 0.02$). No differences were found on the Global Cognitive Score between high and low Lawton IADL scores in the moderate VO_2 group ($U = 22$, $p = 1$).

Discussion

The main finding of the present study is that even in subjects of advanced age with similar education level, health and mental status, improved aerobic fitness is associated with superior global cognitive function.

We found a significant difference in the Global Cognitive Score, which is based on the collective results of all cognitive domains tested. While the differences in the individual tests comprising the Mindstreams battery did not reach significance in most cases, the trend for better cognitive scores in the moderate-fitness compared to the lower-fitness groups was clear (the direction of scores was consistently in favor of the moderate VO2). This was demonstrated in all cognitive measures without exception, reflecting both accuracy and reaction time (Table 3) and indices of cognitive domains (Table 4). These results support the assumption that cardiovascular fitness is associated with cognitive capacity (Colcombe *et al.* 2004), and conform to results from previous studies indicating a relationship between aerobic fitness and various aspects of cognitive functioning (Etnier and Landers, 1997; Barnes *et al.*, 2003; Netz *et al.*, 2009).

The present study is innovative in that it extends the evidence regarding this relationship to more advanced ages than previously reported. Furthermore, the VO_2 scores observed in the present study for both groups are considered very poor (below the 10th percentile) relative to normal values for those older than 60 years (ACSM, 2006a). However, even within those low scores, the group exhibiting higher scores evidently functions better cognitively. This suggests that even at more advanced old age, where a lower level of cardiovascular function is typical, small improvements in physical fitness, usually related to the level of physical activity, may have a positive impact on cognitive capacity.

Not surprisingly, participants at a higher level of fitness also reported that they were more

Table 4. Mindstreams cognitive function index scores (means and SDs) for low and moderate fitness groups

INDEX SCORES (COGNITIVE DOMAINS)	LOW FITNESS, PREDICTED PEAK VO_2 >18.5 $ml*kg^{-1}*min^{-1}$ (N = 18)	MODERATE FITNESS, PREDICTED PEAK VO_2 ≤18.5 $ml*kg^{-1}*min^{-1}$ (N = 20)	MANN-WHITNEY	P VALUE	PEAK VO_2 SPEARMAN CORRELATION	P VALUE
Memory	91.35 (15.01)	98.35 (15.84)	123.00	0.145	0.27	0.11
Attention	94.79 (24.20)	107.70 (5.76)	102.00	0.036	0.37	0.02
Visual spatial	96.01 (17.05)	101.97 (18.71)	137.00	0.301	0.14	0.4
Executive function	99.12 (13.93)	105.34 (10.73)	116.5	0.150	0.39	0.02
Global cognitive score	94.77 (14.78)	103.34 (9.34)	97.00	0.04	0.38	0.02

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active, although their level of physical activity was relatively low (Baecke *et al.*, 1982). One possible interpretation is that at such an old age, even a small challenge (physical activity) can be sufficient to trigger changes in the cardiovascular system, which mediates cognitive functioning (Colcombe *et al.*, 2004). Of note is the fact that we did not find an association between physical activity and cognition, consistent with previous studies suggesting that physical fitness and not physical activity is related to cognition (Etnier *et al.*, 2003; Netz *et al.*, 2009). One possible explanation for this lack of association may be the limited range of scores obtained in the physical activity questionnaire. However, this also reflects the zero score on the occupation index of physical activity, since most participants were retirees as expected at this older age. In addition, the methodological limitation of a self-report measurement may explain these findings.

Apart from the Global Cognitive Score, significant differences in the level of attention between the two fitness groups were also observed. Attention in the present study was evaluated by means of a combination of choice reaction time measurements. It should be emphasized that the high variability in reaction time scores in the low functioning group found in the present study is not uncommon (Der and Deary, 2006). These differences on attention conform to the findings of a recent review reporting the effects of increased cardiorespiratory fitness on cognitive speed and auditory and visual attention, in particular (Angevaren *et al.*, 2008). The significant relationship between fitness and executive functions (Table 4) are in line with a previous review (Colcombe and Kramer, 2003) and with recent studies emphasizing the beneficial effect of exercise and fitness predominantly on executive functions (Hillman *et al.*, 2006; Themanson *et al.*, 2006). The differences between the two fitness groups on executive functions were not significant; however, it is not unlikely that significant differences may be found in a larger sample.

Although there is agreement that executive function refers to the ability to plan and perform goal-directed activities (Spreen and Strauss, 1998), and that it involves planning, scheduling, working memory, interference control and task coordination, it has also been proposed that it is closely linked to the ability to focus on a given task necessitating attention (Spreen and Strauss, 1998). As a result, Barnes *et al.* (2003), in their longitudinal study on cardiorespiratory fitness and cognitive function, integrated both attention and executive functions into one category. Thus, the classification of these cognitive functions is not uniform in the literature.

It is clear that the tasks and task components proposed for measuring cognitive processes can only rarely be neatly and orthogonally arranged into one category (Colcombe and Kramer, 2003). Consequently, there is a great deal of variability in classifying cognitive tasks into categories, as demonstrated in recent reviews examining the same type of studies and/or cognitive tasks (Colcombe and Kramer, 2003; Angevaren *et al.*, 2008). It should be noted that the methodology used in these reviews was not uniform in that they compared different population groups evaluated by the use of various cognitive tasks. Our study, therefore, has the clear advantage of using a uniform computerized battery assessing multiple cognitive domains within a specific population.

Our study has a number of limitations. The estimated (predicted) peak VO_2 is not as precise as the measured VO_2. While it is accepted that the estimated peak VO_2 provides a reasonably accurate reflection of an individual's fitness at a lower cost and reduced risk (ACSM, 2006a) and is thus widely used, the precision of these estimates in the older study cohort has not been adequately determined. The error in estimating exercise capacity from prediction equations is more significant in advanced-age adults with chronic diseases than in young individuals (ACSM, 2006b). Thus, even if gold standards for adults aged 77.5 years (the mean age of our study participants) were available, the discrepancy between the estimated scores and the actual measured score is expected to be larger than in young adults. On the other hand, while this error may result in the spurious elevation of the estimated peak VO_2 (ACSM, 2006b), the estimated scores in the present study were so low that it is questionable whether the real scores were much lower than these. Further data providing actual VO_2 in very old subjects with chronic diseases will define the gold standard for VO_2 in this population. Since no such data were available at the time our study was conducted, we had to rely on estimated peak VO_2 based on data from younger subjects.

In addition, although this study is innovative in assessing aerobic fitness at a more advanced age than previously reported, the risk involved in a maximal stress test (HRmax) and an emphasis on the safety of the subjects limited eligibility, raising the possibility of selection bias and thus questioning the external validity of the study. On the other hand, it is quite likely that any study assessing aerobic fitness at such an advanced age will face similar limitations. It is therefore not surprising that the published norms at age 60+ are based on a much small number of individuals compared to younger ages (ACSM, 2006a).

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Another limitation of our observational study is that the differences demonstrated in cognitive function between the moderate and lower fitness groups do not necessarily indicate a causal relationship between physical fitness and cognition. It is known that the adoption of exercise as a lifestyle is related to a higher level of education and socioeconomic status, both associated with better cognitive function (Etnier and Landers, 1997). However, participants in our study, both in the moderate as well as the low fitness groups, represent subjects of the same relatively high socioeconomic class and education level. Further, the difference found between the two groups with regard to antihypertensive medications does not seem to be related to cognitive function. On the other hand, the differences between groups in IADL do seem to be related to cognitive function. That is, the moderately fit participants seemed to function better than those who are less fit, in addition to their superior cognitive function. This is not surprising, as instrumental activities of daily living, such as handling finances or planning and preparing meals, require cognitive skills. It is clear that these differences between the groups limit the findings of our study.

In conclusion, this pilot study involving relatively healthy residents of a sheltered housing facility demonstrates a positive association between physical fitness and multidomain cognitive function in a group of subjects older than those previously studied. This suggests that the maintenance of higher levels of cardiovascular fitness may be beneficial to cognitive function even at an advanced age in this population group. An adequately powered randomized controlled trial involving a more heterogenic population of community dwelling older subjects should be performed to further evaluate this hypothesis.

Conflict of interest

None.

Description of authors' roles

YN designed the study, supervised the physical fitness data collection, performed the statistical analyses, and wrote the paper. TD designed the study, obtained Ethics Committee approval, performed medical evaluations of the subjects and wrote the paper. EA coordinated the collection of data, formulated the statistical design and interpreted the data. YZ designed the study, coordinated the collection of data, and interpreted the data. RA coordinated the collection of data, and interpreted the data.

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