Aerobic capacity and cognitive performance in a cross-sectional aging study

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ABSTRACT

VAN BOXTIEL, M. P. J., F. G. W. C. PAAS, P. J. HOUX, J. J. ADAM, J. C. TEEKEN, and J. JOLLES Aerobic capacity and cognitive performance in a cross-sectional aging study. Med. Sci. Sports Exerc. Vol. 29, No. 10, pp. 1357–1365, 1997. In a population unselected for aerobic fitness status, aerobic fitness (VO2max) and its interaction with age were used to predict performance on several cognitive measures known to be affected by chronological age. It was hypothesized that, in particular, cognitively demanding tasks would be sensitive to aerobic capacity. Healthy subjects between 24 and 76 yr of age (N = 132) were recruited from a larger study into determinants of cognitive aging (Maastricht Aging Study—MAAS). All participants took part in a submaximal bicycle ergometer protocol and an extensive neurocognitive examination, including tests of intelligence, verbal memory, and simple and complex cognitive speed. Participants engaged more hours a week in aerobic sports and felt healthier than the nonparticipants of the same age did. No group differences were found in the basic anthropometric characteristics height, weight, and BMI. Two of four subtasks that reflect complex cognitive speed (Stroop color/word interference and Concept Shifting Test) showed main and interaction effects with age of aerobic capacity in a hierarchical regression analysis, accounting for up to 5% of variance in parameter score after correction for age, sex, and intelligence main effects. These findings fit well within a moderator model of aerobic fitness in cognitive aging. They add to the notion that aerobic fitness may selectively and age-dependently act on cognitive processes, in particular those that require relatively large attentional resources.

AGING, AEROBIC FITNESS, COGNITIVE FUNCTION, HEALTHY POPULATION STUDY

It has been convincingly demonstrated that the aging process is accompanied by a deterioration of cognitive functions, such as memory, attention, reaction time, and speed of information processing (23,32,37). Also, differences in cognitive performance within groups of individuals of the same age tend to increase as a function of chronological age (29). Age-extrinsic factors such as physical fitness may play a role in explaining the increase with age in variability of cognitive performance within birth cohorts (17,18,30).

The most important functional aspect of physical fitness is the cardiorespiratory component, known as the aerobic capacity (VO2max), which is defined as the oxygen uptake capacity of the body during maximal physical exercise (13,24). Two basic mechanisms have been suggested to explain the effect of aerobic fitness on cognitive processes, namely, the cerebral circulation hypothesis (induction of regional cerebral blood flow, also known as the oxygen hypothesis) (35) and the neurotrophic stimulation hypothesis, which predicts a beneficial effect of neuromuscular activity on higher brain centers (42), or a combination of both (neural efficiency hypothesis). Experimental evidence for either mechanism in humans is, however, largely circumstantial (for review, see (7)).

The positive relation between physical fitness and cognitive performance is not consistent for specific cognitive domains (6), with the exception of performance in timed task paradigms, where differences between very fit and relatively unfit elderly subjects have been demonstrated repeatedly (43). Intervention studies that employed exercise programs to improve aerobic capacity to test the effect of this manipulation on cognitive performance have shown mixed results (5). Dustman et al. (11) found improvement in a group of 55 to 70-yr-old sedentary subjects after an aerobic training program of 4 months on the critical flicker fusion threshold (CFF), digit symbol substitution test (DSST), simple reaction time and Stroop interference, but did not use a nonexercise control group. Other controlled longitudinal community studies of middle-aged subjects (3) and healthy elderly subjects (12,27,31) found no beneficial effect of aerobic training.

A recent study using a 12-month aerobic intervention program in a group of 87 sedentary older adults found no improvement in cognitive task performance associated with the increase in VO2max compared with a nonexercising control group (16). In contrast, Riikli and Edwards (34) reported a decrease in reaction time in older women between 57 and 85 yr of age after a 3-yr exercise program compared with inactive controls. They suggest that the duration of the intervention may be a critical factor in
establishing a beneficial effect of aerobic training on brain function.

A common design in cross-sectional studies to test the effect of physical fitness on cognitive processes is to randomize discrete age cohorts in different subgroups on the basis of their reported level of physical activity (8,33,40) because aerobic capacity is determined in part by regular participation in vigorous physical activity (24). However, the relation between self-reports of physical activity and measures of cardiorespiratory fitness is weak, and many factors (e.g., genetic constitution or inaccuracy of recall) may contribute to the error variance (24). Apart from the potential subjective bias in activity classification based on self-report, one can argue that selection of highly active or fit subjects neglects other personal background characteristics that may confound the effect of activity on cognition, such as mood, life style, motivational drive, or educational level (41,44).

No clear conclusion can be drawn from earlier studies about what can be expected from the cognitive effect of aerobic fitness in a normal aging population. We therefore studied aerobic capacity as a potential predictor of performance in different cognitive task paradigms. A healthy population sample, aged between 24 and 76 yr, was recruited from a larger group of participants in a cognitive aging study, independent of their aerobic capacity status. This procedure enabled a comparison between the participating and nonparticipating groups on several background characteristics and thereby some evaluation of the potential effect of the inclusion procedure on study outcome. We hypothesized that after removal of the effects of age, sex, and intelligence, some additional variance in cognitive performance could be explained by aerobic capacity or the age by aerobic capacity interaction term. The latter expresses the age dependency of the relation between aerobic capacity and cognition. We expected these effects to be most prominent in tasks that require some form of effortful process-

ing, as performance tasks in this category have most consistently shown activity or aerobic capacity effects (7).

**Method**

**Subjects.** The study program was part of a larger cross-sectional study into the determinants of cognitive aging (Maastricht Aging Study, MAAS (23)). Subjects in MAAS were randomly drawn from a register of family practices in the region of Maastricht, The Netherlands (28), stratified for age (12 discontinuous age groups of 25 ± 1 yr, 30 ± 1 yr, . . . , 80 ± 1 yr) and sex. The sample register contains all relevant past and present health problems of all registered patients. Subjects from the register were not eligible for the MAAS study if they had specific morbidity that could be related to brain health (18): cerebrovascular disease, chronic neurological pathology (e.g., dementia, epilepsy, and parkinsonism), mental retardation, or psychotic drug use. All 471 participants in the first panel study of MAAS took part in an extensive neuropsychological test program lasting 3 h. All 245 subjects in the six discrete age groups of 25 ± 1 yr, 35 ± 1 yr, . . . , 75 ± 1 yr were invited to take part in an additional fitness test session. Of this group, 55 subjects did not want to participate. In the remaining group 30 subjects had some degree of cardiovascular morbidity (e.g., angina pectoris, prior myocardial infarction, cardiac insufficiency, or arrhythmia) and 22 subjects had other medical conditions (in particular pulmonary and musculoskeletal morbidity) that resulted in their exclusion. Finally, strict criteria were used to control for a homogenous distribution of IQ within the age groups: six subjects with extreme IQ scores (five below 90 and one above 140) were not included in the study group, resulting in a total group of 132 subjects. Sociodemographic and anthropometric characteristics of the study sample are presented in Table 1.
Test procedure. The additional fitness protocol was administered within 3 wk after the neuropsychological test session. On this occasion additional anthropometric measurements were made and \( \dot{V}O_{2\text{max}} \) was determined in a submaximal ergometer protocol (see below). All tests were administered under medical surveillance and informed consent in writing was obtained from all participants. As part of MAAS all participants filled out an extensive questionnaire pertaining to sociodemographic characteristics and physical and mental health. Subjects were asked to rate in hours their average weekly participation in aerobic sports, for example, jogging, swimming, and racket sports.

Physical Fitness Measurements

Anthropometry. Body height and weight were measured to the nearest centimeter and kilogram. The method of Durnin and Womersley (10) was employed to calculate the fat-free body mass from the body weight and the biceps and triceps skinfold thickness on the left arm.

Submaximal cycle ergometer test. Maximal aerobic capacity (\( \dot{V}O_{2\text{max}} \)) was estimated in a submaximal endurance protocol (38), to maximize compliance to the study while keeping health hazards for some untrained individuals in the sample at an acceptable level. Subjects were instructed to maintain a constant cycling rate of 50 rotations per minute on a cycle ergometer (ERICH JAEGER ER800). Heart rate (HR) was monitored using a standard chest lead connected to a digital pulse transmitter (POLAR Sporttester PE3000, Polar Electro, Kempele, Finland). A wristwatch-type receiver on the arm of the subject displayed the on-line HR. For each subject the HR at 70% of maximal aerobic capacity was estimated using the formula: \( HR_{70\%} = 0.7 * (220 \cdot \text{age [years]}) \), in beats-per-minute (BPM). The initial workload of the cycle test was 25 W. Workload was increased every 2 min in 25-W steps until HR was at or above the target HR\(_{70\%}\). The subject had to maintain this final workload (\( W_{\text{max}} \)) for at least another 2 min to reach a steady-state HR (\( HR_{ss} \)). For male subjects under 35 yr the protocol was different. The initial workload was 50 W and increased in 50-W steps every 2 min until HR was between 60 and 70% of the estimated maximal HR. Then the workload was increased every 2 min in 25-W steps until the 70% limit was reached. Again, \( HR_{ss} \) was recorded after at least 2 min of cycling. The average duration of the endurance protocol was 8 min.

\( \dot{V}O_{2\text{max}} \) was calculated for men and women differently, using the following regression equations (age in years, HR in BPM, \( \dot{V}O_{2\text{max}} \) in L \( \times \) min\(^{-1} \)) (1,38):

Men:

\[
\dot{V}O_{2\text{max}} = 0.348 \cdot X - 0.035 \cdot \text{age} + 3.011 \left( \frac{\text{where } X = (174.2 - W_{\text{ss}} + 4.020)(103.2 - HR_{ss}) - 6.299}{\text{}} \right)
\]

Women:

\[
\dot{V}O_{2\text{max}} = 0.302 \cdot X - 0.019 \cdot \text{age} + 1.593 \left( \frac{\text{where } X = (163.8 - W_{\text{ss}} + 3.780)(104.4 - HR_{ss}) - 7.514}{\text{}} \right)
\]

The endurance protocol was validated in a healthy population aged between 20 and 70 yr and the outcome can be considered as a safe and reliable measure of cardiovascular fitness that correlated (0.94) with direct measurements of \( \dot{V}O_{2\text{max}} \) (38). To compensate for the systematic decrease in fat-free mass with age (22), and because body fat can be regarded as a metabolically relatively inert tissue, \( \dot{V}O_{2\text{max}} \) was corrected for weight and percentage body fat using the fat-free mass (ffm). This procedure yielded a \( \dot{V}O_{2\text{max}} \) in mL \( \times \) min\(^{-1} \) \( \times \) kg-ffm\(^{-1} \).

Cognitive Assessment

A set of neuropsychological tests was used to tap the cognitive domains of memory and memory-related functions, simple psychomotor speed, and information processing speed. These tests were selected for their robustness in detecting age effects in normal aging populations (23). A short description of each test is given below.

**General intelligence.** The Groningen Intelligence Test (GIT) is the commonly used Dutch estimate of formal IQ (26).

**Memory.** Visual verbal learning test (VVT). This test evaluates the ability to acquire and retrieve new verbal information (4). A fixed sequence of 15 frequently used monosyllabic words was presented on a computer screen. Subjects were asked to reproduce the words after each of five subsequent trials. The total of correctly reproduced words in five trials was recorded (immediate recall), together with the number of correctly reproduced words 20 min after the last trial (delayed recall).

**Verbal fluency.** The results of this test reflect the level of organization in memory of clusters of meaningful related words. The number of animal names correctly produced in 60 s was recorded (26).

**Simple psychomotor speed.** Continuous tapping. The continuous tapping task required the subject to press the button of an electronic counting device at maximum frequency for 30 s, using the index finger of the dominant hand. The total tap count was recorded as index of peripheral motor speed ((25) pp. 672–673).

**Information processing speed.** Concept Shifting Test (CST). This test evaluates behavioral planning and evaluation (20). The subject’s ability to alternate two psychological concepts during task performance is measured, i.e., cancellation of numbers and letters in the correct order. A test sheet contains 16 small diameter circles (Ø 15 mm) arranged in a larger circle (Ø 16 cm). The digit version (Part A) presents the numbers 1 to 16 in random order in the circles, a letter version (Part B)
depicts random letters, and finally a number/letter version (Part C) alternates the numbers 1 to 8 and letters A to H. The subject is instructed to cross out the circles in correct order as fast as possible without making errors. The outcome is the time required to complete each task separately.

**Motor Choice Reaction Test (MCRT).** A computer test was used that evaluates reaction times as a function of the complexity of task requirements (17). It consists of a simple and a complex choice reaction subtask. In the simple task the subject is required to push a central button on a switch panel with the index finger of the dominant hand. When a white button 5 cm above the central button lights up, the subject is instructed to push this button and then to return the finger to the central button. The complex task introduces a decision component: one of three adjacent white buttons (that are positioned on a 90° arc: 5 cm above the central red button) may light up in a random order, again requiring the subject to push the button that is lit as fast as possible. Target parameters are median initiation time (decision making and motor preparation) and actual movement time, calculated after 30 trials for both subtasks.

**Letter Digit Substitution Test (LDST).** This paper-and-pencil test is a modification of the Symbol Digit Modalities Test and measures fundamental processing speed (SDMT (39)). The subject is instructed to copy numbers in cells indexed by a letter. The letter refers to nine letter/number combinations at the top of the form. The number of correctly copied corresponding numbers in 90 s is recorded.

**Stroop Color Word Test (SCWT).** This perceptual interference test consists of three subtasks. Each subtask consists of a test sheet containing four rows of ten columns of color names or colored spots. The test measures the speed at which color names are read (subtask I) and the speed at which color spots are named (subtask II). Subtask III involves color names again, but the printing of the word is different from the color name. The speed at which the color of the printing ink of the words is named is recorded. The time to complete this subtask reflects the ability to inhibit overlearned responses and shows robust effects of chronological age (19).

In particular, the complex subtask of the MCRT, the letter/digit version (Part C) of the CST and Stroop subtask III can be regarded as being on the effortful extreme of the effortless versus automatic cognitive processing demand continuum (7).

**Statistical Analysis**

Differences between participating and nonparticipating groups on several measures of mood and physical activity were studied using ANCOVA, with age and sex as covariates. All cognitive outcome measures were tested for age, sex, and age by sex interaction effects with ANCOVA after correction for differences in general intelligence. The effects of aerobic capacity (VO₂max) and VO₂max by age interaction on cognitive performance were tested in several multiple hierarchical regression models in which age, sex, and IQ were entered together in the first step of the analysis. In this way the effects of aerobic capacity on residual scores of the cognitive parameters were tested. Goodness-of-fit of the models was described in terms of variance explained by the variables in the equation, expressed as (adjusted) R². The increase in variance explained by the model was tested for significance after each step. Residual scores were screened for systematic trends, but these were not identified in the fitted models.

**RESULTS**

Comparison of participating and nonparticipating groups showed that the participating subjects were more active in playing aerobic sports than the subjects who did not participate (2.0 vs 0.9 h wk⁻¹, F(1,241) = 7.77, P = 0.006) and rated themselves higher on the general health dimension (4.0 vs 3.6, F(1,239) = 7.94, P = 0.005). No group differences were observed at or below the P = 0.05 level between nonparticipating and participating subjects for years of formal education (11.0 vs 11.3 yr, F(1,241) = 1.81), or general intelligence (GIT-IQ 113.2 vs 112.0, F(1,241) < 1). Furthermore, the anthropometric measures body height (1.68 vs 1.71 m), weight (72.9 vs 74.4 kg), and body mass index (BMI; 25.6 vs 25.3 kg m⁻²) were not differentially distributed in the two groups (F(1,238) < 1). Table 1 displays the mean anthropometric variables by age group and sex of the participating group. The results, by age group and sex, of the neuropsychological tests are presented in Table 2.

Women and older subjects had a lower aerobic capacity, both corrected and uncorrected for body composition, than did men and younger subjects (Table 3). An age by sex interaction effect was found only for the aerobic capacity uncorrected for body fat, indicating lower values of VO₂max with increasing age in men, when compared with women. No effect of age was observed on the general ability measure GIT-IQ, indicating a homogeneous distribution of IQ after the exclusion of six subjects with extreme values. The IQ scores of the women tended to be somewhat lower than those of the men. All cognitive measures were more or less strongly age and IQ sensitive, showing lower average performance values for older age groups and lower IQ scores. Men outperformed women on movement times of the simple and choice reaction time tasks (SRT and CRT, respectively), on the concept shifting test (CST) subtasks letter and digit/letter cancellation, and on finger tapping speed. However, the opposite was true for the immediate and delayed recall of learned words (VLT), where women had higher scores. Age interacted with sex on CST digit cancellation, where
TABLE 2. Mean ± SD cognitive outcome measures, by age group and sex (N = 132).

<table>
<thead>
<tr>
<th>Age Group (yr)</th>
<th>IQ</th>
<th>VVLT: recall total</th>
<th>VVLT: delayed recall</th>
<th>SRT: initiation (ms)</th>
<th>SRT: movement (ms)</th>
<th>CRT: initiation (ms)</th>
<th>CRT: movement (ms)</th>
<th>Stransk: I. words (s)</th>
<th>Stransk: II. colors (s)</th>
<th>Stransk: III. color/words (s)</th>
<th>CST: numbers (s)</th>
<th>CST: letters (s)</th>
<th>Tapping</th>
<th>Fluency</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 ± 1</td>
<td>110.0 (11.0)</td>
<td>47.3 (10.3)</td>
<td>10.4 (2.7)</td>
<td>319.6 (48.3)</td>
<td>104.2 (22.5)</td>
<td>349.3 (33.2)</td>
<td>110.4 (23.8)</td>
<td>41.6 (6.2)</td>
<td>55.3 (8.2)</td>
<td>83.1 (14.3)</td>
<td>15.8 (3.6)</td>
<td>21.7 (8.1)</td>
<td>203.6 (25.4)</td>
<td>23.6 (6.6)</td>
</tr>
<tr>
<td>35 ± 1</td>
<td>117.3 (10.2)</td>
<td>49.4 (3.4)</td>
<td>10.2 (2.9)</td>
<td>311.0 (34.0)</td>
<td>141.1 (23.8)</td>
<td>357.4 (37.4)</td>
<td>120.7 (27.4)</td>
<td>43.6 (6.7)</td>
<td>55.4 (8.4)</td>
<td>81.8 (12.6)</td>
<td>18.3 (4.9)</td>
<td>22.2 (6.3)</td>
<td>237.6 (22.2)</td>
<td>24.3 (6.6)</td>
</tr>
<tr>
<td>45 ± 1</td>
<td>115.3 (13.1)</td>
<td>44.3 (6.4)</td>
<td>9.5 (2.4)</td>
<td>326.4 (57.6)</td>
<td>121.8 (27.2)</td>
<td>302.7 (27.2)</td>
<td>123.6 (27.4)</td>
<td>45.5 (8.2)</td>
<td>55.2 (8.5)</td>
<td>80.0 (18.5)</td>
<td>18.4 (4.1)</td>
<td>22.5 (6.3)</td>
<td>187.9 (28.9)</td>
<td>23.1 (4.6)</td>
</tr>
<tr>
<td>55 ± 1</td>
<td>113.4 (13.3)</td>
<td>45.0 (6.8)</td>
<td>8.6 (2.4)</td>
<td>341.5 (55.5)</td>
<td>134.1 (36.9)</td>
<td>367.2 (36.8)</td>
<td>137.0 (36.9)</td>
<td>47.3 (6.5)</td>
<td>60.8 (9.0)</td>
<td>103.5 (18.3)</td>
<td>21.4 (3.7)</td>
<td>27.7 (6.3)</td>
<td>176.0 (26.1)</td>
<td>21.9 (4.6)</td>
</tr>
<tr>
<td>65 ± 1</td>
<td>113.3 (&lt;1)</td>
<td>37.5 (&lt;1)</td>
<td>8.8 (&lt;1)</td>
<td>150.0 (&lt;1)</td>
<td>154.5 (&lt;1)</td>
<td>360.0 (&lt;1)</td>
<td>147.4 (&lt;1)</td>
<td>46.9 (&lt;1)</td>
<td>62.2 (&lt;1)</td>
<td>104.3 (&lt;1)</td>
<td>23.9 (&lt;1)</td>
<td>29.4 (&lt;1)</td>
<td>171.6 (&lt;1)</td>
<td>22.9 (&lt;1)</td>
</tr>
<tr>
<td>75 ± 1</td>
<td>119.5 (11.0)</td>
<td>34.9 (&lt;1)</td>
<td>7.7 (&lt;1)</td>
<td>135.4 (38.3)</td>
<td>134.5 (39.3)</td>
<td>363.0 (37.3)</td>
<td>146.8 (37.3)</td>
<td>46.6 (&lt;1)</td>
<td>54.0 (&lt;1)</td>
<td>127.5 (&lt;1)</td>
<td>24.6 (&lt;1)</td>
<td>29.2 (&lt;1)</td>
<td>146.4 (&lt;1)</td>
<td>22.9 (&lt;1)</td>
</tr>
<tr>
<td>M</td>
<td>116.2 (10.8)</td>
<td>42.2 (&lt;1)</td>
<td>8.9 (10.5)</td>
<td>323.5 (39.3)</td>
<td>154.0 (39.3)</td>
<td>363.0 (37.3)</td>
<td>146.8 (37.3)</td>
<td>46.6 (&lt;1)</td>
<td>54.0 (&lt;1)</td>
<td>127.5 (39.3)</td>
<td>24.6 (&lt;1)</td>
<td>29.2 (&lt;1)</td>
<td>146.4 (&lt;1)</td>
<td>22.9 (&lt;1)</td>
</tr>
<tr>
<td>F</td>
<td>111.7 (10.8)</td>
<td>46.6 (&lt;1)</td>
<td>10.3 (10.5)</td>
<td>339.5 (39.3)</td>
<td>142.0 (39.3)</td>
<td>363.0 (37.3)</td>
<td>146.8 (37.3)</td>
<td>46.6 (&lt;1)</td>
<td>54.0 (&lt;1)</td>
<td>127.5 (39.3)</td>
<td>24.6 (&lt;1)</td>
<td>29.2 (&lt;1)</td>
<td>146.4 (&lt;1)</td>
<td>22.9 (&lt;1)</td>
</tr>
</tbody>
</table>

1. Groningen Intelligence Test (SIT) — IQ; VVLT, Visual Verbal Learning Test; SRT, Simple Reaction Time; CRT, Complex Reaction Time; CST, Concept Shifting Test; LDST, Letter Digit Substitution Test.

the time required to complete the task tended to increase more with age in women than in men.

Before the regression models were fitted, zero-order correlations were computed between independent and dependent variables in the subsequent analysis (Table 4).

All cognitive measures (except CRT movement time) were correlated with chronological age and intelligence level in the expected direction, lower performance being associated with lower IQ levels or higher age. VO2max was strongly correlated with cognitive measures, except

TABLE 3. Results of repeated ANCOVA on aerobic capacity and cognitive outcome: tests for main and interaction effects of age and sex, with IQ as covariate (N = 132).

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex F(6,119)=</th>
<th>Sex F(1,119)=</th>
<th>Age×Sex F(5,119)=</th>
<th>IQ F(1,119)=</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2max (mL/min·kg⁻¹)</td>
<td>47.99***</td>
<td>113.89***</td>
<td>3.03*</td>
<td>1.49</td>
</tr>
<tr>
<td>VO2max (mL/min·kg⁻¹·fmin⁻¹)</td>
<td>34.41***</td>
<td>50.14***</td>
<td>1.79</td>
<td>1.25</td>
</tr>
<tr>
<td>GTQ</td>
<td>1.69</td>
<td>6.18</td>
<td>&lt;1</td>
<td>4.20</td>
</tr>
<tr>
<td>VVLT: recall total</td>
<td>9.77**</td>
<td>17.86**</td>
<td>1.11</td>
<td>4.36*</td>
</tr>
<tr>
<td>VVLT: delayed recall</td>
<td>5.99***</td>
<td>13.23***</td>
<td>&lt;1</td>
<td>23.53***</td>
</tr>
<tr>
<td>SRT: initiation time</td>
<td>5.38***</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>5.72*</td>
</tr>
<tr>
<td>SRT: movement time</td>
<td>8.63***</td>
<td>16.79***</td>
<td>&lt;1</td>
<td>12.04***</td>
</tr>
<tr>
<td>CRT: initiation time</td>
<td>5.74***</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>14.73***</td>
</tr>
<tr>
<td>CRT: movement time</td>
<td>9.21***</td>
<td>19.93***</td>
<td>1.74</td>
<td>5.11</td>
</tr>
<tr>
<td>Stransk: I. word naming</td>
<td>5.83***</td>
<td>1.70</td>
<td>2.38*</td>
<td>7.40*</td>
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<tr>
<td>Stransk: II. color naming</td>
<td>4.06**</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>13.73***</td>
</tr>
<tr>
<td>CST: number cancellation</td>
<td>13.80***</td>
<td>1.70</td>
<td>2.38*</td>
<td>7.40*</td>
</tr>
<tr>
<td>CST: color cancellation</td>
<td>6.81***</td>
<td>7.22*</td>
<td>&lt;1</td>
<td>13.73***</td>
</tr>
<tr>
<td>CST: number/letter cancellation</td>
<td>23.67***</td>
<td>5.08*</td>
<td>2.14</td>
<td>21.62***</td>
</tr>
<tr>
<td>LDST</td>
<td>10.72***</td>
<td>1.05</td>
<td>2.22</td>
<td>13.31***</td>
</tr>
<tr>
<td>Tapping</td>
<td>16.96***</td>
<td>2.68</td>
<td>1.46</td>
<td>5.16</td>
</tr>
</tbody>
</table>

VO2max estimated maximal aerobic capacity (mL/min·kg⁻¹); VO2max.fmin⁻¹ estimated maximal aerobic capacity, corrected for body fat (%). IQ, Groningen Intelligence Test — GTQ, VVLT, Visual Verbal Learning Test; SRT, Simple Reaction Time; CRT, Complex Reaction Time; CST, Concept Shifting Test; LDST, Letter Digit Substitution Test.

1 Result of ANOVA with only age and sex as independent variables.

** P = 0.05; *** P = 0.01; **** P = 0.001.
in word fluency. This may be in part a result of the intermediate factor age, which was associated with both cognitive and physical performance measures. Higher levels of the age by aerobic capacity interaction term were associated with higher VVLT recall total scores and faster CRT initiation, Stroop III performance, and CST digit/letter cancellation, indicating that the effect of aerobic capacity was dependent on the subject's age.

In the final phase of the analysis, hierarchical regression models were fitted for all cognitive measures to test the predictive value of VO\textsubscript{max} (in step 2) and of the VO\textsubscript{2max} by age interaction term (in step 3), after linear correction for main effects of age, sex, and IQ in step 1 (Table 5). By far the largest proportion of the increase in R\textsuperscript{2} was observed in step 1 for all cognitive measures, which confirms the effects already present in the ANCOVA's. When VO\textsubscript{2max} was entered, there was an increase in R\textsuperscript{2} of 1% and 2% for the interaction version (III) of the Stroop and concept letter cancellation, respectively. Again, R\textsuperscript{2} increased significantly for both tests on introduction of the interaction term VO\textsubscript{2max} by age in step 3, by 2% and 5%, respectively. In addition, R\textsuperscript{2} of the movement time of the choice reaction time task increased by 2% in step 3. All other outcome measures remained unaffected by the aerobic capacity measures in the final two steps of the analysis.

### Table 5. Results of multiple hierarchical regression analysis: Age, Sex and GRT-IQ were entered in Step 1 of the analysis, VO\textsubscript{2max} and Age by VO\textsubscript{2max} interaction term in Step 2 and 3, respectively. Displayed are standardized regression coefficients (Betas) in the final model, R\textsuperscript{2} (equivalent to the proportion of explained variance) and significance of R\textsuperscript{2} change after each step.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age</th>
<th>Sex*</th>
<th>IQ</th>
<th>VO\textsubscript{2max}</th>
<th>Age×VO\textsubscript{2max}</th>
<th>R\textsuperscript{2} after step 1</th>
<th>R\textsuperscript{2} after step 2</th>
<th>R\textsuperscript{2} after step 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>VVLT: recall total</td>
<td>-0.37</td>
<td>0.37</td>
<td>0.26</td>
<td>0.14</td>
<td>0.05</td>
<td>0.29**</td>
<td>0.29</td>
<td>0.30</td>
</tr>
<tr>
<td>VVLT: delayed recall</td>
<td>-0.22</td>
<td>0.22</td>
<td>0.26</td>
<td>0.19</td>
<td>0.03</td>
<td>0.21**</td>
<td>0.22</td>
<td>0.22</td>
</tr>
<tr>
<td>CRT: initiation time</td>
<td>0.25</td>
<td>0.25</td>
<td>0.29</td>
<td>0.17</td>
<td>0.08</td>
<td>0.32***</td>
<td>0.33</td>
<td>0.33</td>
</tr>
<tr>
<td>CRT: movement time</td>
<td>0.23</td>
<td>-0.08</td>
<td>-0.31</td>
<td>-0.17</td>
<td>-0.06</td>
<td>0.17***</td>
<td>0.17</td>
<td>0.17</td>
</tr>
<tr>
<td>Stroop I: word reading</td>
<td>0.44</td>
<td>0.39</td>
<td>0.39</td>
<td>0.29</td>
<td>0.36</td>
<td>0.23***</td>
<td>0.33</td>
<td>0.33</td>
</tr>
<tr>
<td>Stroop III: word reading</td>
<td>0.30</td>
<td>0.07</td>
<td>0.31</td>
<td>0.14</td>
<td>0.06</td>
<td>0.24**</td>
<td>0.24</td>
<td>0.24</td>
</tr>
<tr>
<td>Stroop III: color naming</td>
<td>0.06</td>
<td>-0.07</td>
<td>-0.37</td>
<td>-0.05</td>
<td>-0.13</td>
<td>0.17***</td>
<td>0.16</td>
<td>0.16</td>
</tr>
<tr>
<td>Stroop III: color/word</td>
<td>0.44</td>
<td>-0.08</td>
<td>-0.42</td>
<td>-0.15</td>
<td>-0.18</td>
<td>0.42***</td>
<td>0.43**</td>
<td>0.46**</td>
</tr>
<tr>
<td>CST: digit cancellation</td>
<td>0.61</td>
<td>-0.04</td>
<td>0.28</td>
<td>0.06</td>
<td>0.16</td>
<td>0.35**</td>
<td>0.35</td>
<td>0.35</td>
</tr>
<tr>
<td>CST: letter cancellation</td>
<td>0.33</td>
<td>0.33</td>
<td>0.28</td>
<td>0.13</td>
<td>0.07</td>
<td>0.29**</td>
<td>0.30</td>
<td>0.30</td>
</tr>
<tr>
<td>CST: digit/letter</td>
<td>0.48</td>
<td>-0.18</td>
<td>0.37</td>
<td>-0.18</td>
<td>-0.23</td>
<td>0.44***</td>
<td>0.45**</td>
<td>0.51***</td>
</tr>
<tr>
<td>LDST</td>
<td>0.47</td>
<td>0.08</td>
<td>0.34</td>
<td>0.02</td>
<td>0.10</td>
<td>0.45**</td>
<td>0.44</td>
<td>0.45</td>
</tr>
<tr>
<td>Tapping</td>
<td>-0.52</td>
<td>0.27</td>
<td>0.25</td>
<td>0.05</td>
<td>0.11</td>
<td>0.38**</td>
<td>0.38</td>
<td>0.38</td>
</tr>
</tbody>
</table>

IQ, Stroop Intelligence Test - IQ; VO\textsubscript{2max}, estimated maximal aerobic capacity-corrected for body fat (in ml·min\textsuperscript{-1}·kg\textsuperscript{-1}·fat-free mass); VVLT, Visual Verbal Learning Test; SRT, Simple Reaction Time; CRT, Concept Shifting Test; LDST, Letter Digit Substitution Test.

* P = 0.05; ** P = 0.01; *** P = 0.001.
AEROBIC CAPACITY, AGING AND COGNITION

DISCUSSION

Our chief aim of this study was to assess the relationship between aerobic capacity (VO$_2$$_{max}$) and cognitive test performance in a healthy, normal aging population, in particular without a priori stratification for the physical fitness level. After evaluation and control for relevant background characteristics, a positive association was found between VO$_2$$_{max}$ and the VO$_2$$_{max}$ by age interaction on the one hand and two measures of information processing speed (Stroop III and CST digit/letter cancellation) on the other. Test outcome related to memory and simple psychomotor speed was relatively unaffected by aerobic capacity, except for an isolated association between CRT movement time and VO$_2$$_{max}$ by age interaction. These findings are evaluated in the light of earlier research.

Study population characteristics. There was no difference between parameters of mood, years of formal education, or general intelligence between the participating and nonparticipating groups. However, differences in perceived general health and hours per week spent on aerobic activities between participating and nonparticipating groups suggest that some selection bias may have been present, in part owing to the health exclusion criteria that were used. The reason for our strict scrutiny of the health status was to exclude any potential bias resulting from cardiopulmonary pathology on study outcome (e.g., 15) and to prevent any health hazard for participants as the result of the fitness protocol. It cannot be ruled out that as levels of aerobic activity and functional health may be directly related to actual aerobic capacity (9, 24), this bias may have resulted in a “restriction of range” of VO$_2$$_{max}$ in the study group, thereby attenuating the effects of VO$_2$$_{max}$ on cognitive outcome. This is a well-known methodological problem in developmental research where the ultimate goal is to obtain unbiased estimates of change (14). Furthermore, although there were no differences in overall IQ between participating and nonparticipating groups (112.0 vs 113.2, respectively), the averages were in the high-normal range (26). A higher level of IQ has been shown to protect against age-related memory performance deficits (21). As all measures of cognitive test performance were positively related to IQ, it cannot be ruled out that the study population was less likely to benefit from a higher aerobic capacity. Higher IQ and the aforementioned “restriction of range” phenomenon therefore may have attenuated the observed effects of aerobic capacity.

The values for VO$_2$$_{max}$, uncorrected for body fat, that were obtained in this study (in mL x min$^{-1}$ x kg$^{-1}$ body weight) were somewhat higher than those of the Siconolfi et al. validation study (38), in which a comparable inclusion procedure and approximately the same age groups, balanced for sex, were used. Their averages ranged from 37.2 (SD 7.9) in the 20–29 yr group to 20.6 (SD 6.1) in subjects between 60 and 70 yr. Lower values for VO$_2$$_{max}$ in our study may in part be attributable to a relative under-representation of women.

Speed of information processing and aging. It was recently suggested that cognitively demanding tasks are likely to be sensitive to physical fitness, in particular those tasks where processing speed is the target variable and in tasks of high complexity and low S–R compatibility (6, 7). Both the Stroop task III (interference) and the complex concept shifting task (Part C), which showed effects of aerobic capacity in this study, can be classified as tasks that require effortful cognitive processing. Both task variables, which were combined in a compound score, were also sensitive to habitual physical activity, as measured by questionnaires in a healthy group of older adults (45). Furthermore, the age by fitness interactions found are consistent with the “moderator model” proposed by Stones and Kozma (44). The moderator model predicts an augmentation of fitness effects with age if adequate levels of physical fitness protect the individual against age-related decline in attentional resources. Within a theoretical framework that defines cognitive aging in terms of resource limitation, it is clear that tasks that draw heavily on the central information processing capacity generally show the greatest effects of chronological age (36). Along these lines, but from a developmental perspective, Baltes (2) has argued that when one is “testing the limits” of the cognitive reserve capacity the age-related differences between individuals come to light even more clearly. Additional support for such notions with respect to physical fitness has been found in several other studies that showed an association between complex reaction time (CRT) and physical activity level (42) or CRT and improvement in VO$_2$$_{max}$ after an aerobic training intervention (34). Our results, however, indicated that CRT initiation time, which is known to represent the time needed for stimulus evaluation and response formation, did not covary with aerobic capacity or its interaction with age. Of course, this may in part be the result of procedural differences in the task used in this study compared with those in earlier studies. The absence of an effect of aerobic fitness on digit copying (LDST) is less troublesome to explain; when using a stage model of information processing, the basic sensorimotor speed component in this task is quite substantial and may overshadow the central processing speed component in the overall test outcome parameter.

In summary, aerobic capacity and the aerobic capacity by age interaction explained some of the variance seen in two of four tasks that measure speed of information processing. These findings add to the notion that aerobic capacity, measured as a continuous
variable in a healthy adult population sample, may act selectively in task paradigms that require cognitive effort. Our findings indicate that aerobic fitness per se is a factor of moderate importance in cognitive aging research. However, we feel that any evidence for the existence of a factor that may prevent or postpone age-related cognitive decline and which is amenable for intervention should be fully explored and also justifies further research that uncovers the underlying mechanism of action in more detail.

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