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Low cognitive ability in early adulthood is associated with reduced lung function in middle age: The Vietnam Experience Study

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Running head: Cognitive ability and lung function

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Abstract

Objective: Reduced lung function has been linked to poorer cognitive ability later in life. In the present study we examined the converse: whether there was a prospective association between cognitive ability in early adulthood and lung function in middle age. **Methods:** Participants were 4256 male Vietnam-era US veterans. Cognitive ability was assessed by the Army General Technical Test on enlistment when participants were, on average, 20 years old (range: 17 to 34). Data on ethnicity and place of service were extracted from army files. Smoking behaviour, alcohol consumption, basic socio-demographics, and whether participants suffered from a physician diagnosed chronic disease were determined by telephone interview in middle-age in 1985. Forced expiratory volume in one second (FEV1) was measured by spirometry at a 3-day medical examination in 1986. Height and weight were also measured. **Results:** In linear regression models, poor cognitive ability in early adulthood was associated with reduced lung function in middle age, first adjusting for age and height, $\beta = .17$, $p < .001$, then additionally adjusting for circumstantial, sociodemographic, lifestyle, and health factors, $\beta = .12$, $p = .001$. The same results obtained when the analysis was confined to non-smokers. **Conclusion:** Not only is lung function related to subsequent cognitive ability, but poor cognitive ability earlier in life is associated with reduced lung function in middle age.

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INTRODUCTION

Low cognitive ability, assessed in childhood, adolescence, or early adulthood, has been associated with a range of subsequent adverse health outcomes. A recent systematic review of nine cohort studies from various countries indicated that the research was uniform in showing an inverse association between early life cognitive ability and increased all cause mortality risk (1). More recently, a study of over one million Swedish men compared cognitive ability at military service conscription and mortality in middle age and found that low cognitive ability was not only associated with a greater risk of prematurely dying from all causes, it was also related to risk of death from specific causes, such as coronary heart disease, suicide, and accidents (2). In addition, low cognitive ability in youth is associated with a range of clinical and behavioural risk factors from premature mortality, such as obesity (3, 4), hypertension (4-6) markers of inflammation (7, 8); cigarette smoking (4, 5, 9), excessive alcohol consumption (10), and psychiatric illness (11, 12).

Poor lung function, typically indexed by low forced expiratory volume (FEV1), has also been shown to predict all-cause, cause specific mortality, and a range of adverse health outcomes (13-15), even in non-smokers (16, 17). A number of studies have now examined the association between lung function and cognitive ability; all have found that relatively poor lung function is associated with relatively low cognitive ability. However, the majority of studies to date have been cross-sectional (18-20), or, if longitudinal, have focused on the association between lung function and future cognitive ability and cognitive decline (21-25). Only two studies, as far as we are aware, have additionally examined the relationship between cognitive ability in youth and later lung function. In the British 1946 birth cohort, cognitive ability was measured in adolescence and FEV1 in middle age in 1778 study members; low cognitive ability was related to poorer subsequent lung function (24). In the other study, cognitive ability was assessed at age 11, as part of the Scottish Mental Survey 1932, and FEV1 measured 68 years later in 460 participants; again, low cognitive ability was related to poorer subsequent lung function (25).

Given the paucity of previous research, we examined the association between cognitive ability in youth and subsequent lung function in a substantially larger cohort of over 4,000 US male Vietnam era veterans. Cognitive ability data from early adulthood, that is, on army enlistment, were available and FEV1 was measured at a subsequent medical examination 18 years later when the men were middle aged. The two previous studies adjusted for only a few of the many potentially confounding variables. Due to the richness of the current data set we were able to correct for a range of circumstantial, socio-demographic, behavioural, and health-related covariates.

METHODS

Sample

Participants were Vietnam-era male military veterans. The effective sample size was 4256. Ethical approval for the study was given by various bodies, including the US Centers for Disease Control and participants gave informed consent. Details of sampling at each stage of data collection are described more fully elsewhere (26, 27). Inclusion

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criteria were: entered military service between January 1, 1965 and December 31, 1971; served only one term of enlistment and at least 16 weeks of active duty; earned a military specialty other than “trainee” or “duty soldier”; had a military pay grade at discharge no higher than sergeant.

Data collection

Information on place of service, Vietnam, other overseas, US only; ethnicity, white, black, other; and cognitive ability, was extracted from the military archives. On induction, i.e., during early adulthood, participants completed the Army General Technical Test (28), which consists of verbal and arithmetic reasoning items and generates an intelligence quotient (IQ) score (29). The Army General Technical test has been validated against components of the Wechsler Adult Intelligence Scale and found to show good correspondence (30). The mean age when IQ was assessed was 20.4 years (range: 17.0 to 33.8). From a telephone survey in 1985, socioeconomic position was measured using household income in midlife (≤$20,000; $20,000 - $40,000; > $40,000) and the grade from which participants left school (≤11;12; >12). Participants were also asked if they suffered from a range of physician-diagnosed somatic health problems: diabetes, hypertension, coronary heart disease, and cancer. Alcohol consumption (units per week), smoking habits (smoker; ex smoker; never smoker), and marital status (married; divorced, separated, widowed; never married) were ascertained using standard questions. Sixteen thousand three hundred and forty nine veterans were invited for interview and 15,288 (94%) actually participated.

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In 1986, 6443 participants, selected at random, were invited to attend a thorough 3-day medical examination; 4462 (69%) attended and full data, as indicated, were available for 4256. Mean age at medical examination was 38.3 yr. (range: 31.1 to 49.0). Height and weight were measured using standard protocols. FEV1 was determined by spirometry. Flow volume loops were recorded by a MedScience 570 Wedge Spirometer and a Digital DEC Writer 111 used to transmit the analogue data from the spirometer to a pulmonary function computer. The spirometer was calibrated daily; at the beginning of each day, atmospheric pressure and temperature were entered into the computer. For quality control, on each day one participant was randomly selected for repeat testing by a different examiner. Reproducibility was good and the coefficient of variation was 4.4%.

Statistical analyses

Analyses were undertaken using PASW Statistics, version 18, software. We tested multiple linear regression models, with lung function, i.e., FEV1, as the dependent variable and cognitive ability, that is, IQ score, as the independent variable. First, we tested a hierarchical model that, at step 1, adjusted for only age and height. Age and height have routinely been shown to affect lung function. IQ was entered at step 2. Second, we tested a further model that, in addition to age and height, adjusted at step 1 for weight, smoking, alcohol consumption, place of service, ethnicity, marital status, household income in midlife, education grade achieved, chronic disease (i.e., physician diagnosed diabetes, hypertension, coronary heart disease, and cancer). These are all variables that could be potential confounders of any association between IQ and FEV1. IQ was again entered at step 2 in this model. The following association statistics are

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reported: β, the standardized regression coefficient, ΔR^2, the proportion of additional variance in FEV1 explained by IQ. Associations were considered statistical significant if $p < .05$. In order to explore the impact of using alternative computations of lung function, FEV1 was also characterised as FEV1/height^2 (31) and as percentage of predicted FEV1, using a standard algorithm involving age and height to calculate predicted FEV1 (32). Since smoking has such a profound effect on lung function, it was considered important to determine whether any association between IQ and lung function was evident in non-smokers. Accordingly, the fully adjusted model above was re-run excluding smokers (16,17).

RESULTS

The participant characteristics are presented in Table 1. In the linear regression model that adjusted only for age at the medical examination and height, IQ was positively associated with FEV1 18 years later, $\beta = .17$, $p < .001$, $\Delta R^2 = .026$. A 1-point reduction in IQ was associated with a 7ml drop in FEV1. In addition, as would be expected, age at the medical examination was negatively associated and height positively associated with FEV1, $p < .001$. The association between IQ and FEV1 is illustrated in Figure 1 which plots quartiles of IQ against FEV1; the FEV1 data are estimated means following adjustment for age and height. Inspection of Figure 1 indicates a dose response relationship between IQ and FEV1. In the regression model that additionally adjusted for all the other covariates, the association between IQ and FEV1 was somewhat attenuated but remained statistically significant, $\beta = .12$, $p = .001$, $\Delta R^2 = .008$. In this case, a 1-point

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reduction in IQ was associated with a 5ml drop in FEV1. In addition to the association between age and height and FEV1, poorer lung function characterized those who smoked, consumed more alcohol, weighed more, were not white, and had a diagnosed major disease. The full model is presented in Table 2.

[Insert Tables 1 and 2 and Figure 1 about here]

We again ran the fully adjusted models for the two other representations of lung function, FEV1/height^2 and FEV1/FEV1predicted;for the former we no longer adjusted for height and for the latter, neither height nor age were entered. The outcomes were virtually identical to those reported above; IQ was associated with FEV1/height^2, $\beta = .12$, $p < .001$, $\Delta R^2 = .009$ and FEV1/FEV1predicted, $\beta = .12$, $p < .001$, $\Delta R^2 = .009$. Current smoking had a substantial effect on FEV1, mean (SD) for never smokers, ex-smokers, and current smokers was 4.15 (0.66), 4.14 (0.65), and 3.92 (0.66); Analysis of Variance, $F(2, 4253) = 66.52$, $p < .001$, indicated that the three smoking groups varied in lung function. Post hoc tests using the Newman-Keuls method indicated that the current smokers had poorer lung function than the ex- or never smokers ($p < .05$ in each case). Finally, the original FEV1 fully adjusted analysis was re-run excluding smokers. Again, the results were similar to those reported above, $\beta = .13$, $p = .001$, $\Delta R^2 = .010$.

DISCUSSION

Low cognitive ability in early adulthood was associated with poorer lung function in middle age in a large cohort of male Vietnam era army veterans. As such, our results add weight to the findings of the two previous smaller scale studies that also show a positive association between cognitive ability and FEV1 (24, 25). In the present study, the relationship between low cognitive ability and poorer lung function remained statistically significant despite adjusting for a wide range of potential confounders, using alternative derivations of lung function, and when the analysis was restricted to participants who were not current smokers. This testifies to the robustness of the relationship.

As described, several studies have now shown that reduced lung function is related to future cognitive ability and cognitive decline (21-25). The present results, along with those from the two earlier reports (24, 25) also indicate that low cognitive ability in youth increases the risk of reduced lung function later in life. Taken together, the evidence now suggests that cognitive ability and lung function have a bi-directional relationship. This is not without precedent. For example, there is evidence linking markers of inflammation, such as C-reactive protein, earlier in life with future cognitive decline (33, 34). We have also recently shown in the present cohort that low cognitive ability was associated with a higher subsequent erythrocyte sedimentation rate, another marker of inflammation (8).

The association between FEV1 and subsequent cognitive ability is generally explained in terms of processes such as inflammation, impaired fibrinolytic activity, oxidative stress, and hypoxia associated with compromised respiratory function (35, 36). Various pathways have been suggested that might link low cognitive ability with subsequent adverse health outcomes, including impaired lung function, have been suggested. For example, a greater propensity for unhealthy behaviour, including smoking, alcohol consumption, and poorer medical adherence and surveillance, among those with low cognitive ability has been cited (1). However, the present associations survived adjustment for both alcohol consumption and smoking and the positive relationship between cognitive ability and future lung function was of the same order of magnitude in analyses restricted to non-smokers. Another possibility is that low cognitive ability might be a marker of poorer 'system integrity', such that various physiological systems mount less resistance to injurious environmental exposures across the life course (37). Finally, both poor lung function and low cognitive ability have also been regarded as markers of early life adversity including exposure to suboptimal nutrition, poverty, chronic childhood illness, and psychosocial stress (16, 38). Accordingly, it is possible that low cognitive ability and poor lung function are parallel products of shared antecedents, either genetic, epigenetic, or early environmental (25, 39). The present dataset is insufficient to determine the relative merits of these various possibilities.

The present study is not without other limitations. First, only men were included and thus the issue of generalisation arises. However, there are no compelling reasons for believing the present association to be sex-specific. The two previous studies demonstrating a relationship between cognitive ability and future lung function were conducted on mixed samples (24, 25). Second, the effect sizes could be regarded as modest. Nevertheless, they are of the same order as those reported in the two previous studies (24, 25). Third, without a measure of lung function in early adulthood, it is impossible to ascertain the direct of causality, as the association between cognitive ability and lung function could already have existed at the earlier age. Fourth, observational studies are prone to confounding by poorly measured or unmeasured variables (40).

However, we adjusted for a more complete set of potentially relevant confounders than previous studies. Further, in this context, our rather crude characterization of smoking behaviour, (smoker; ex smoker; never smoker) rather than pack years, may have underestimated the effects of smoking on association between cognitive ability and lung function. Nevertheless, the association between cognitive ability and later lung function was of the same order in analysis restricted to non-smokers as it was in the whole sample. Finally, undoubtedly the present study's greatest limitation is the absence of measures of environmental, including occupational, exposures to air borne toxins and pollutants. However in this, our study is hardly unique; neither of the other two studies of cognitive ability and subsequent lung function were able to draw on such measures (24, 25), perhaps testimony to the difficulty of collecting these sort of data. Nevertheless, it is quite conceivable that such environmental exposures were more common among those with poorer cognitive ability and, accordingly, mediated the relationship between cognitive ability and lung function. However, we would contend that that income and education may be reasonable proxies for whether participants were more or less likely to be living in environments and working in occupations with such exposures; similarly, service in Vietnam could be considered a fair proxy for such exposures during military service. Our main finding withstands correction for income, education, and place of service.

In conclusion, low cognitive ability in early adulthood was associated with reduced lung function, as indicated by lower FEV1, in middle age. This association was still evident following adjustment for a range of socio-demographic, anthropometric, lifestyle,

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and health variables, and was evident with different representations of FEV1. Thus, it would appear that not only does lung function affect later cognitive ability, but also that poor cognitive ability earlier in life is associated with reduced lung function later in life.

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Table 1. Characteristics of participants

Variable		Mean	SD
FEV1 litres		4.04	0.66
FEV1% of predicted FEV1		99.54	14.63
Height in metres		1.78	0.07
Weight in kgs		82.50	13.55
Age at medical examination in years		38.33	2.52
Units of alcohol per week (median and IQR)		2.00	9.00
Standardised IQ score from enlistment		101.37	15.19
		Percent	
Ethnicity	white	82	
	black	12	
	other	6	
Place of service	Vietnam	55	
	other overseas	26	
	US only	19	
Smoking status	smoker	46	
	ex smoker	28	
	non smoker	26	
Education grade	≤ 11	12	
	12	37	
	> 12	51	
Household income midlife	≤ $20,000	28	
	$20,000 - $40,000	50	
	> $40,000	22	

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Marital status	married	74
	divorced/separated/widowed	18
	never married	8
Physician diagnosed chronic disease		13

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Step 1	β	p	ΔR^2
Height in metres	.40	<.001	
Weight in kg	-.03	.035	
Age at medical examination in years	-.15	<.001	
Units of alcohol per week	-.03	.015	

Table 2. Predictors of lung function in the fully adjusted regression model

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Ethnicity	-.09	<.001	
Place of service	-.02	.123	
Smoking status	-.17	<.001	
Education grade	-.02	.248	
Household income midlife	.02	.325	
Marital status	.01	.430	
Physician diagnosed chronic disease	-.05	<.001	.238
Step 2			
Standardised IQ score from enlistment	.12	<.001	.008

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Competing Interests

The authors have no competing interests.

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Figure Caption:

Figure 1: Mean FEV1 by quartile of IQ; the error bars are standard errors