The relationships among pulmonary function, aerobic fitness, and cognitive functioning in older COPD patients

By: Jennifer Etnier, Rebecca Johnston, Dale Dagenbach, R. Joy Pollard, W. Jack Rejeski, and Michael Berry

Etnier, J.L., Johnston, R., Dagenbach, D., Pollard, R.J., Rejeski, W.J., & Berry, M. (1999). The relationships between pulmonary function, aerobic fitness, and cognitive functioning in older COPD patients. *Chest, 116* (4), 953-960.

Made available courtesy of Elsevier: https://doi.org/10.1378/chest.116.4.953

Abstract:

Study objectives: To study the predictive relationships among age, pulmonary function, aerobic fitness, and cognition in people with COPD. **Design:** Observational study conducted during baseline testing with COPD patients who volunteered to participate in an exercise intervention. **Participants:** Older adults (age, 56 to 80 years) with COPD. **Measurements and results:** Age, depression, education level, aerobic fitness, blood oxygen saturation levels, and pulmonary function were assessed. Participants were randomly assigned to take cognitive tests of (1) fluid intelligence, (2) processing speed and working memory span, or (3) processing speed and inhibition. After controlling for education and depression ($F_{2,57} = 7.43$; $r^2 = 0.21$), performance on the 6-min walk ($F_{1,56} = 15.27$; $r^2 = 0.17$) and age ($F_{1,55} = 7.52$; $r^2 = 0.08$) were significant predictors of fluid intelligence. On the speed-of-processing task, performance on the 6-min walk ($F_{1,30} = 8.17$; $r^2 = 0.20$), maximum voluntary ventilation ($F_{1,29} = 5.81$; $r^2 = 0.16$), and age ($F_{1,28} = 5.26$; $r^2 = 0.10$) were significant predictors. FVC was a significant predictor ($F_{1,25} = 6.37$; $r^2 = 0.18$) of working memory span. The ability to inhibit a response was not significantly predicted by any of the variables assessed. **Conclusions:** In an older COPD sample, age, aerobic fitness, and pulmonary function are predictive of cognitive performance on various tasks. In particular, age and aerobic fitness are predictive of speed of processing, which is a cognitive variable that may itself underlie performance on a majority of cognitive tasks.

Keywords: mental health | mental processes | respiratory mechanics

Article:

Abbreviations: CESD = Center for Epidemiological Studies Depression Scale; GXT = graded exercise test; MEL = Micro Experimental Lab; MVV = maximum voluntary ventilation; REACT = Reconditioning Exercise and COPD Trial; SpO_2 = oxygen saturation of hemoglobin; VE = minute ventilation; VO_2peak = peak oxygen consumption

The age-related decline in the cognitive functioning of healthy adults is a well-documented phenomenon.[1,2] As healthy people advance in age beyond the sixth decade, they typically experience declines in a variety of cognitive functions. However, while these age-related declines are well established, the cause of these declines remains unclear. One hypothesis which has been proposed is that the declines in cognitive functioning are due to a decrease in the transport of oxygen to the cerebral environment.[3] Indirect support for this hypothesis is provided by evidence that older deconditioned individuals have decreased oxygen transport to the brain.[4,5] The hypothesis contends that decreased oxygen transport to the brain results in a decline in cognitive capabilities.

While the impact of advancing age on cognitive functioning has been studied extensively in normal healthy samples, changes in cognitive functioning in older impaired individuals have not been studied as frequently. Because of the proposed link between cognitive functioning and oxygen transport, the study of cognitive functioning capabilities in older individuals with COPD is of particular interest. Arterial oxygen desaturation may develop in these patients as a result of their disease.[6] This decline in arterial oxygen content could subsequently result in a decrease in oxygen transport to the brain. Additionally, this decrease in arterial oxygen content may cause dyspnea during activity, which typically results in an avoidance of activity and facilitates further deconditioning. Thus, older individuals who have COPD may be affected in three ways that are relevant to cognitive functioning. They may experience age-related declines in blood flow, disease-related declines in arterial oxygen content, and both age- and disease-related declines in physical activity. The combination of these three factors makes this population an interesting one to study to glean information about the relationship between aerobic fitness, arterial oxygen content, and cognitive functioning.

There has been research examining the cognitive functioning of COPD patients. This research has typically indicated that COPD individuals experience declines in a number of cognitive functions, such as reaction time,[7,8] memory,[8-10] abstract reasoning skills,[8] and complex visual-motor processes,[11] relative to normal adults. However, while many of these authors looked at the relationship between arterial oxygenation (as assessed with PaO_2) and cognitive performance in these COPD samples, none of these studies looked at the role that aerobic fitness may play in this relationship.

There is one series of studies in which the relationship between aerobic fitness and cognition in a COPD sample was examined,[8,12,13] In the first of these studies, there was not a significant relationship between exercise level attained and any of the cognitive variables once education had been controlled.[8] The sample used in this study was then combined with individuals from the Nocturnal Oxygen Therapy Trial,[12] and a regression analysis was conducted to examine the predictive ability of exercise level on cognitive factors.[13] The results indicated that exercise level was a significant predictor only for the cognitive factor simple motor, which included a tapping task and grip strength. However, the results of these studies must be interpreted with caution because sufficient detail regarding the fitness test was not provided for interpretation of the results.

Therefore, the purpose of the present study is to investigate the relationship between age, pulmonary function, aerobic capacity, and cognitive performance in a sample of COPD patients. It is hypothesized that there will be a negative relationship between age and cognitive performance, while there will be a positive relationship between aerobic fitness and cognitive performance and between measures of pulmonary function and cognitive performance.

MATERIALS AND METHODS

Participants

Participants were 98 individuals who were taking part in the Reconditioning Exercise and COPD Trial (REACT). The REACT study is an 18-month exercise intervention in which all participants complete 3 months of exercise before being randomly assigned to either return to their normal lifestyle or to continue exercising for an additional 15 months. For the purposes of this study, only data from the initial screening visits were examined. Individuals with COPD were recruited from the community through physician referral, pamphlet distribution, and advertisements in local newspapers and on local television stations. To qualify for the study, participants had to be between the ages of 55 and 80 years. Additionally, they had to display an expiratory airflow limitation such that the ratio of FEV_1 to FVC was < 70% and the FEV_1 was > 20% of predicted. This expiratory airflow limitation could not be reversible by medication, with reversibility defined as > 12% and/or 200 mL improvement in the FEV_1 after inhalation of 200 µg of albuterol via metered-dose inhaler using a cylindrical spacer device. Finally, participants also had to report difficulties in performing various activities of daily living due to dyspnea. Individuals were not allowed to participate if they had been involved in a regular exercise or pulmonary rehabilitation program during the preceding 6 months. A complete list of exclusion criteria is given in Table 1. Participants' age, sex, and years of education were recorded by self report. Of the 98 participants, 34 reported that they were not taking any medications, 54 reported taking sympathomimetic bronchodilators, 27 reported taking anticholinergic bronchodilators, 33 reported taking steroidal anti-inflammatory agents, 25 reported taking diuretics, 24 reported taking calcium channel blockers, and < 20 reported taking any of the other categories of medications. Patients were asked to refrain from using inhaled or oral bronchodilators for 3 to 4 h prior to being tested.

Table 1. Exclusion Criteria

Criteria	**Characteristics That Would Result in Exclusion**	**Screening Methods**
Health	Active treatment for cancer; severe congestive heart failure, stroke, peripheral vascular disease, coronary artery disease, major psychiatric disease, severe anemia, liver or renal disease, uncontrolled diabetes or hypertension, orthopedic impairment, blindness, or deafness	History, physical examination, graded exercise test, personal physician
COPD with disability	FEV_1/FVC >70%, FEV_1 <20% of predicted, or absence of reported disability, oxygen desaturation during exercise to <90% at a heart rate <50% of age predicted maximum without supplemental O_2	Pulmonary function test, history, graded exercise test
Ability to comply with exercise interventions	Inability to perform exercise due to physical disability or positive exercise stress test	History, physical examinations, graded exercise test
Alcohol use	Consumption (current or proceeding 2 mo) of >2 drinks/d	History
Inability to complete study	Living >50 miles from center of planning to move	History

Materials

Pulmonary Function Measures: Spirometry and lung volume measurements were performed with a body plethysmograph (MedGraphics model 1085; Medical Graphics Corp; Minneapolis, MN). Spirometry and lung volume measurements were made using the guidelines of the America Thoracic Society.[14,15]

Graded Exercise Test: During all graded exercise tests (GXTs), spirometry and respiratory gas analysis were performed with a cardiopulmonary exercise system (CPX/d; Medical Graphics Corp). During the exercise test, oxygen saturation of hemoglobin (SpO_2) was monitored using a pulse oximeter (Armstrong Medical/BCI International; Waukesha, WI) and was defined as the lowest value that occurred during the test. Peak oxygen consumption (VO_2peak) was recorded in mL/kg/min and was defined as the highest VO_2 that was attained during the GXT. Minute ventilation (VE) was measured in L/min and was defined as the VE at the point that a VO_2peak was attained. All GXTs were conducted on a treadmill using a modified Naughton treadmill protocol[16] and the American College of Sports Medicine termination criteria.[17] Most tests were terminated because of shortness of breath or general fatigue.

Six-minute Walk Test: Participants were asked to walk a measured course for 6 min, attempting to cover as much distance as possible in the given time. Participants walked at a self-selected pace and were advised to decrease their pace or to stop if perceived symptoms became excessive. Just prior to the end of the 6 min, an exercise technician approached the subject and placed a finger probe from the pulse oximeter on the subject. SpO_2 was assessed immediately after the participants stopped walking. No feedback was given during the test.

Depression: Research has indicated that depression may influence performance on a cognitive functioning test.[18] For this reason, the Center for Epidemiological Studies Depression Scale (CESD) was used as a self-administered questionnaire.[19,20] The CESD has been found to be reasonably good at screening to identify the nondepressed.[21] Reliability as a measure of internal consistency of the CESD is 0.85.[19]

Cognitive Tests: A battery of cognitive tests was used because of the interest in examining the differential influence of the physiologic and psychological parameters on tasks that differ in their cognitive demands. Fluid intelligence, reaction time, and working memory span were examined because of the past evidence that COPD subjects are deficient in the capability to perform these types of tasks.[7-10] Additionally, a measure of inhibition was incorporated because there is substantial evidence that suggests that inhibition ability declines as a function of aging.[22-26]

Fluid Intelligence: Fluid intelligence is the basic power of reasoning and problem solving.[27] Form A of Scale 3 of the Culture Fair Intelligence Test (Institute for Personality and Ability Testing; Champaign, IL) was administered because it is designed for use with an educated adult population. To reduce test anxiety and to minimize the effects of speed of performance on fluid intelligence, the recommended time limit for each subtest was doubled. Validity of the Culture Fair Intelligence Test as a measure of fluid intelligence ranges between 0.71 and 0.84[28]; reliability of the test ranges from 0.71 to 0.92 when administered as a power test as opposed to a speed test.[29] Instructions were read to participants from the manual. Breaks and verbal encouragement were provided between subtests.

Processing Speed: This test was developed by Salthouse[30] and is patterned after the Wechsler Adult Intelligence Scale-Digit Symbol Subtest.[31] The participant's task was to determine whether or not a number and symbol pair presented as a stimulus were properly matched, as determined by the display bar, and then to depress the appropriate key on the keyboard. Equal emphasis was placed on speed and accuracy. Participants were given 20 practice trials and 90 measured presentations. Stimulus presentation and response time collection routines were computed using appropriate software (Micro Experimental Lab [MEL] software; Psychology Software Tools; Pittsburgh, PA), allowing millisecond accuracy for both. The Wechsler Adult Intelligence Scale digit-symbol test has a validity of 0.91[32] and a reliability of 0.92.[33]

Working Memory Span: Working memory span is a limited capacity memory system used to hold information that is used in cognitive activities such as reasoning, problem solving, and comprehension. Engle et al[34] developed the operation-word span procedure used. Participants were asked to determine the accuracy of an arithmetic problem and then were to read aloud and remember the single word presented after the problem. Participants were instructed to remember all words presented until the "recall" command was given. At this point, participants wrote all remembered words on the answer sheet. The grand score of working memory span (range, 2 to 6) was determined as the largest number of words completely recalled in two of the three presentations. The program was administered using MEL software.

Reaction Inhibition: Reaction inhibition is a measure of the ability to stop a response after it has been initiated. The negative priming task developed by Kane et al[35] was used. In the first 10 trials, participants were asked to identify whether a letter or a number was presented. Participants were encouraged to respond rapidly and accurately. An average response time was generated for the correctly answered trials. In the next 10 trials, an inhibition signal (a beep) was occasionally added after presentation of the stimulus. In the absence of a beep, participants were to respond exactly as they had responded during the first trial block. However, if a beep was present, participants were instructed not to respond to the stimulus.

During the final 100 trials, the time from presentation of the stimulus to the beep was varied in order to measure the shortest time to full motor inhibition. Beeps were given five times each at either 75, 150, 225, or 300 ms following stimulus presentation. Stopping accuracy (the number of trials in which the participant correctly chose not to respond divided by five) was determined for each inhibition signal time. MEL software was used to administer the trials and to collect participant responses.

Procedure

Program Entry: Participants completed three screening-day visits prior to their completion of the cognitive tests. The institutional review board for research with human subjects approved all procedures. During the first screening visit, informed consent forms were supplied, explained, and signed. Participants then completed a pulmonary function test and a series of questionnaires, including the CESD and a medical history questionnaire. During the second screening visit, participants underwent a medical examination conducted by a physician and completed a GXT. During the third screening visit, participants completed questionnaires that were not related to this study and then completed the 6-min walk test. Participants who met all the necessary criteria for participation were asked to return to the laboratory to complete the cognitive tests.

Randomization: Because involvement in the REACT study required extensive testing and because the cognitive measures were not a primary outcome variable for REACT, participants were only available for 30 min of cognitive testing. Therefore, participants were randomly assigned to either Test Battery 1 (fluid intelligence, or "Fluid"), Test Battery 2 (processing speed and working memory span, or "Speed" and "Span"), or Test Battery 3 ("Speed" and reaction inhibition, or "Stopping"). Assignments were made on a random basis in all cases except when more than one participant was to be tested at the same time. In these cases, because only one computer was available for testing, the participants were all assigned to Test Battery 1. Completion of each test battery took approximately 30 min.

Statistical Analysis

All analyses were conducted using computer software (Statistical Package for Social Sciences, version 7.5 for Windows 95; SPSS Inc; Chicago, IL). Age, education level, depression score, pulmonary function variables, and fitness variables were used to predict performance on the cognitive functioning tests. For all tests, significance was set at $\alpha = 0.05$.

Separate regressions were performed for each of the measures of cognitive functioning. Additionally, for the speed-of-processing task, performance was measured in terms of both accuracy of response and speed of response. A separate regression analysis was performed for each of these measures. To control for the potential confounding effects of education and depression on cognitive performance, CESD score and education level were forced into the first level of each regression. After controlling for these variables, age, the measures of pulmonary function (FVC, predicted FVC, FEV_1, predicted FEV_1, ratio of FEV_1 to FVC, maximum voluntary ventilation [MVV], ratio of MVV to predicted MVV, and ratio of MVV to VE), the measures of oxygen saturation (SpO_2 during GXT, SpO_2immediately after 6-min walk), and the measures of aerobic fitness (VO_2peak, 6-min walk distance) were entered stepwise. For the stopping task, the time delay from the stimulus to the stopping signal was also entered as a predictor variable in the second level of the regression.

RESULTS

There were a total of 98 participants in the study, ranging in age from 56 to 80 years old. Of these 98 subjects, data is available for 60 people who completed testing for Fluid, 34 people who completed Speed, 29 people who completed Span, and 31 people who completed Stopping. Descriptive data for each of the subsamples tested is presented in Table 2.

Fluid

CESD score and education level were entered into the first level of the regression and explained 21% of the observed variance in Fluid ($r^2 = 0.46$; $F_{2,57} = 7.43$; $p < 0.001$). Distance on the 6-min walk was stepped into the equation next and added significantly to the prediction of variance ($Fchange_{1,56} = 15.27$; $p < 0.001$; $r^2change = 0.17$; $\beta = 0.0056$). Age was stepped into the equation next and accounted for a significant increase in the explained variance ($Fchange_{1,55} = 7.52$; $p < 0.01$; $r^2change = 0.08$; $\beta = -0.35$). The addition of VO_2peak data, the other pulmonary function data, and the oxygen saturation data did not add significantly to the prediction of the variance.

Table 2. Descriptive Data for Each of the Samples

Sample/Variable	Overall	Culture Fair	Speed	Span	Stopping
Sex					
Male	54	33	19	15	17
Female	44	27	15	14	14
Education†	6.97 ± 2.15	7.12 ± 2.16	6.79 ± 2.07	6.76 ± 2.13	6.57 ± 2.11
CESD	8.70 ± 8.48	8.85 ± 8.94	8.62 ± 8.11	8.55 ± 8.36	8.10 ± 8.38
Age. yr	67.76 ± 6.01	67.88 ± 5.78	67.24 ± 6.65	66.34 ± 6.19	66.50 ± 6.17
VO_2peak, mL/kg/min	17.27 ± 3.84	17.55 ± 3.96	17.18 ± 3.68	17.25 ± 3.88	17.51 ± 3.68
6-min walk, feet	1,562.69 ± 332.77	1,568.53 ± 368.21	1,557.41 ± 279.51	1,580.79 ± 249.58	1,589.43 ± 221.90
FEV_1, L	1.57 ± 0.53	1.59 ± 0.54	1.57 ± 0.55	1.58 ± 0.57	1.59 ± 0.52
FEV_1, % predicted	58.34 ± 16.41	58.63 ± 15.40	58.50 ± 18.89	58.38 ± 17.22	59.91 ± 18.19
FEV_1,/FVC	54.29 ± 9.80	55.02 ± 9.87	52.85 ± 10.08	53.17 ± 8.98	53.45 ± 10.33
MVV, L/min	66.50 ± 27.90	67.67 ± 28.43	65.44 ± 28.74	66.38 ± 27.95	65.45 ± 25.37
SpO_2 after GXT	93.06 ± 3.07	93.17 ± 3.16	92.85 ± 3.07	92.76 ± 3.03	92.77 ± 3.06
SpO_2 after 6-min walk	97.09 ± 3.03	93.98 ± 3.09	94.12 ± 2.85	94.14 ± 2.92	94.42 ± 2.88

*Data are presented as mean ± SD or as No.

†Education was coded according to the following scale: 1 = no formal education; 2 = grade school (grades 1 to 4); 3 = grade school (grades 5 to 8); 4 = some high school (grades 9 to 11); 5 = high school graduate or equivalence; 6 = vocational or training school after high school; 7 = some college; 8 = associate degree (AD or AA degree); 9 = college graduate (BA or BS degree); 10 = some college or professional school after college; 11 = master's degree; 12 = completed a doctoral degree.

Speed

Results of the regression analysis indicated that education and CESD did not predict a significant portion of the variance in speed of processing ($F_{2,31} = 1.24$; $p > 0.05$). Distance on the 6-min walk test was stepped into the equation as a significant predictor of speed of processing ($Fchange_{1,30} = 8.17$; $p < 0.01$; $r^2change = 0.20$, $\beta = 1.18$). Then, MW was stepped into the equation and further contributed to the explanation of the variance ([Fchange.sub.1,29] = 5.81; $p < 0.03$; $r^2change = 0.16$; $\beta = 9.17$). Finally, age added further to the prediction of the variance ($Fchange_{1,28} = 5.26$; $p < 0.03$; $r^2change = 0.10$; $\beta = 25.43$). Thus, 6-min walk distance, age, and MVV predicted 46% of the variance in speed of processing ($F_{5,25} = 5.45$; $p < 0.01$). None of the other predictors reached the criterion required for entrance into the equation.

Span

Education and CESD did not predict a significant portion of the variance in performance ($F_{2,26} = 1.44$; $p > 0.05$). However, the addition of FVC did allow for the prediction of a significant proportion of the variance in performance ($Fchange_{1,25} = 6.37$; $p < 0.02$; $r^2change = 0.18$; $\beta = 0.59$).

Stopping

The temporal location of the stopping signal relative to the stimulus had the predicted impact on the subjects' ability to inhibit their response. The mean accuracy was as follows: at 75 ms, 0.69; 150 ms, 0.65; 225 ms, 0.62; and 300 ms, 0.55.

The ability to inhibit a response was not significantly predicted by education or depression ($F_{2,89} = 1.24$; $p > 0.05$). None of the other variables was a significant predictor of the variance in accuracy.

DISCUSSION

It has been proposed that the mechanism underlying the negative relationship between age and cognitive functioning is cerebral oxygenation.[3] Further, it has been proposed that an explanation for individual differences in cognitive functioning among older adults may be aerobic fitness level because of its impact on cerebral oxygenation.[3] Patients with COPD may have a reduced VO_2peak for several reasons. These patients may be limited by their cardiovascular system, similar to normal healthy individuals and cardiac patients, or they may have pulmonary abnormalities that impose limitations in oxygen transport. Therefore, examination of these patients may provide clues as to the relationship between aerobic fitness, age, and cognitive functioning. To examine these relationships, cognitive performance on a variety of tasks was assessed in a sample of older adults with COPD, and prediction equations were generated using age, measures of pulmonary function, measures of oxygen saturation, and measures of aerobic fitness.

The Culture Fair Intelligence Test is designed to assess fluid intelligence, and past evidence has shown that increasing age is associated with a decrease in performance on this task.[1,2,36-42] The results of this study support this conclusion because age predicted a significant portion of the variance in performance and was negatively related to performance. Additionally, past cross-sectional research has provided support for the hypothesis that greater levels of aerobic fitness may be associated with a lessening of the normal age-related declines in cognitive functioning.[43-45] This conclusion was also supported by the results of this study because a significant portion of the variance in fluid intelligence performance was explained by performance on the 6-min walk test and the direction of this relationship was positive. Thus, in a COPD sample of older adults, age is negatively associated and aerobic fitness is positively associated with fluid intelligence. The strength of this relationship is also worthy of mention because these variables were able to predict 28% of the variance in performance after we controlled for education and depression.

Some may question why performance on the 6-min walk test was a significant predictor of performance while VO_2peak was not a significant predictor. Evidence suggests that even in normal older populations, as many as half of the participants may be unable to attain true maximum oxygen uptake.[46] Additionally, older patients with chronic diseases often become exhausted after a short time period during conventional maximal exercise testing,[47] and some patients with COPD may terminate an exercise test early because of difficulty with the mouth piece.[48,49] As a result, maximal or peak aerobic capacity may be underestimated. Because of these limitations, the 6-min walk test may be considered a better measure of the patient's functional capacity. If this is true, then the findings of this study are in line with past research with normal samples and provide further support for the idea that aerobic fitness may serve to ameliorate age-related declines in cognitive functioning.

On the speed-of-processing task, 6-min walk performance accounted for 20% of the variance in performance. The relationship was such that those who could walk further during the 6-min (and thus who had higher levels of aerobic fitness) had faster responses. Thus, aerobic fitness had a positive impact on performance of this task. Additionally, age was a significant predictor of performance. The nature of this relationship was such that older subjects had slower responses. These findings are of special interest because past research has shown that speed of processing may be one of two cognitive variables that are capable of explaining a large proportion of the age-related variance in cognitive functioning.[50] In other words, aerobic fitness was found to be associated with the maintenance of speed of processing, which suggests the possibility that cardiovascular mechanisms may mediate the relationship between age and speed of processing and ultimately between age and performance on many cognitive tasks.

MVV was also a significant predictor of performance on the speed-of-processing task; however, the direction of the relationship was counter to that which was hypothesized. That is, subjects who performed better on the MVV task also had slower performances on the speed-of-processing task. This variable was included to assess factors that may limit VO_2 and thus may have an effect on cognitive function. Because VE is one component of VO_2 and patients with COPD may have a maximal VE that equals their MVV, it was expected that a decrease in MVV would be associated with poorer performance on the speed-of-processing task. However, it is possible that MVV is not a meaningful indicator of task performance because the cognitive tasks were all performed at submaximal levels of ventilation.

Surprisingly, once education and CESD were controlled for on the working memory span test, age did not contribute significantly to the prediction of the variance. This is in contrast to a wealth of research that has established that declines in working memory are associated with aging.[51] There are several possible reasons for these contradictory findings. One possibility is that because only older adults were used in this study, there was not enough variance in performance or in age for age to be predictive; i.e., because the data were only examined at one end of the age and performance continuum, the relationship may not have been apparent. This possible explanation is further strengthened by the fact that the range of performance on the memory task was quite small. This task provides scores in a short range, from 2 to 6, and it is possible that this range is too small to make age-related differences apparent in a sample consisting of all older individuals.

Interestingly, FVC was able to explain 18% of the variance in performance on the memory span task. This finding suggests that this measure of pulmonary function may be related to working memory span. Another explanation relates to the fact that FVC has also been shown to be related to timed walk distance.[52] While neither 6-min walk distance nor VO_2peak entered into the equation for the prediction of working memory span, there was a significant correlation between each of these two variables and the FVC (6-min walk distance, $r = 0.55$ and $p < 0.01$; VO_2peak, $r = 0.57$ and $p < 0.01$). Therefore, the fact that FVC entered into the equation may be more of a problem of multicollinearity among FVC, 6-min walk distance, and VO_2peak than the fact that

FVC is predictive of working memory span. Additionally, it is probably worthy of mention that while these results are indicative of a statistically significant relationship, they cannot ascertain the level of practical significance. Therefore, while this measure of pulmonary function was a statistical predictor of memory span, it is unlikely that it is a meaningful predictor from a practical standpoint.

The ability to inhibit a response was not predicted by any of the variables assessed in this study. It is somewhat surprising that age was not associated with accuracy of performance because this relationship has been established in the past.[24] However, there are two likely explanations for these contradictory findings. First, it is possible that inhibition abilities in a COPD population are not affected by age. Second, it is possible that the variations made to simplify the stopping task made it less sensitive to age-related differences in performance. The design of this research does not allow us to clearly identify the reason for these findings. However, examination of the accuracy of responses by the participants suggests that the second explanation is most viable because there was very little variance in the accuracy of performance on this task, with most participants performing at a level of 60% accuracy.

The fact that the findings with regard to the pulmonary function variables were inconsistent suggests several possible interpretations. The most likely explanation is that the pulmonary function variables assessed were not meaningful in the examination of the relationship. This could be true because the participants in this study were primarily only mildly to moderately impaired (95% of the sample). Therefore, the participants were not experiencing desaturation and were not limited in their oxygen delivery at submaximal levels of performance. It could also be that the measures that were taken in this study were not the ideal in terms of assessing limitations, which could influence the cerebral environment. For example, some researchers who have used PaO_2 as their measure of oxygenation have found that there is a relationship between PaO_2 and cognitive functioning.[8,10,13] A third explanation for the discrepant results is that the cerebral environment may be resistant to declines in pulmonary function. This notion is supported by past research[7,10,13,53] and is suggestive of a threshold model in the relationship between pulmonary function and cognition. It is also possible that the demands of the tasks are differentially related to disease state and pulmonary function so that on some tasks, there is a positive relationship, while in others there is a negative relationship. Finally, it is possible that the use of different samples for the different cognitive measures resulted in the differing results. However, random assignment was used to minimize the likelihood of systematic differences existing between the samples.

In conclusion, on a fluid intelligence task and on a speed-of-processing task, support was found for the idea that age and aerobic fitness have the predicted relationship with cognitive performance in a COPD sample. This finding adds to the growing literature suggesting that aerobic fitness may serve to minimize or slow the normal age-related declines in cognitive functioning. This finding also extends the past literature by providing evidence that aerobic fitness may lessen age-related declines in cognition even in a sample of participants with pulmonary limitations. However, it is necessary to conduct further research in this area to determine the precise relationship between these variables and cognition and to further examine the mechanisms underlying the relationship. In addition, a study is needed in which aerobic fitness is actually manipulated so that the mechanisms underlying this relationship can be more closely examined and so that a cause and effect relationship can be tested.

REFERENCES

[1] Jacewicz MM, Hartley AA. Age differences in the speed of cognitive operations: resolution of inconsistent findings. J Gerontol 1987; 42:86-88

[2] Schaie KW. The course of adult intellectual development. Am Psychol 1994; 49:304-313

[3] Dustman RE, Emmerson R, Shearer D. Physical activity, age, and cognitive-neuropsychological function. J Aging Phys Act 1994; 2:143-181

[4] Hagstadius S, Risberg J. Regional CBF characteristics and variations with age in resting normal subjects. Brain Cogn 1989; 10:28-43

[5] Marchal G, Rioux P, Petit-Taboue MC, et al. Regional cerebral oxygen consumption, blood flow, and blood volume in healthy human aging. Arch Neurol 1992; 49:1013-1020

[6] Hansen P. Pathophysiology of chronic diseases and exercise training. In: Durstine JL, ed. Resource manual for guidelines for exercise testing and prescription. 2nd ed. Philadelphia, PA: Lea & Febiger, 1993; 187-197

[7] Della Sala S, Donner CF, Sacco C, et al. Does chronic lung failure lead to cognitive failure? Schweiz Arch Neurol Psychiatr 1992; 143:343-354

[8] Prigatano GP, Parsons O, Wright E, et al. Neuropsychological test performance in mildly hypoxemic patients with chronic obstructive pulmonary disease. J Consult Clin Psychol 1983; 51:108-116

[9] Fioravanti, M, Nacca D, Amati S, et al. Chronic obstructive pulmonary disease and associated patterns of memory decline. Dementia 1995; 6:39-48

[10] Huppert FA. Memory impairment associated with chronic hypoxia. Thorax 1982; 37:858-860

[11] Fix AJ, Golden CJ, Daughton D, et al. Neuropsychological deficits among patients with chronic obstructive pulmonary disease. Int J Neurosci 1982; 16:99-105

[12] Grant I, Heaton RK, McSweeny AJ, et al. Neuropsychologic findings in hypoxemic chronic obstructive pulmonary disease. Arch Intern Med 1982; 142:1470-1476

[13] Grant I, Prigatano GP, Heaton RK. Progressive neuropsychologic impairment and hypoxemia: relationship in chronic obstructive pulmonary disease. Arch Gen Psychiatr 1987; 44:999 -1006

[14] ATS statement: Snowbird workshop on standardization of spirometry. Am Rev Respir Dis 1979; 119:831-838

[15] Standardization of spirometry: 1987 update--statement of the American Thoracic Society. Am Rev Respir Dis 1987; 136:1285-1298

[16] Berry MJ, Brubaker PH, O'Toole ML, et al. The prediction of [VO.sub.2] during treadmill exercise in older individuals with osteoarthritis of the knee and cardiovascular disease. Med Sci Sport Exer 1996; 28:808-814

[17] Mahler DA, Froelicher VF, Miller NH, et al. Clinical exercise testing. In: Kenney WL, Humphrey RH, eds. ACSM's guidelines for exercise testing and prescription. 5th ed. Baltimore, MD: Williams & Wilkins, 1995

[18] Kennelly KJ, Hayslip B, Richardson SK. Depression and helplessness-induced cognitive deficits in the aged. Exp Aging Res 1985; 11:169-173

[19] Radloff LS. The CES-D scale: a self report depression scale for research in the general population. Appl Psychol Measures 1977; 3:385-401

[20] Radloff LS, Teri L. Use of the Center for Epidemiological Studies-Depression Scale with older adults. Clin Gerontol 1986; 5:119-136

[21] Roberts RE, Vernon SW. The Center for Epidemiologic Studies Depression Scale: its use in a community sample. Am J Psychiatr 1983; 140:41-46

[22] Hartley AA, Kieley JM. Adult age differences in the inhibition of return of visual attention. Psychol Aging 1995; 10:670-683

[23] Hasher L, Stoltzfus ER, Zacks RT, et al. Age and inhibition. J Exp Psychol Learn Mere Cogn 1991; 17:163-169

[24] Kramer AF, Humphrey DC, Larish JF, et al. Aging and inhibition: beyond a unitary view of inhibitory processing in attention. Psychol Aging 1994; 9:491-512

[25] McDowd JM, Filion DL. Aging and negative priming in a location suppression task: the long and short of it. Psychol Aging 1995; 10:34-47

[26] McDowd JM, Oseas-Kreger DM. Aging, inhibitory processes, and negative priming. J Gerontol 1991; 46:P340-P345

[27] Cattell RB. Abilities: their structure growth and action. Boston, MA: Houghton Mifflin, 1971

[28] Bajard G. Validation differentielle et analyze factorielle d'une batterie de tests. Bull ANOP 1955; 11:38-58

[29] Knapp RR. The effects of time limits on the intelligence test performance of Mexican and American subjects. J Educ Psychol 1960; 51:14-20

[30] Salthouse T. What do adult age differences in the Digit Symbol Substitution Test reflect? J Gerontol 1992; 47:P121- P128

[31] Wechsler D. The Wechsler Adult Intelligence Scale-Revised. New York, NY: Psychological Corp, 1981

[32] Morgan SF, Wheelock J. Comparability of WAIS-R Digit Symbol and the Symbol Digit Modalities Test. Percept Mot Skills 1995; 80:631-634

[33] Hanson RK, Hunsley J, Parker KCH. The relationship between WAIS subtest reliability, "g" loadings, and meta-analytically derived validity estimates. J Clin Psychol 1988; 44:557-563

[34] Engle R, Cantor J, Carullo J. Individual differences in working memory and comprehension: a test of four hypotheses. J Exp Psychol Learn Mem Cogn 1992; 18:972-992

[35] Kane MJ, Hasher L, Stoltzfus ER, et al. Inhibitory attentional mechanisms and aging. Psychol Aging 1994; 9:103-112

[36] Birren JE, Woods AM, Williams MV. Behavioral slowing with age: causes, organization, and consequences. In: Poon LW, ed. Aging in the 1980s: psychological issues. Washington, DC: American Psychological Association, 1980; 293-308

[37] Botwinick J. Intellectual abilities. In: Birren JE, Schaie KW, eds. Handbook of the psychology of aging. New York, NY: Van Nostrand Reinhold, 1977; 580-605

[38] Cunningham W. Intellectual abilities and old age. In: Schaie KW, ed. Annual review of gerontology and geriatrics. Vol 7. New York, NY: Springer, 1987; 117-134

[39] Horn JL. Human ability systems. In Baltes PB, ed. Life-span development and behavior. Vol 1. New York, NY: Academic Press, 1978

[40] Horn JL. Remodeling old models of intelligence. In: Wolman BB, ed. Handbook of intelligence: Theories, measurements, and applications. New York, NY: Wiley, 1985

[41] Horn JL. Cognitive diversity: a framework of learning. In: Ackerman PL, Sternberg RJ, Glasser R, eds. Learning and individual differences. New York, NY: Freeman, 1989; 61-116

[42] Stankov L, Chen K. Can we boost fluid and crystallized intelligence? A structural modeling approach Aust J Psychol 1988; 40:363-376

[43] Clarkson-Smith L, Hartley AA. Relationships between physical exercise and cognitive abilities in older adults. Psychol Aging 1989; 4:183-189

[44] Elsayed M, Ismail AH, Young RJ. Intellectual differences of adult men related to age and physical fitness before and after an exercise program. J Gerontol 1980; 35:383-387

[45] Etnier JL, Landers DM. The influence of age and fitness on performance and learning. J Aging Phys Act 1997; 5:175-189

[46] White TA, Fehlauer S, Hanover R, et al. Is [VO.sub.2]max an appropriate fitness indicator for older adults? J Aging Phys Act 1998; 6:303-309

[47] Steele B. Timed walking tests of exercise capacity in chronic cardiopulmonary illness. J Cardpulm Rehabil 1996; 16:25-33

[48] Beaumont A, Cockcroft A, Guz A. A self-paced treadmill walking test for breathless patients. Thorax 1985; 40:459-464

[49] Morrison DA, Collins M, Stovall JR, et al. Reduced exercise capacity of chronic obstructive pulmonary disease patients exercising with noseclip/mouthpiece. Am J Cardiol 1989; 15:1180-1184

[50] Salthouse TA. How many causes are there of aging-related decrements in cognitive functioning? Dev Rev 1994; 14:413-437

[51] Craik FIM, Jennings JM. Human memory. In: Craik FIM, Salthouse TA, eds. The handbook of aging and cognition. Hillsdale, NJ: Lawrence Erlbaum Associates, 1992; 51-110

[52] Mahler DA, Weinberg DH, Wells CK, et al. The measurement of dyspnea: contents, interobserver agreement, and physiologic correlates of two new clinical indexes. Chest 1984; 85:751-758

[53] Prigatano GP, Levin AC. The impact of disease on behavior. In: Tarter RE, Van Thiel DH, Edwards KL, eds. Medical neuropsychology. New York, NY: Plenum Press, 1988; 11-26