Published in final edited form as:

J Epidemiol Community Health. 2015 March ; 69(3): 261–265. doi:10.1136/jech-2014-204143.

Individual differences in cognitive ability at age 20 predict pulmonary function 35 years later

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Abstract

Background—Poor pulmonary function is associated with mortality and age-related diseases, and can affect cognitive performance. However, extant longitudinal studies indicate that early cognitive ability also affects later pulmonary function. Despite the multifaceted nature of pulmonary function, most longitudinal studies were limited to a single index of pulmonary function: forced expiratory volume in 1 s (FEV1). In this study, we examined whether early adult cognitive ability predicted five different indices of pulmonary function in mid-life.

Methods—Mixed modelling tested the association between young adult general cognitive ability (mean age=20), measured by the Armed Forces Qualification Test (AFQT), and mid-life

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Contributors All authors contributed to study design and interpretation of the results, critically reviewed the draft, and approved the final version. TV conducted data analyses. TV, CEF, WSK and KCJ contributed to drafting the paper. All authors attest to the accuracy and integrity of this work.

Competing interests None.

Ethics approval The study was approved by Institutional Review Boards at both Boston University and the University of California, San Diego.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The data-set used for this work (wave 1 of the Vietnam-Era Twin Study of Aging, VETSA) is publicly available. More details can be obtained from contacting the study's Principal Investigators.

pulmonary function (mean age=55), in 1019 men from the Vietnam Era Twin Study of Aging. Pulmonary function was indexed by per cent predicted values for forced vital capacity (FVC%p), FEV1%p, maximum forced expiratory flow (FEFmax%p), and maximal voluntary ventilation (MVV%p), and by the ratio of FEV1 to FVC (FEV1/FVC), an index of lung obstruction.

Results—After adjusting for smoking, pulmonary disease, occupation, income and education, age 20 AFQT was significantly ($p<0.05$) associated with mid-life FVC%p ($\beta=0.10$), FEV1%p ($\beta=0.13$), FEFmax%p ($\beta=0.13$), and MVV%p ($\beta=0.13$), but was not significantly associated with FEV1/FVC ($\beta=0.03$, $p=0.34$).

Conclusions—Early adult cognitive ability is a predictor of multiple indices of aging-related pulmonary function 35 years later, including lung volume, airflow and ventilator capacity. Cognitive deficits associated with impaired aging-related lung function may, thus, be partly pre-existing. However, results also highlight that early life risk factors may be differentially related to different metrics of later-life pulmonary health.

INTRODUCTION

Pulmonary function is associated with mortality and many age-related diseases, such as coronary heart disease.¹² Additionally, pulmonary function has been associated with cognitive ability in young, middle and older adulthood, and with cognitive decline.³ However, the relationship between cognition and pulmonary function appears to be bidirectional. A small number of studies have examined the longitudinal association between cognitive ability in youth and pulmonary function in later life. In the Scottish Mental Health Survey, general cognitive ability at age 11 was positively correlated with forced expiratory volume in 1 s (FEV1), a measure of lung volume that is used as an indicator restrictive and obstructive diseases, at age 79.⁴ Likewise, in an all-male sample from the Vietnam Experience Study, lower cognitive ability in young adulthood (17–34 years) was related to poorer FEV1 18 years later after adjusting for a range of health and lifestyle factors.⁵ Finally, findings from the British 1946 Birth Cohort demonstrated that after accounting for a wide range of covariates, higher cognitive ability at age 15 was related to better FEV1 at age 43.⁶

There are several possible mechanisms that may underlie the relationship between cognition in young adulthood/adolescence and later life pulmonary function. For example, cognition has been linked to the selection of health behaviours, such as physical activity and diet, in later life.⁷ Furthermore, others have postulated that cognition plays a key role in a person's ability to understand health messages and to make informed health decisions, which may impact later life health outcomes.⁸ Additionally, poor cognition may be an overall marker of poor 'system integrity' that can influence the functions of multiple physiological systems.⁵ Alternatively, a 'common cause' may underlie respiratory function and cognitive capacity.⁹ For example inflammation and stress have been linked to cognition and pulmonary function.¹⁰⁻¹⁴

Pulmonary function is an important biomarker of aging, undergoing normative age-related decline that is influenced by biological and environmental factors. Moreover, pulmonary function is a multifaceted phenotype that can be indexed by lung volume, lung obstruction,

ventilatory capacity and airflow. Spirometry indices of lung function are useful tools in assessing both obstructive lung diseases such as asthma, chronic obstructive pulmonary disease (COPD), and chronic bronchitis, and restrictive lung diseases such as pulmonary fibrosis and sarcoidosis. FEV₁, along with forced vital capacity (FVC, total volume of air expired after a full inspiration), are the two most common spirometry indices and are clinically-relevant diagnostic indicators of restrictive and obstructive disease.¹⁵ Although FEV and FVC are the most frequently studied indices of pulmonary function, there are other measures that have clinical relevance. For example, the ratio of FEV₁/FVC is a commonly used index of lung obstruction.¹⁵ Forced expiratory flow (FEF) indexes airflow or speed of air during expiration. Measured during the FVC manoeuvre, FEF provides additional information regarding obstructive disease and may be a more sensitive indicator for asthma.¹⁶ Finally, maximal voluntary ventilation (MVV) measures the maximum volume of air inspired and expired over 1 min under instructions to breathe as hard and as fast as possible without getting dizzy. MVV, also referred to as ventilatory capacity, reflects breathing reserve during exercise, inspiratory muscle strength and general core body fitness.¹⁵

Despite this diverse range of lung function indices, with only one exception, the aforementioned longitudinal studies of early cognition and later pulmonary function examined only a single index of pulmonary function: FEV₁. In the study using the British 1946 Birth Cohort, early cognitive ability was related to FEV₁, but was not related to FEV₁/FVC, a finding the authors attributed to possible measurement error.⁶ No study has extensively examined the long-term effect of cognitive ability in youth on multiple indices of later-life pulmonary function, which may reflect different disease processes. Thus, the present study investigates how general cognitive ability in young adulthood is associated with various indices of lung volume, obstruction, ventilatory capacity/fitness and airflow measured 35 years later in late middle age.

METHODS

Sample

Pulmonary function and covariates were obtained from Wave 1 of the Vietnam Era Twin Study of Aging (VETSA), a longitudinal study of cognition and aging beginning in mid-life (51–60 years old).¹⁷ VETSA participants are part of the Vietnam Era Twin Registry, a nationally representative sample of male–male twin pairs who served in the US military sometime between 1965 and 1975.^{18,19} VETSA twins resemble those of the larger Registry sample and are representative of the general population of similarly-aged adult males in terms of health and lifestyle characteristics.²⁰ Wave 1 of VETSA included 1237 twins with an average age of 55.4 years (SD=2.5, range=51–60). Recruitment and data collection for Wave 1 occurred between 2002 and 2008. Young adult general cognitive ability was measured at the participant's induction into the armed forces (mean age=19.8 years, SD=1.3, range=17–26); data were obtained from military records from the Vietnam Era Twin Registry.

The study was approved by Institutional Review Boards at Boston University and the University of California, San Diego. All participants signed written informed consent documents prior to participation.

Measures

Pulmonary function—Pulmonary function was recorded with commercially available software (Breeze Suite; MedGraphics, St Paul, Minnesota, USA). Per cent predicted values were calculated for FVC%p, FEV1%p, MVV%p and maximum FEF (FEFmax%p) using existing reference equations, which include measures of body size and age.²¹⁻²³ FEV1/FVC was also included and was adjusted for height and age to closely match the per cent predicted values for other measures. Pulmonary function values used for analysis represent the ‘best effort’ from multiple trials (typically three trials). Per cent predicted values <10% or >200% are unlikely to occur in a non-patient ambulatory population, and appeared to be errors resulting from incorrect attempts during the tasks. Owing to other errors in the data recording equipment or failed/non-attempts by participants, between 100 and 170 participants had invalid pulmonary function data for each measure. After recoding invalid data as missing, values 3 SD above or below the mean for each measure were considered outliers and were coded as missing.

General cognitive ability—General cognitive ability in young adulthood was indexed using the Armed Forces Qualification Test (AFQT).²⁴ The AFQT is a 100-item multiple-choice test that is highly correlated with other general cognitive ability tests, including the Wechsler Adult Intelligence Scale ($r=0.84$).²⁵ The AFQT assesses four domains of cognitive ability: vocabulary, arithmetic word problems, knowledge and tool/mechanical reasoning.²⁶

Confounding variables—Smoking was included as a covariate due to its demonstrated influence on lung health.²⁷ Smoking was indexed by pack years (number of cigarettes smoked per day $\times$ number of years smoked)/20. Additionally, smoking status (current smoker, ex-smoker and non-smoker) was recoded into two dummy variables with non-smokers as the reference group. Pulmonary diseases, which are commonly diagnosed using spirometry,¹⁵ were classified as a single no/yes measure for individuals having a diagnosis of asthma, emphysema and/or bronchitis. In addition, previous studies have demonstrated that socioeconomic status is related to pulmonary health, although cognitive ability was not necessarily taken into account in those reports.²⁸ Thus, to investigate the effects of cognitive ability on pulmonary function independent of socioeconomic status, education and income were included as covariates. Education was measured by number of years of formal education. Current income was coded on a scale from 1 to 13, with values corresponding to each participant’s income bracket for the most recent year (ranging from less than \$10 000 to \$120 000 or more). Finally, two variables were included to index potential workplace exposure to health risk factors. First, occupation was recoded as blue collar (eg, labourers) versus white collar (eg, administrators, professionals) because previous research has demonstrated that blue collar workers are at a greater risk of being exposed to health hazards, including second-hand smoke.²⁹ Additionally, participants were asked to what extent their occupations exposed them to accidents or injury.³⁰ This item was coded 0 (none at all or a little) versus 1 (some or a lot). After inclusion of all covariates, the sample sizes

ranged from 924 to 992 across each pulmonary measure, with per cent of missing data ranging from 20% to 25% compared to the full sample (n=1237). The final sample, including individuals who had at least one complete pulmonary function measure and complete data for AFQT and covariates, was 1019.

Statistical analysis

All analyses were conducted in SAS V.9.3. All measures were assessed at the individual level. However, because our sample consisted of twins, we used a linear mixed modelling approach to account for the clustering of twins within families by including family ID variable as a random effect. Separate analyses were performed for each pulmonary measure. Standardised scores were used for all outcome measures and for AFQT, education and income. Model 1 tested the effects of age 20 AFQT on pulmonary function. Model 2 tested whether the effects of age 20 AFQT were significant after including covariates. Significant associations were determined using the type III fixed effects. Associations were considered statistically significant at $p < 0.05$, two tailed.

RESULTS

Sample characteristics are reported in table 1. The mean age of the study sample was the same as that of the full VETSA sample (55.4 years). Nearly 24% of participants were current smokers and 12% had some type of pulmonary disease. These estimates are similar to national estimates and rates reported in other middle-aged populations.²⁰³¹ The mean years of education was 13.8. The mean AFQT percentile score at induction was 61.4, which translates into a Wechsler IQ of 104.

Results from the mixed modelling analyses are reported in table 2. In model 1, age 20 AFQT had statistically significant positive associations with FVC%p, FEV1%p, FEFmax%p, and MVV%p, at age 55 ($\beta = 0.10 - 0.13$). However, this association was not statistically significant for FEV1/FVC ($\beta = 0.03$, $p = 0.34$).

Results from model 2 indicated that the effects of AFQT remained significant for FVC%p, FEV1%p, FEFmax%p and MVV%p after controlling for the effects of the covariates. In addition, pack years, current smoking status, and pulmonary disease had significant, negative associations with a majority of the pulmonary indices. Education and current income were significantly associated only with FEFmax%p. Occupation and occupational risk were not significantly associated with any pulmonary index.

DISCUSSION

The present study examined the relationship between general cognitive ability in young adulthood and pulmonary function in middle age. General cognitive ability in young adulthood had a significant positive association with mid-life lung volume, ventilatory capacity and airflow, even after controlling for health, education, income and occupational exposure. Overall, our findings extend previous research by demonstrating that cognition in young adulthood is significantly associated with lung function in middle age, and that this association is evident for a variety of previously unexplored pulmonary phenotypes.⁴⁻⁶

On the other hand, we did not find a significant association between early adult cognitive ability and lung obstruction, as measured by FEV1/FVC. This finding is consistent with one previous study, by Richards *et al*,⁶ that examined the relationship between cognitive ability at age 15 with FEV1 and FEV1/FVC at age 43. Although authors of that previous study speculated that the lack of relationship might be due to less accurate measurement of FVC, our data do not give any indication of reduced accuracy as the variability of FEV1 and FVC, and their associations with cognitive ability, were strikingly similar. FEV1/FVC is an indicator of COPD, which describes a group of diseases (including emphysema and chronic bronchitis) that cause progressive airway limitation. COPD-related air limitations can be caused by a variety of mechanisms, including damage to alveoli (air sacs) in the lung, mucus hypersecretion and narrowing of airways.³² In keeping with other literature on obstructive lung diseases,²⁷ we found that FEV1/FVC was most strongly associated with smoking behaviour (ie, current smoking and pack years) and pulmonary disease diagnosis, which included emphysema and chronic bronchitis. This further supports the validity of our FEV1/FVC measure.

Thus, this study adds to a growing body of research indicating that the aetiology of FEV1/FVC differs from that of other pulmonary function phenotypes. For example, pneumonia occurring between 2 and 7 years old is significantly associated with lung volume (FEV1 and FVC), but not lung obstruction (FEV1/FVC), at age 34–35 years, even after adjusting for confounding factors such as smoking, socioeconomic status and body size.³³ In addition, genetic studies of pulmonary function, including our own previous research on the VETSA sample, have demonstrated that the majority of the genetic and environmental influences underlying FEV1/FVC are distinct from other pulmonary measures (FEV1%p, MVV %p, FEFmax%p).^{34–36} Thus, results from the current study indicating that poorer cognitive ability in young adulthood is associated with reduced lung volume, ventilator capacity and airflow in mid-life, but not with processes more specifically associated with lung obstruction (eg, narrowing of the airways), may, in part, reflect different genetic aetiology. Genetic risk may, in turn, be exacerbated by behavioural factors and/or disease status rather than early life risk factors. For example, high genetic risk plus smoking—which was associated with FEV1/FVC in the present study—may combine to increase risk for narrowing of the airways and other physiological aspects of lung obstruction in mid-life.

Although our study revealed that young adult cognitive ability predicted multiple aspects of mid-life lung function using a longitudinal design, we still cannot be certain of the direction of causality. First, it is possible that lung function during earlier developmental periods may have influenced our measures of young adult cognitive ability. Indeed, other studies have found that more severe childhood respiratory problems such as sleep disordered breathing, hypoxia and nocturnal asthma are associated with lower academic performance in adolescence.³³ This explanation seems unlikely in the present study, however, because individuals with these types of severe breathing problems would be unlikely to be accepted into the military, and would therefore not be included in the study sample. In support of this, we note that rates of self-reported asthma diagnoses in the present sample (7.5%) are lower compared with Center for Disease Control and Prevention data for American men ages 45–64 (10.8%).³⁷ Nevertheless, future research examining cognition and pulmonary function

during childhood, early adulthood and later adulthood would be needed to definitively address directions of causality.

Second, the present study cannot identify the precise mechanisms underlying the association between early adult cognitive ability and mid-life pulmonary function. There is evidence that higher cognitive ability is associated with greater health literacy and better health habits (eg, dietary and exercise habits), and this might be a pathway through which cognition in adolescence and young adulthood affects later pulmonary function.⁷⁸ While we were able to account for smoking habits in these analyses, we did not have information on these other potential intervening variables.

Third, we note that other unmeasured factors underlying cognition and lung function may explain why these two factors covary. For example, the ‘common cause hypothesis’ of cognitive aging postulates that a biologically-based factor is responsible for age-related deterioration of cognitive and non-cognitive processes.⁹ Although age-related changes in biological factors are unlikely to be associated with cognition measured in young adulthood, we cannot definitively rule this hypothesis. Shared psychosocial factors may also play a role, with previous research demonstrating that stress and mood dysregulation are related to lung function and cognitive function.¹⁰⁻¹²³⁸ Similarly, shared genetic factors may also influence both characteristics.³⁹

Finally, several limitations should be considered when evaluating results from this study. Because there were too few women enlisted in the military at the time the VET Registry was created, the present study comprised only male participants, so our results may not generalise to women. Similarly, our participants were mostly non-Hispanic Caucasians (88%), so our results may not generalise to other ethnicities. However, these limitations are not likely to have biased our findings because the effect sizes in the present study were similar to those reported in previous studies using other samples. As noted above, if we had measures of earlier pulmonary function, we could have drawn more firm conclusions about the direction of causality among the observed associations. Future studies accounting for childhood/adolescent pulmonary function and other health factors, such as incidence of respiratory illness, would help to provide a more complete understanding of the complex relationship between cognition in early life and pulmonary function in later life. Nevertheless, our results add to a growing body of research linking individual differences in early cognitive ability with pulmonary function in later life, yet also suggest that the FEV1/FVC measure of lung obstruction has a different aetiology compared with other measures of pulmonary function.

Acknowledgements

The U.S. Department of Veterans Affairs provides financial support for the development and maintenance of the Vietnam Era Twin (VET) Registry. Numerous organizations provided invaluable assistance in the conduct of the VET Registry, including: Department of Defense; National Personnel Records Center, National Archives and Records Administration; Internal Revenue Service; National Opinion Research Center; National Research Council, National Academy of Sciences; the Institute for Survey Research, Temple University. All statements, opinions, or views are solely of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government, the NIA, or the NIH. Most importantly, the authors gratefully acknowledge the continued cooperation and participation of the members of the VET Registry and their families. Without their contribution this research would not have been possible. We also appreciate the time and energy of

many staff and students on the VETSA projects. The present study was also, in part, supported with resources of the VA San Diego Center of Excellence for Stress and Mental Health.

Funding The present work was supported by a NIH/NIA NRSA Individual Postdoctoral Fellowship (F32AG039954) and the Vietnam-Era Twin Study of Aging was supported by grants from NIH/NIA (R01AG018386, R01AG018384, R01AG022381, and R01AG022982).

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What is already known on this subject?

- ▶ Pulmonary function is associated with cognitive ability during each stage of adulthood.
- ▶ There is evidence that cognitive function in childhood and adolescence predicts lung volume in adulthood.

What this study adds?

- ▶ The relationship between general cognitive ability in young adulthood and pulmonary function in middle age exists for a variety of pulmonary function indices, including lung volume, airflow and ventilator capacity, but is not associated with forced expiratory volume in 1 s/forced vital capacity, a measure of lung obstruction.
- ▶ The relationship between general cognitive ability in young adulthood and pulmonary function in middle age remained after controlling for smoking, education, income and occupation.

Table 1

Characteristics of study sample from the Vietnam-Era Twin Study of Aging (VETSA), N=1019

Characteristic	Value
FVC%p, mean (SD) *	106.1 (21.2)
FEV1%p, mean (SD) *	101.2 (21.9)
Ratio of, FEV1/FVC (percentage), mean (SD) *	76.7 (8.2)
MVV%p, mean (SD) *	112.1 (29.2)
FEFmax%p, mean (SD) *	112.3 (29.2)
AFQT at age 20 (percentile), mean (SD)	61.4 (22.2)
Non-smoker, (%)	35.1
Ex-smoker, (%)	40.9
Current smoker, (%)	23.9
Pack years mean (SD)	19.0 (22.9)
Pulmonary disease, (%)	12.2
Education (years), mean (SD)	13.8 (2.1)
Current Income, median income bracket [†]	\$50 000–59 000
Occupation, (% blue collar)	38.7
Occupational risk (% some or a lot) [‡]	44.8
Age (years), mean (SD)	55.4 (2.5)

AFQT, Armed Forces Qualification Test; FEFmax%p, per cent predicted maximum forced expiratory flow; FEV1%p, per cent predicted forced expiratory volume in 1 s; FVC%p, per cent predicted forced vital capacity; MVV%p, per cent predicted maximal voluntary ventilation.

* Owing to patterns of missing data described in the Methods, Ns for individual pulmonary function measures ranged from 924 to 992.

[†] Income was coded on a scale from 1 to 13 with values corresponding to each participant's self-identified income bracket for the most recent year (ranging from less than \$10 000 to \$120 000 or more).

[‡] Participants were asked 'to what extent are (were) you exposed to the risk of accident or injury on your job'; responses for these analyses were coded as 0 (not at all or a little) and 1 (some or a lot).

Table 2

Mixed modelling results

Model	FVC%p N=951		FEV1%p N=956		FEV1/FVC N=946		MVV%p N=924		FEFmax%p N=992	
	1 β (SE)	2 β (SE)	1 β (SE)	2 β (SE)	1 β (SE)	2 β (SE)	1 β (SE)	2 β (SE)	1 β (SE)	2 β (SE)
Intercept	0.01 (0.03)	0.12 (0.09)	0.01 (0.03)	0.16 (0.09)	0.01 (0.04)	0.21* (0.08)	0.02 (0.03)	0.27* (0.09)	0.02 (0.03)	0.14 (0.08)
AFQT (age 20)	0.10** (0.03)	0.10* (0.04)	0.13** (0.03)	0.10** (0.03)	0.03 (0.03)	-0.02 (0.03)	0.13** (0.03)	0.10** (0.03)	0.13** (0.03)	0.10** (0.03)
Ex-smoker		0.01 (0.09)		0.04 (0.08)		0.01 (0.08)		-0.10 (0.09)		-0.01 (0.08)
Current smoker		-0.19 [†] (0.11)		-0.38** (0.11)		-0.54** (0.10)		-0.59** (0.11)		-0.42** (0.10)
Pack years		-0.04 (0.04)		-0.11** (0.04)		-0.51** (0.09)		0.01 (0.04)		-0.08* (0.04)
Pulmonary disease		-0.14 (0.10)		-0.29** (0.09)		-0.51** (0.09)		-0.34** (0.09)		-0.27** (0.09)
Education		-0.01 (0.04)		0.02 (0.04)		0.05 (0.04)		0.06 (0.04)		0.07* (0.04)
Current income		0.03 (0.03)		0.02 (0.03)		0.01 (0.03)		0.02 (0.03)		0.09** (0.03)
Occupation		-0.08 (0.08)		-0.08 (0.07)		0.01 (0.07)		-0.06 (0.07)		-0.04 (0.06)
Occupational risk		-0.01 (0.07)		0.02 (0.07)		-0.05 (0.07)		0.03 (0.07)		0.09 (0.06)

Statistically significant effects are in bold.

AFQT, Armed Forces Qualification Test; FEFmax%p, per cent predicted value maximum forced expiratory flow; FEV1 %p, per cent predicted value forced expiratory flow in 1 s; FEV1/FVC, ratio of forced expiratory volume in 1 s to forced vital capacity; FVC%p, per cent predicted value forced vital capacity; MVV%p=per cent predicted value maximal voluntary ventilation.

[†] p<0.10

* p<0.05

** p<0.01.