Cognitive Ability in Early Adulthood and Risk of 5 Specific Psychiatric Disorders in Middle Age
The Vietnam Experience Study

Citation for published version:

Digital Object Identifier (DOI):
10.1001/archpsyc.65.12.1410

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Peer reviewed version

Published In:
Archives of General Psychiatry

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Cognitive ability in early adulthood and risk of five specific psychiatric disorders in mid life: the Vietnam Experience Study

Catharine R Gale PhD¹,², Ian J Deary PhD¹, Stephen H Boyle PhD³, John Barefoot PhD³, Laust H Mortensen MS⁴, G David Batty PhD¹,⁵

¹Medical Research Council Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, Edinburgh, UK
²Medical Research Council Epidemiology Resource Centre, University of Southampton, Southampton, UK
³Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, USA
⁴Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark
⁵Medical Research Council Social & Public Health Sciences Unit, University of Glasgow, Glasgow, UK

Correspondence to:
Catharine Gale
MRC Epidemiology Resource Centre
(University of Southampton)
Southampton General Hospital
Southampton
SO16 6YD
UK
Email: crg@mrc.soton.ac.uk, Tel: 44 (0)23 80764080 Fax: 44 (0)23 704021
Context: Lower cognitive ability is a risk factor for some forms of psychopathology, but much of the evidence for this is based on individuals who required specialist care. It is unclear whether lower ability influences risk of particular patterns of comorbidity.

Objective: To examine the relation between pre-morbid cognitive ability in early adulthood and risk of major depression, generalized anxiety (GAD), post-traumatic stress disorder (PTSD), alcohol and drug abuse or dependence and comorbid forms of these conditions in mid life.

Design: Prospective cohort study in which cognitive ability was measured on enlistment into military service at a mean age of 20.4 years and psychiatric disorder was assessed by structured diagnostic interview at a mean age of 38.3 years.

Setting: USA.

Participants: 3258 male veterans, participants in the Vietnam Experience Study.

Main outcome measures: Major depression, GAD, PTSD, alcohol or drug abuse or dependence, since enlistment and currently, diagnosed according to the American Psychiatric Association’s Diagnostic and Statistical Manual, edition 3.

Results: Lower cognitive ability was associated with an increased risk of depression, GAD, alcohol abuse/dependence and PTSD, and some patterns of comorbidity. For a standard deviation decrease in cognitive ability, unadjusted odds ratios (95% CI) for having these disorders currently were: 1.32 (1.12-1.56) for depression, 1.43 (1.27-1.64) for GAD, 1.20 (1.08-1.35) for alcohol abuse/dependence, 1.39 (1.18-1.67) for PTSD, 2.50 (1.41-4.55) for PTSD plus GAD, 2.17 (1.47-2.43) for PTSD plus GAD plus depression, and 2.77 (1.12-6.66) for all four disorders. Most associations remained statistically significant after adjustment for confounders.

Conclusions: Lower cognitive ability is a risk factor for several psychiatric disorders including some forms of comorbidity. Understanding the mechanisms whereby ability is
linked to individual patterns of psychopathology may inform intervention.

**Unstructured abstract**

Lower cognitive ability is a risk factor for some forms of psychopathology, but much of the evidence is based on individuals who required specialist care. Whether lower ability influences risk of particular patterns of comorbidity is unclear. We examined the relation between pre-morbid cognitive ability in early adulthood and risk of major depression, generalized anxiety (GAD), post-traumatic stress disorder (PTSD), alcohol and drug abuse or dependence and comorbid forms of these conditions in 3258 male veterans who underwent a structured diagnostic interview in mid life as part of the Vietnam Experience Study. Lower cognitive ability was associated with an increased risk of depression, GAD, alcohol abuse/dependence and PTSD, and some patterns of comorbidity. For a standard deviation decrease in cognitive ability, unadjusted odds ratios (95% CI) for having these disorders currently were: 1.32 (1.12-1.56) for depression, 1.43 (1.27-1.64) for GAD, 1.20 (1.08-1.35) for alcohol abuse/dependence, 1.39 (1.18-1.67) for PTSD, 2.50 (1.41-4.55) for PTSD plus GAD, 2.17 (1.47-2.43) for PTSD plus GAD plus depression, and 2.77 (1.12-6.66) for all four disorders. Most associations remained statistically significant after adjustment for confounders. Lower cognitive ability is a risk factor for several specific psychiatric disorders and some forms of comorbidity.
Introduction

There is increasing evidence that children or adolescents who gain lower scores on standard tests of intelligence may be more vulnerable to psychopathology later in life. Lower cognitive ability in childhood or adolescence has been associated with an increased risk of developing schizophrenia, severe depression or other non-affective psychoses, post-traumatic stress disorder (PTSD), GAD, and alcohol or drug abuse. While these findings suggest that cognitive ability may be a risk factor for many forms of psychiatric disorder, much of the evidence is based on individuals whose disorders were severe enough to require admission to hospital or treatment by secondary care mental health services. A few recent longitudinal studies of the relation between cognitive ability and subsequent psychiatric disorder have used structured diagnostic interviews to assess psychopathology over a wider spectrum of severity, but while these have produced consistent findings linking cognitive ability with risk of PTSD, results on the relation between cognitive ability and anxiety disorders were inconsistent, and the only study to examine its link with depression found no association.

None of these studies has examined whether cognitive ability is linked with susceptibility to particular patterns of psychiatric comorbidity. The co-occurrence of two or more psychiatric diagnoses – sometimes involving alcohol or drug abuse or dependence – is common and has major consequences in terms of increased service use, greater functional disability, and higher levels of distress. Learning whether particular combinations of disorders show stronger associations with cognitive ability earlier in life may help us better understand the nature of the link between cognitive ability and psychopathology.
The Vietnam Experience Study (VES) is a longitudinal study of male US Army veterans who had their cognitive ability assessed on enlistment in early adulthood and took part in a psychological examination in middle-age, when psychiatric morbidity was assessed. We used these data to examine the relation between cognitive ability in early adulthood and risk of major depression, GAD, PTSD and alcohol or drug abuse and dependence, since enlistment and currently, and to investigate whether it influenced risk of comorbidity among these conditions.

**Methods**

*Data collection in late adolescence/early adulthood*

The Vietnam Experience Study was conducted by the Centers for Disease Control. Participants were identified retrospectively using military records, as described elsewhere.\(^{18, 19}\) In brief, 18,313 former military personnel were drawn randomly from approximately five million US army veterans who had served in Vietnam and elsewhere and whose service files were stored at the National Personnel Records Center. Information on place of service, rank, ethnicity and cognitive ability were extracted from military archives. Based on rank at army discharge (mean age 22.5 yr., range: 17.9 to 36.8), monthly income based on 1964 pay scales was derived. Ethnic origin was classified as ‘white’, ‘black’, or ‘other’; the latter group comprising Hispanics, Asians, Pacific Islanders, American Indians, and Alaskan Natives.

On enlistment, participants took a general aptitude test: the General Technical Section of the Army Classification Battery.\(^{20}\) This consists of two subtests, verbal and arithmetic reasoning. Scores on the General Technical Section correlate highly with scores on standard tests of intelligence.\(^{20}\) We were able to validate this test by comparing scores from it with those from two subtests of the Wechsler Adult Intelligence Scale, a comprehensive and widely used test of cognitive ability, that were administered to participants during the psychological
examination in middle-age (described below). Despite this intervening period, total General Technical scores were strongly correlated with scores on the information subtest (r; 95% CI: 0.74; 0.73, 0.76) and block design subtest (0.51; 0.49, 0.55) of the Wechsler Adult Intelligence Scale. Mean age at army entry when cognitive ability was assessed was 20.4 yr. (range: 17.0 to 33.8). For ease of interpretation, we converted total scores on the General Technical section to an IQ equivalent (mean 100, SD 15).

Data collection in middle-age

Of 18,313 former military personnel who qualified for inclusion in the original study cohort, 446 died post-discharge. The remainder (N=17,867) were considered to be alive on December 31st 1983 and eligible for follow-up through interview and examination. In all, 15,288 men (85.6% of target population) participated in a telephone survey in 1985-6. A random sample of respondents (N=6443) were invited to attend a three-day medical and psychological examination; 4462 attended (69.3% of those invited). Participants signed a consent form on the first day. Mean age at examination was 38.3 yr. (range: 31.1 to 49.0), and mean time since enlistment was 17.4 yr (range 13 to 22). Psychological health was assessed using the Diagnostic Interview Schedule (DIS).21 The DIS is a standardized questionnaire designed to assess the prevalence of psychiatric conditions according to the DSM-III 22 criteria of the American Psychiatric Association. The DIS was administered by trained psychology technicians under the supervision of clinical psychologists. Participants reported the age at which they experienced symptoms and age at onset of disorder was determined from this. Participants completed a 12-item Combat Exposure Questionnaire which enquired about the frequency with which they had experienced various combat-related events.23
We used DIS data on the prevalence of major depression, GAD, PTSD, and alcohol or drug abuse or dependence since enlistment or in the last 12 months. Participants were considered as having a diagnosis of a particular condition since enlistment if they reported ever having a pattern of symptoms that met the full DSM-III criteria and onset occurred after enlistment. In total, 1126 participants reported first experiencing symptoms at an age that pre-dated enlistment (81% of these had alcohol abuse or dependence). Participants were considered as having the diagnosis currently if they reported a pattern of symptoms in the past 12 months that met the full criteria. To allow the study of comorbidity, the optional DSM-III exclusion rules were not used. Participants were considered to have a 'pure' form of a disorder if they did not meet the DIS criteria for any other condition within the same period (i.e., this was their sole diagnosis). Participants were considered to have a comorbid condition if they met the criteria for two or more of the disorders under study.

By definition, individuals cannot be at risk for PTSD unless they had a history of exposure to a traumatic event. The version of the DIS used in the Vietnam Experience Study does not permit the identification of participants who were exposed to trauma but did not develop symptoms, only of those who did develop symptoms. In order to use a trauma-exposed comparison group in our analyses of PTSD, we therefore restricted these analyses to a subgroup who had served in Vietnam and scored 1 or more on the Combat Exposure questionnaire indicating that they had experienced combat. DIS criteria for PTSD within the last year did not require trauma exposure to have occurred within this time period, only symptoms.
Analytical sample

The present analyses are based on a sample of men with complete information on cognitive ability at enlistment, DIS data, and all the covariates available from their army records - age at enlistment, ethnicity, place of service and army income. These covariates were included as potential confounders of the relation between cognitive ability and psychiatric disorder. After exclusion of men with onset of psychiatric disorder prior to enlistment, the sample consisted of 3258 men. This group represents 18% of the target population for the telephone interview and 51% of those invited for examination. We compared the distribution of baseline characteristics (age, army income, place of service, ethnicity and IQ equivalent scores) between our analytical sample and those who took part in the telephone survey but were excluded from our sample because they did not take part in the examination. Men in the excluded group had a lower IQ equivalent score than those in the analytical sample (mean (SD) 100.2 (14.9) vs 101.1 (15.2), t=3.25, p=0.001, Cohen’s d = 0.06); they were also more likely to be in the lowest category of army income (12.8% vs 10.8%, $\chi^2=8.90$, p=0.012), and less likely to be black (11.1% vs 12.7%, $\chi^2=6.32$, p=0.036). There were no differences between the groups in age at enlistment. Thus, these few differences were marginal, achieving statistical significance owing to the large numbers.

Statistical analysis

We used ANOVA, correlation coefficients and the $\chi^2$-test to examine the characteristics of the participants. We used logistic regression to examine associations between these characteristics and risk of psychiatric morbidity and to examine how the relation between cognitive ability and risk of morbidity changed on adjustment for potential confounding factors.
Results

Cognitive ability in relation to demographic and army service characteristics

Table 1 shows cognitive ability scores at enlistment in relation to characteristics in early adulthood. Cognitive ability was greater in men with a higher socio-economic position during service (as indicated by army income), in those who were white, in those whose place of service did not include Vietnam and in those who were older at the time of enlistment.

Cognitive ability and risk of psychiatric disorders

Table 2 show the unadjusted odds ratios for major depression, GAD, alcohol or drug abuse or dependence, and PTSD since enlistment, or currently, according to cognitive ability. Lower cognitive ability was associated with a significantly increased risk of major depression, GAD and PTSD since enlistment and currently. Lower cognitive ability was also associated with an increased risk of alcohol abuse or dependence but, in contrast to the other disorders, it was slightly more strongly linked with risk of ever having the condition since enlistment than with risk of having it currently. Risk of drug abuse or dependence since enlistment or currently was slightly higher in men of lower cognitive ability but these relations were not statistically significant.

Likelihood of all psychiatric disorders was increased in men with a lower income during their army service, in those who served in Vietnam, and in those who were younger at the time of enlistment. Men from non-white ethnic groups also tended to have a higher risk of all disorders. We examined whether the relations between cognitive ability and risk of psychiatric disorder were attenuated by adjustment for potential confounders. We did not adjust for age at enlistment in these analyses because, as Table 1 shows, there were large
differences in cognitive ability between age groups that are likely to be caused by brighter men taking college deferments before entering the military. Adjustment for age could therefore result in an underestimation of the effect of cognitive ability.

Table 3 shows the adjusted odds ratios for major depression, GAD, PTSD and alcohol abuse or dependence since enlistment or currently according to cognitive ability; the relation between cognitive ability and drug abuse or dependence remained non-significant with adjustment for covariates so was not considered further. Odds ratios for major depression, GAD and alcohol abuse or dependence were adjusted separately and then together for ethnicity, army income and place of service. Odds ratios for PTSD, based on a subgroup of combat-exposed Vietnam veterans, were adjusted for ethnicity and army income.

The relation between cognitive ability and risk of major depression was slightly attenuated by adjustment for army income and place of service; adjustment for ethnicity had little effect (Table 3). After full adjustment, the relation between cognitive ability and risk of depression since enlistment ceased to be statistically significant, but cognitive ability remained significantly associated with risk of depression currently: the odds ratio (95% CI) for a SD decrease in ability was 1.23 (1.03 to 1.47). The relation between cognitive ability and risk of GAD was stronger than that with depression. Adjustment for potential confounding factors had only slight attenuating effects and after full adjustment lower cognitive ability continued to be associated with increased risk of GAD both since enlistment and currently: the odds ratios (95% CI) for a SD decrease in ability were 1.16 (1.04 to 1.30) and 1.39 (1.19 to 1.61) respectively. The relation between cognitive ability and risk of alcohol abuse or dependence was attenuated most strongly by adjustment for army income. After controlling for all potential confounding factors, cognitive ability ceased to be significantly associated with risk
of alcohol abuse or dependence currently, but remained a significant predictor of alcohol
abuse or dependence since enlistment: the odds ratio (95% CI) for a SD decrease in cognitive
ability was 1.19 (1.10 to 1.30). In the subgroup of participants exposed to combat during
service in Vietnam, the strong association between lower cognitive ability and increased risk
of PTSD either since enlistment or currently was only slightly weakened by adjustment for
army income.

Of the 1377 men who had ever had major depression, GAD, PTSD or alcohol abuse or
dependence since enlistment, only 670 (49%) had a single disorder with no accompanying
comorbidity. There was a similar pattern among the 543 men who had these disorders
currently, where 296 (55%) had a single disorder. We examined whether the strength of the
relation between cognitive ability and risk of these disorders varied according to whether the
condition was present in a pure or comorbid form (Figure 1 & Table 4). As before, we
restricted analyses of PTSD to a sub-group of combat-exposed Vietnam veterans.

**Risk of having a pure disorder**

Cognitive ability was not associated with risk of having pure depression or pure GAD, either
since enlistment or currently (Figure 1 & Table 4). Risk of having PTSD in a pure form was
raised in men with lower cognitive ability. Numbers with this condition were small and the
relations were not statistically significant in unadjusted analyses, though adjustment for
potential confounders strengthened the association with current disorder. Far larger numbers
of men had pure alcohol abuse or dependence. As in the case of an overall diagnosis of
alcohol abuse or disorder (Table 3), lower cognitive ability was associated with a significantly
increased risk of having alcohol abuse or dependence in a pure form since enlistment. This
relation was slightly strengthened when potential confounding factors were added to the
multivariable model. The association between cognitive ability and risk of having this form of the disorder currently was weaker and not statistically significant.

*Risk of having a comorbid disorder*

Numbers of cases with comorbidity involving depression, GAD, alcohol abuse or dependence or PTSD were often very small, so odds ratios based on these need to be interpreted with caution. In general, men with lower cognitive ability appeared to have a higher risk of comorbid as opposed to single disorders, particularly those involving GAD and PTSD, though only a few of these associations were statistically significant. Associations between lower cognitive ability and increased risk of alcohol abuse or dependence in combination with either GAD or depression were weakened by adjustment for potential confounding factors and ceased to be significant. Associations between lower cognitive ability and heightened risk of some forms of comorbid PTSD tended to be little attenuated or slightly strengthened by adjustment, albeit based on very small numbers of cases: for a SD decrease in cognitive ability, after adjustment, odds ratios (95% CI) for disorders since enlistment were 1.51 (1.08, 2.10) for PTSD plus alcohol abuse or dependence and 1.65 (1.08, 2.52) for PTSD plus alcohol abuse plus depression plus GAD, while odds ratios for disorders currently were 2.49 (1.35, 4.56) for PTSD plus GAD, 2.02 (1.32, 3.10) for PTSD plus GAD plus depression, and 2.89 (1.15, 7.26) for PTSD plus GAD plus alcohol abuse or dependence plus depression.

**Discussion**

In this study of former US soldiers followed up in middle age men who had lower cognitive ability in early adulthood had an increased risk of major depression, GAD, alcohol abuse or dependence, PTSD and some comorbid forms of this disorder.
**Previous studies**

Higher pre-morbid cognitive ability has been associated with a lower risk of PTSD in previous studies. In a New Zealand cohort, men and women who had a higher IQ at age 5 had a reduced risk of developing PTSD by age 32. Similar findings have been reported from a small US cohort, where higher IQ at age 6 was linked to a lower likelihood of being exposed to trauma and a reduced risk of developing PTSD by age 17. Studies of military samples have also implicated cognitive ability as a risk factor for this condition. In a small prospective study of US veterans, men with higher IQ on enlistment were less likely to develop PTSD, though interpretation of this finding is difficult as there was no adjustment for prior socio-economic status. A recent co-twin-control study of 2386 Vietnam-era veterans found a significant dose-response relation between higher IQ at induction into the military and lower risk of PTSD in both between-twin and within-pair analyses. In our study, higher cognitive ability was associated with a reduced risk of PTSD in combat-exposed Vietnam veterans.

None of these studies of PTSD examined the potential influence of premorbid cognitive ability on the psychiatric comorbidity that frequently accompanies the condition. Our results on this need to be treated with caution as the number of cases were small, but they suggest that lower cognitive ability may be a risk factor for comorbid forms of PTSD, perhaps particularly those involving GAD and alcohol abuse or dependence. Lower intelligence has previously been associated with hospitalisation for psychiatric disorder, Our findings on comorbidity provide further indications of a link between lower cognitive ability and severity of psychiatric disorder.
Existing evidence on the relation between IQ and subsequent risk of GAD is sparse. In a small follow-up of members of the National Collaborative Perinatal Project when they were in their mid thirties, a SD increase in IQ at age seven was associated with a 50% reduction in lifetime risk of GAD. The unadjusted odds ratio (95% CI) for GAD with onset in adulthood was 0.81 (0.52 to 1.27) per SD increase in IQ. This is similar in magnitude to the association found in the present study where the equivalent odds ratio for onset of GAD since enlistment was 0.83 (0.76-0.92) per SD increase in cognitive ability. Higher childhood IQ was linked with a lower risk of anxiety disorders overall (GAD, phobias and panic disorder) in adolescence or early adulthood in the Christchurch Health and Development Study, but the relation was severely attenuated and no longer significant after adjustment for potential confounding factors. The present study was based on larger numbers than either of these investigations. That factor together with the older age of our study sample may in part explain why we found a more robust association between IQ and GAD than these earlier studies. The prevalence of GAD increases substantially with age.

Few previous studies have examined the link between cognitive ability and depression and findings have been inconsistent. In a study of hospital admissions over a 27 year period, risk of severe depression was significantly higher in men with a lower IQ in late adolescence. Lower IQ in childhood was associated with greater depression and anxiety at age 53, as measured by the General Health Questionnaire (GHQ-28), though only in women. However, in a follow-up study of another cohort where depression was assessed by structured diagnostic interview, there was no evidence to link IQ in childhood with risk of depression by age 25. In this study, men with lower cognitive ability in late adolescence experienced a significantly increased risk of developing depression. We found no link between cognitive ability and depression when it co-occurred with GAD. The reasons for this are unclear. This
pattern of comorbidity occurs frequently in the population and individuals with pure GAD or GAD plus major depression tend to show a similar risk history.\textsuperscript{28}

Only one previous study has examined the link between IQ and drug abuse. In a longitudinal study of a Danish male cohort, those with higher cognitive ability at age 12 had a reduced risk of drug or alcohol abuse, as measured by diagnosis on hospital admission or mention on death certificates, over a 30-year follow-up period.\textsuperscript{8} In the present study, we found no significant association between IQ and risk of drug abuse or dependence. It is likely that the relatively few cases of drug abuse found among the men who took part in the psychological examination were at the milder end of the spectrum compared to the cases observed in the Danish cohort whose disorder was severe enough to have caused their hospitalisation or death.

Higher IQ in childhood was also associated with a reduced risk of alcohol abuse or dependence in this Danish cohort.\textsuperscript{8} This is consistent with findings linking higher IQ with healthier behaviours in terms of smoking,\textsuperscript{29, 30} diet and exercise.\textsuperscript{31} In this study, we found that men with higher cognitive ability were at significantly lower risk of alcohol abuse or dependence at any time after enlistment, though the relation between cognitive ability and risk of alcoholism in the year prior to the mid-life examination was weaker and attenuated by adjustment, particularly for army income.

Recent findings from two UK national birth cohorts found a very different association between IQ and risk of alcohol abuse to that found here. In follow-ups of the 1970 British Cohort Study and the 1946 National Survey of Health and Development, carried out when the participants were aged 30 and 53 years respectively, higher IQ in childhood was associated
with an increased risk of scoring positive for alcohol problems on the CAGE inventory.\textsuperscript{27, 32}

The CAGE has been validated against the DIS and found to be an effective screening instrument.\textsuperscript{33} The reasons for the discrepancy between these findings and the results of the present study and that in Denmark are unclear,\textsuperscript{8} but one explanation might be that data on the UK cohorts was collected at a time and in a society where more frequent drinking tends to be associated with higher income and greater educational attainment.\textsuperscript{34}

\textit{Plausible mechanisms}

The mechanisms that underlie the link between cognitive ability and risk of psychopathology are still unclear. One possible explanation is that lower cognitive ability is acting as a marker of impaired neurodevelopment that itself affects the development of psychiatric disorder.\textsuperscript{3, 9}

The suggestion in our findings that lower cognitive ability may be more strongly linked to risk of having comorbid rather than pure disorders could indicate that individuals with such conditions have more vulnerable brains. This vulnerability might be genetically mediated. In a study of pre-morbid cognitive ability and risk of PTSD in twins, the variance in PTSD explained by cognitive ability was accounted for entirely by common genetic factors.\textsuperscript{6} There is evidence that several of the disorders studied here share some genetic influences.\textsuperscript{35, 36} Twin studies suggest that common genetic liability explains a large part of the comorbidity between major depression and PTSD,\textsuperscript{37} and major depression and GAD,\textsuperscript{38, 39} although shared environmental factors largely accounted for the association between PTSD and conduct disorder,\textsuperscript{40} perhaps due to adverse family environment in childhood. Another explanation for the link between lower cognitive ability and psychiatric disorder might be that people with a lower IQ have a reduced perception of control over their lives. Having an internal locus of control or a stronger sense of self-efficacy decreases the risk of anxiety and depression,\textsuperscript{41} and PTSD.\textsuperscript{42} Evidence in children suggest that an internal locus of control is more common in
individuals with a higher IQ. A further potential mechanism might be that individuals with a higher IQ are less likely to experience socio-economic disadvantage in adult life. Socio-economic disadvantage is linked with a high risk of experiencing depression or anxiety. Although we controlled for army income as a potential confounding factor, this might be an over-adjustment as intelligence could have influenced the rank they attained and thereby their risk of psychiatric disorder. It is also possible that individuals with greater cognitive resources are better able to interpret stressful or potentially traumatic stimuli or events in a way that nullifies or reduces their impact on mental equilibrium and prevents them succumbing to PTSD.

**Strengths and limitations**

The strengths of this study are its size and the availability of data on factors that might potentially confound the relations between cognitive ability and psychiatric disorder. The study also has some limitations. Firstly, there has been some criticism of the psychiatric diagnoses in the Vietnam Experience Study, particularly of PTSD, because the prevalence of this disorder was markedly lower than those found in the National Vietnam Veterans Readjustment Study, and in other surveys conducted at the same time. That some cases of psychiatric disorder in the VES participants may have been unidentified could result in an underestimate of the true strength of the relation between cognitive ability and later risk of psychiatric disorder, particularly PTSD. Secondly, we examined risk of generalized anxiety disorder only. It is possible that our results might have been different had we examined other forms of anxiety disorders. Thirdly, selection into military service is likely to have excluded men with severe early-onset psychopathology, so the cases of psychiatric disorder in our sample may be predominantly those with mild or moderate disease. This reduced variance may also have resulted in an underestimation of the true effect of cognitive ability on later
risk. Thirdly, the diagnosis of PTSD did not permit us to identify men who had experienced traumatic events but had no symptoms. In order to restrict our analyses of PTSD to men who had been exposed to trauma, we had to use a subgroup of combat-exposed Vietnam veterans; this means that some men who had a diagnosis of PTSD after non-combat related trauma were excluded, though numbers of such cases were low (n=34 for disorder since enlistment). Fourthly, retrospective self-report of first age at onset of symptoms may be subject to error, resulting in misclassification as to timing of disease onset. Such reports are widely used in large-scale psychiatric surveys and have shown good reliability and validity over the short term, but to collect lifetime prevalence data respondents have to recall the presence and co-occurrence of symptoms, possibly many years after their first occurrence. Problems with recall can cause underestimation of lifetime prevalence. This may explain why cognitive ability, and all risk factors, tended - with the exception of alcohol abuse or dependence - to be more strongly associated with current disorder than with disorder since enlistment. Finally, although we excluded men with prior psychiatric disorder, it is possible that some men’s cognitive performance may have been influenced by the presence of disease.

The results of this study suggest that lower cognitive ability is a risk factor for several forms of psychopathology, including, perhaps, some patterns of comorbidity. Distinct mechanisms may underlie some of these associations, particularly those where the disorder has a strong behavioural component, such as alcohol abuse or dependence. Understanding the mechanisms whereby cognitive ability is linked to individual patterns of psychopathology may help inform intervention.
Acknowledgments

Catharine Gale is supported by the Medical Research Council, Laust Mortensen by The National Institute of Public Health, Denmark, and John Barefoot and Stephen Boyle by the National Heart Lung and Blood Institute and the National Institutes on Aging at NIH (grant no. RO1-HL54780). David Batty is a UK Wellcome Trust Fellow (WBS U.1300.00.006.00012.01). Ian Deary is the recipient of a Royal Society-Wolfson Research Merit Award. Catharine Gale carried out the statistical analysis, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References


(3) Zammit S, Allebeck P, David AS et al. A longitudinal study of premorbid IQ Score and risk of developing schizophrenia, bipolar disorder, severe depression, and other nonaffective psychoses. *Arch Gen Psychiatry* 2004;61:354-60.


(24) Breslau N, Lucia VC, Alvarado GF. Intelligence and other predisposing factors in exposure to trauma and posttraumatic stress disorder: a follow-up study at age 17 years. *Arch Gen Psychiatry* 2006;63:1238-45.


Table 1. Cognitive ability score at enlistment according to demographic and army service characteristics (N=3258)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
<th>Mean (SD) cognitive ability score</th>
<th>Correlation with cognitive ability score</th>
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<tr>
<td>Age at enlistment (yrs)</td>
<td></td>
<td></td>
<td>0.23*</td>
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<tr>
<td>≤ 18</td>
<td>408 (12.5)</td>
<td>97.4 (12.9)</td>
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<tr>
<td>19 - 22</td>
<td>2522 (77.4)</td>
<td>101.1 (15.1)</td>
<td></td>
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<tr>
<td>≥ 23</td>
<td>328 (10.1)</td>
<td>106.2 (17.6) *</td>
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<tr>
<td>Army income (US$/week)</td>
<td></td>
<td></td>
<td>0.30*</td>
</tr>
<tr>
<td>83-119</td>
<td>352 (10.8)</td>
<td>93.2 (13.2)</td>
<td></td>
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<td>120-144</td>
<td>1621 (49.8)</td>
<td>98.7 (15.3)</td>
<td></td>
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<tr>
<td>145</td>
<td>1285 (39.4)</td>
<td>106.3 (14.0) *</td>
<td></td>
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<td>Place of service</td>
<td></td>
<td></td>
<td>-</td>
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<tr>
<td>Ever in Vietnam</td>
<td>1753 (53.8)</td>
<td>100.0 (14.9)</td>
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<td>Other overseas</td>
<td>685 (26.6)</td>
<td>101.5 (15.6)</td>
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<td>US only</td>
<td>640 (19.6)</td>
<td>103.6 (15.5) ¶</td>
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<td>Ethnic group</td>
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<td>White</td>
<td>2634 (80.8)</td>
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<td>Other</td>
<td>209 (6.4)</td>
<td>93.7 (14.3) ¶</td>
<td></td>
</tr>
</tbody>
</table>

*p for trend<0.001. ¶ p for difference<0.001
Table 2: Unadjusted odds ratios for psychiatric disorders since enlistment or currently according to cognitive ability

<table>
<thead>
<tr>
<th></th>
<th>No of cases (%)</th>
<th>Odds ratios (95% CIs) per SD decrease in cognitive ability, unadjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Based on all participants (n=3258)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>242 (7.4)</td>
<td>1.15 (1.01, 1.30)</td>
</tr>
<tr>
<td>Currently</td>
<td>145 (4.5)</td>
<td>1.32 (1.12, 1.56)</td>
</tr>
<tr>
<td>GAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>473 (14.5)</td>
<td>1.20 (1.09, 1.32)</td>
</tr>
<tr>
<td>Currently</td>
<td>221 (6.8)</td>
<td>1.43 (1.27, 1.64)</td>
</tr>
<tr>
<td>Alcohol abuse or dependence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>1035 (32.4)</td>
<td>1.25 (1.16, 1.35)</td>
</tr>
<tr>
<td>Currently</td>
<td>308 (9.5)</td>
<td>1.20 (1.08, 1.35)</td>
</tr>
<tr>
<td>Drug abuse or dependence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>318 (9.8)</td>
<td>1.09 (0.97, 1.22)</td>
</tr>
<tr>
<td>Currently</td>
<td>80 (2.5)</td>
<td>1.11 (0.90, 1.39)</td>
</tr>
<tr>
<td><strong>Based on combat-exposed Vietnam veterans (n=1659)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>161 (9.7)</td>
<td>1.32 (1.12, 1.56)</td>
</tr>
<tr>
<td>Currently</td>
<td>131 (8.1)</td>
<td>1.39 (1.18, 1.67)</td>
</tr>
</tbody>
</table>
Table 3: Odds ratios for psychiatric disorders since enlistment or currently according to cognitive ability, adjusted separately then together for potential confounders

<table>
<thead>
<tr>
<th></th>
<th>Based on all participants (n=3258)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Ethnicity</td>
<td>Adjustments</td>
<td>Adjustments</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Army income</td>
<td>Place of service</td>
<td></td>
</tr>
<tr>
<td>Major depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>1.15 (1.01, 1.30)</td>
<td>1.18 (1.02, 1.35)</td>
<td>1.12 (0.99, 1.32)</td>
<td>1.12 (0.99, 1.29)</td>
<td>1.11 (0.96, 1.30)</td>
</tr>
<tr>
<td>Currently</td>
<td>1.32 (1.12, 1.56)</td>
<td>1.32 (1.11, 1.56)</td>
<td>1.28 (1.09, 1.52)</td>
<td>1.30 (1.11, 1.54)</td>
<td>1.23 (1.03, 1.47)</td>
</tr>
<tr>
<td>GAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>1.20 (1.09, 1.32)</td>
<td>1.20 (1.09, 1.33)</td>
<td>1.16 (1.05, 1.28)</td>
<td>1.19 (1.08, 1.30)</td>
<td>1.16 (1.04, 1.30)</td>
</tr>
<tr>
<td>Currently</td>
<td>1.43 (1.27, 1.64)</td>
<td>1.44 (1.25, 1.67)</td>
<td>1.41 (1.23, 1.64)</td>
<td>1.41 (1.23, 1.61)</td>
<td>1.39 (1.19, 1.61)</td>
</tr>
<tr>
<td>Alcohol abuse or dependence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>1.25 (1.16, 1.35)</td>
<td>1.27 (1.18, 1.37)</td>
<td>1.19 (1.10, 1.28)</td>
<td>1.23 (1.15, 1.33)</td>
<td>1.19 (1.10, 1.30)</td>
</tr>
<tr>
<td>Currently</td>
<td>1.20 (1.08, 1.35)</td>
<td>1.14 (1.01, 1.28)</td>
<td>1.12 (1.00, 1.27)</td>
<td>1.19 (1.06, 1.35)</td>
<td>1.04 (0.92, 1.19)</td>
</tr>
<tr>
<td>Based on combat-exposed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vietnam veterans (n=1659)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>1.32 (1.12, 1.56)</td>
<td>1.35 (1.15, 1.61)</td>
<td>1.28 (1.09, 1.52)</td>
<td>-</td>
<td>1.33 (1.11, 1.58)</td>
</tr>
<tr>
<td>Currently</td>
<td>1.39 (1.18, 1.67)</td>
<td>1.39 (1.14, 1.67)</td>
<td>1.33 (1.10, 1.61)</td>
<td>-</td>
<td>1.38 (1.14, 1.66)</td>
</tr>
</tbody>
</table>
Table 4: Odds ratios (95% CI) for having a pure or a comorbid form of psychiatric disorder since enlistment or currently according to cognitive ability

<table>
<thead>
<tr>
<th>Based on all participants (n=3258)</th>
<th>No (% of cases)</th>
<th>Unadjusted</th>
<th>Adjusted for ethnicity, army income and place of service</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure alcohol abuse/dependence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>467 (14.3)</td>
<td>1.11 (1.01, 1.22)</td>
<td>1.14 (1.02, 1.27)</td>
</tr>
<tr>
<td>Currently</td>
<td>192 (5.89)</td>
<td>1.10 (0.95, 1.27)</td>
<td>1.03 (0.88, 1.20)</td>
</tr>
<tr>
<td>GAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>146 (4.48)</td>
<td>0.90 (0.77, 1.05)</td>
<td>0.98 (0.83, 1.20)</td>
</tr>
<tr>
<td>Currently</td>
<td>74 (2.27)</td>
<td>1.19 (0.95, 1.49)</td>
<td>1.23 (0.97, 1.59)</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>57 (1.75)</td>
<td>0.78 (0.59, 1.02)</td>
<td>0.89 (0.66, 1.19)</td>
</tr>
<tr>
<td>Currently</td>
<td>26 (0.01)</td>
<td>1.03 (0.70, 1.49)</td>
<td>1.20 (0.79, 1.85)</td>
</tr>
<tr>
<td>Depression &amp; GAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>49 (1.50)</td>
<td>0.85 (0.64, 1.12)</td>
<td>0.83 (0.61, 1.14)</td>
</tr>
<tr>
<td>Currently</td>
<td>53 (1.63)</td>
<td>1.19 (0.90, 1.53)</td>
<td>1.08 (0.81, 1.45)</td>
</tr>
<tr>
<td>Depression &amp; alcohol abuse/dependence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>36 (1.10)</td>
<td>1.18 (0.86, 1.61)</td>
<td>1.02 (0.72, 1.45)</td>
</tr>
<tr>
<td>Currently</td>
<td>26 (0.01)</td>
<td>1.45 (1.00, 2.23)</td>
<td>1.32 (0.86, 2.00)</td>
</tr>
<tr>
<td>GAD &amp; alcohol abuse/dependence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>125 (3.84)</td>
<td>1.30 (1.10, 1.54)</td>
<td>1.14 (0.94, 1.39)</td>
</tr>
<tr>
<td>Currently</td>
<td>38 (1.17)</td>
<td>1.51 (1.09, 2.04)</td>
<td>1.27 (0.89, 1.79)</td>
</tr>
<tr>
<td>GAD &amp; alcohol abuse/dependence &amp; depression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>38 (1.17)</td>
<td>1.15 (0.84, 1.56)</td>
<td>1.02 (0.74, 1.45)</td>
</tr>
<tr>
<td>Currently</td>
<td>28 (0.01)</td>
<td>1.49 (0.76, 2.94)</td>
<td>1.23 (0.58, 2.63)</td>
</tr>
</tbody>
</table>

Based on combat-exposed Vietnam veterans (n=1659)

<table>
<thead>
<tr>
<th>No (% of cases)</th>
<th>Unadjusted</th>
<th>Adjusted for ethnicity and army income</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure PTSD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>21 (1.27)</td>
<td>1.07 (0.70, 1.66)</td>
</tr>
<tr>
<td>Currently</td>
<td>48 (2.89)</td>
<td>1.21 (0.91, 1.61)</td>
</tr>
<tr>
<td>PTSD &amp; GAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>14 (0.01)</td>
<td>1.33 (0.79, 1.22)</td>
</tr>
<tr>
<td>Currently</td>
<td>12 (0.01)</td>
<td>2.50 (1.41, 4.55)</td>
</tr>
<tr>
<td>PTSD &amp; alcohol abuse/dependence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>38 (2.29)</td>
<td>1.35 (0.99, 1.85)</td>
</tr>
<tr>
<td>Currently</td>
<td>23 (1.39)</td>
<td>1.20 (0.81, 1.82)</td>
</tr>
<tr>
<td>PTSD &amp; GAD &amp; depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Since enlistment</td>
<td>16 (0.01)</td>
<td>1.92 (1.18, 3.13)</td>
</tr>
<tr>
<td>Currently</td>
<td>25 (1.51)</td>
<td>2.17 (1.47, 3.22)</td>
</tr>
<tr>
<td></td>
<td>Since enlistment</td>
<td>Currently 1</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>PTSD &amp; GAD &amp; alcohol abuse/dependence</td>
<td>24 (1.45)</td>
<td>1.64 (1.09, 2.43)</td>
</tr>
<tr>
<td>Currently</td>
<td>1 (-)</td>
<td>-</td>
</tr>
<tr>
<td>PTSD &amp; depression &amp; alcohol abuse/dependence</td>
<td>13 (0.01)</td>
<td>0.90 (0.52, 1.56)</td>
</tr>
<tr>
<td>Currently</td>
<td>3 (0.001)</td>
<td>-</td>
</tr>
<tr>
<td>PTSD &amp; GAD &amp; depression &amp; alcohol abuse/</td>
<td>24 (1.45)</td>
<td>1.63 (1.09, 2.43)</td>
</tr>
<tr>
<td>Currently</td>
<td>5 (0.003)</td>
<td>2.77 (1.12, 6.66)</td>
</tr>
</tbody>
</table>
Legend for Figure 1: Venn diagram showing unadjusted odds ratios for pure and comorbid forms of psychiatric disorder (a) since enlistment and (b) currently for a SD decrease in cognitive ability. N=3258, except for analyses of pure and comorbid forms of PTSD which are based on combat-exposed Vietnam veterans (n=1659)

(a)

Pure depression
0.78 (0.59-1.01)
n=57

0.47 (0.18-1.30)
n=5

0.90 (0.52-1.56)
n=13

1.18 (0.86-1.61)
n=36

Pure GAD
0.90 (0.77-1.05)
n=146

1.92 (1.18-3.13)
n=16

1.63 (1.09-2.43)
n=24

1.15 (0.84-1.56)
n=38

1.30 (1.10-1.54)
n=125

Pure PTSD
1.07 (0.70-1.66)
n=21

1.35 (0.89-1.85)
n=38

Pure alcohol abuse or dependence
1.11 (1.01-1.22)
n=467

(b)

Pure depression
1.03 (0.70-1.49)
n=26

0.89 (0.50-1.49)
n=13

1.45 (1.00-2.23)
n=26

Pure GAD
1.19 (0.95-1.49)
n=74

2.17 (1.47-3.22)
n=25

2.77 (1.12-6.66)
n=5

1.49 (0.76-2.94)
n=28

1.51 (1.09-2.04)
n=38

Pure PTSD
1.21 (0.91-1.61)
n=48

1.20 (0.81-1.82)
n=23

Pure alcohol abuse or dependence
1.10 (0.95-1.27)
n=192