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Intelligence in early adulthood and life span up to 65 years later in male elderly twins

TRACEY HOLSINGER1,2, MICHAEL HELMS2, BRENDA PLASSMAN2
1Durham VA Medical Center, Psychiatry, Durham, NC, USA
2Duke University Medical Center, Psychiatry, Durham, NC, USA

Address correspondence to: Tracey Holsinger. Tel: (919)286-6933; Fax: (919)416-5832. Email: tracey.holsinger@med.va.gov

Abstract

Background: previous research has reported that greater intelligence in early life is associated with longer lifespan. Whether this relationship is mediated by genetic factors or environmental factors, some of which could be modified by an individual, is unclear.

Objective: we examined the association between intelligence test scores, obtained during the 1940s, and age at death in a group of 492 male twin pairs, members of the National Academy of Sciences - National Research Council Twins Registry of WWII veterans.

Design: using self-report information collected in the 1960s, we examined whether modifiable risk factors for mortality, such as use of tobacco and alcohol, cardiovascular disease, and body mass index altered the association between intelligence and longevity.

Results: when each member of a twin pair was treated as an independent observation, higher intelligence test scores were associated with longer life span ($P = 0.0002$). Modifiable risk factors were associated with life span as expected. However, in co-twin control analyses in which one twin served as the control for the other twin, neither intelligence nor any modifiable risk factors showed a significant association with life span.

Conclusion: our findings suggest that genetics and early life environmental factors contribute heavily to lifespan and when one controls for these factors using twins, the effect of intelligence on longevity is diminished.

Keywords: intelligence, survival, twins, risk factors, elderly
Introduction

Previous studies have reported that higher scores on intelligence tests in childhood and young adulthood may predict a longer life span [1–4]. These findings prompted a few researchers to investigate whether the effect of intelligence or educational level on longevity is altered by other well-known risk factors of premature mortality such as tobacco use and cardiovascular disease [5, 6]. The general conclusion from these latter studies is that the effect of intellect is fairly independent of the effect of health behaviours and medical conditions on mortality. However, these studies have not assessed the extent to which genetic influences may explain some of the association between these risk variables and mortality.

Longevity has a genetic component. Estimates of the heritability of life span, as measured in twins, have varied somewhat but are generally estimated around 0.25 [7–9]. This might be due to the effects of specific genes or might be mediated by genetic influences on life-shortening conditions or life-style factors, such as socio-economic status, cardiovascular disease, smoking and body mass index (BMI). Some of these factors, such as smoking, BMI and cardiovascular disease, themselves have been shown to have genetic components [10, 11].

It is possible that the same latent genetic or environmental influences underlie both these various medical conditions and longevity, and that a lack of understanding of such confounding may result in erroneous inferences about the causality in the relationship between such factors and longevity. In the case of BMI and smoking, there does not appear to be an overlap between the genetic and shared environmental influence on these factors and longevity [12]. However, little is known about the overlap in aetiology of some other conditions, such as cardiovascular disease. Given that intelligence also has a genetic component [13, 14], one might ask whether the same issue of potential confounding may explain the reported association between intelligence and longevity.

We examined this question using twins. The study of twins inherently controls for many genetic and early life shared environmental influences. Using the National Academy of Sciences - National Research Council (NAS-NRC) Twin Registry of WWII Veterans from the United States, we examined the association between intelligence in early adulthood and longevity approximately through age 80. We also investigated whether smoking, alcohol use, BMI, and other cardiovascular risk in midlife contributed to mortality, and whether any of these factors altered the association between intelligence and longevity. Finding an association between early life intellect and longevity (independent of the other factors) within-twin pairs who share not only many (or all) of the same genes, but also childhood socio-economic status, would provide support to the unique contribution of IQ to life span.

Materials and methods

Subjects

The subjects were members of the NAS-NRC Twin Registry of WWII Veterans born between 1917 and 1927. To be included in the study, both members of the twin pair had to have a military entrance examination score available and had to have completed a questionnaire that was mailed to Twin Registry members in 1967 to collect information on a number of medical conditions and health behaviours. The resulting cohort included 492 twin pairs who had lived at least into their 40s, of which 301 were monozygotic and 191 were dizygotic. Of these, as of 31 December 2004, both members were deceased in 115 pairs, one twin was deceased in 155 pairs, and both twins were still alive in the remaining 222 pairs. In 72 pairs, zygosity was determined from buccal and blood DNA samples. In 420 pairs, zygosity was determined from the NAS-NRC Twins Registry data based on the best available information from questionnaire responses, fingerprint analysis, and anthropometric data from military records [15, 16]. Methods of establishing zygosity are estimated by cross-validation to be 97% correct [17].

To obtain as complete data as possible, death information was determined from all available sources: (i) the computer-based Beneficiary Identification and Records Locator Subsystem of the Veterans Administration, (ii) telephone calls with the subject’s family, or (iii) the Social Security Death Index database.

Measure of intelligence

As part of the entrance procedures for military service during the 1940s, all army inductees and enrollees in officers candidate school were administered the Army General Classification Test (AGCT) [18], while those entering the navy were administered the General Classification Test (GCT) [19]. The AGCT was developed to be a ‘test of general learning ability’ and the GCT were designed to measure verbal aptitude. Both tests correlate with education ($r = 0.65–0.73$) [20, 21] and with other tests that assess or are correlated with general intellect. For example, results of the AGCT have correlated strongly ($r = 0.83$) with results of the Wechsler–Bellevue Intelligence Scale, which measures verbal and nonverbal factors of intelligence [22].

Test scores for the AGCT and the GCT were standardised to a common metric with a mean of 10 and standard deviation of 1. Assumptions underlying this common standardisation were that the two variable’s population distributions were, in fact, very similar in shape and would not have differed in their mean scale measures had both been administered a common scale. We jointly refer to the scores from these tests as GCT/AGCT scores.

Mailed questionnaires

Information on a number of medical conditions and health behaviours was collected on a questionnaire mailed to the
registry members in 1967. For this study, we selected life-
style factors or medical conditions that previously have been
reported to be associated with longevity, but also have the
total potential to be modified by the individual and are likely
influenced by genes. The factors were defined as follows. BMI
was calculated from self-reported height and weight.
Smoking history required that the individual be a current
smoker (at the time of the 1967 survey) and then was defined
by the number of pack-years smoked. Heavy alcohol use was
defined as any of the following: reported daily consumption
of more than three beers, more than one-half bottle of
wine or more than three drinks of liquor or reported daily
hangover or drinking to intoxication daily.

The Rose Questionnaire, developed as a tool to diagnose
angina pectoris in epidemiological studies [23], was included
in the mailed questionnaire. A positive Rose Questionnaire
required a report: (i) of pain in either the sternum or left arm
and left anterior chest, (ii) provoked by exertion, (iii) requiring
a lessening of exertion or use of nitroglycerin, and (iv) pain
disappearing within 10 min when subject is standing still.
We categorised the responses on the Rose Questionnaire
in two ways; first as a dichotomous variable (i.e. positive versus
negative) as it was designed and then as a continuous variable
from 0 to 4, representing the sum of the Rose items endorsed
to capture all available information. We created an additional
variable ranging from 0 to 4, representing the sum of the Rose items endorsed
for a positive Rose Questionnaire, a history of severe chest pain, and a history of myocardial
infarction.

Data analysis
Means, standard deviations, and frequencies were calculated.
Heritability, the ratio of genetic variation to total variation,
was calculated for GCT/AGCT scores, age at death, a
history of severe chest pain, and a history of myocardial
infarction.

Results
Table 1 provides descriptive statistics grouped by living and
decesed status. Information regarding whether the twins had
lived together during childhood was collected as part of the
mailed questionnaire and indicated that all but one pair had

<table>
<thead>
<tr>
<th>Table 1. Characteristics of twins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
</tr>
<tr>
<td>N</td>
</tr>
<tr>
<td>Age at censoring/death</td>
</tr>
<tr>
<td>Test score</td>
</tr>
<tr>
<td>Body mass index</td>
</tr>
<tr>
<td>Pack-years smoked</td>
</tr>
<tr>
<td>Rose Questionnaire positive</td>
</tr>
<tr>
<td>Vascular score ≥1</td>
</tr>
<tr>
<td>Heavy alcohol use</td>
</tr>
</tbody>
</table>

Note: ‘Alive’ column is all living individuals; ‘Deceased’ column is all deceased; ‘First deceased’ column includes
the twins that died first within a pair; and ‘Second deceased’ or ‘Living’ column includes the co-twins of those
in the First deceased column. ‘Mean’ (standard deviation) or percentages are given. ‘Age at censoring’ refers to
the age as of 31/12/2004 among cohort members still alive. ‘Test score’ is a transformation of GCT or AGCT
test scores. ‘Pack-years smoked’ refers to number of packs of cigarettes smoked a day times the number of years
cigarettes were smoked. The ‘Vascular Score’ is made up of the Rose Questionnaire, a history of severe chest pain
and a history of myocardial infarction midlife. ‘Heavy Drinking’ is defined as any of the following: reported daily
consumption of more than three beers, more than one-half bottle of wine or more than three drinks of liquor or
reported daily hangover or drinking to intoxication daily.

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lived their first 15 years together. Table 2 shows heritability estimates for GCT/AGCT test scores and many of the health variables. Although GCT/AGCT showed substantial heritability, scores on this measure for two members of a twin pair differed on average by 0.55 standardised units (SD = 0.58). For twin pairs in which one twin had died, the mean difference between age at death for that twin and age of censoring for the living twin was 6.7 (SD = 3.7) years. In the twin pairs in which both twins had died, the mean difference between ages of death was 7.7 (SD = 6.5) years.

Case-control analyses

Figure 1 shows that when subjects were analysed as individuals (not members of twin pairs), a longer life span was associated with higher intelligence (hazard ratio (HR) = 0.698 per 2 standard units, \( P = 0.0013 \)). As expected, smoking history, heavy alcohol use, symptoms suggestive of vascular disease both from the Rose Questionnaire and the vascular score, were all correlated with life span. In models that included GCT/AGCT score, source of test score, and age at questionnaire as covariates, the following relationships were found. Smoking, as measured in pack-years, was correlated with increased risk of death (HR 1.29, \( P < 0.0001 \)). Heavy alcohol use was associated with shortened life span (HR 2.26, \( P < 0.0001 \)), Coronary artery disease as measured by a positive Rose Questionnaire was associated with an increased risk of dying (HR 1.67, \( P = 0.045 \)). Using the items of the Rose Questionnaire summed was also associated with an increased risk of dying (HR 1.52, \( P = 0.009 \)). A higher vascular score was also associated with an increased risk of dying (HR 1.76, \( P < 0.0001 \)). Based on previous literature [25], we examined the linear and quadratic function for body mass index and found no association with longevity.

No significant interactions were found for smoking, heavy alcohol use or any vascular scores with IQ as measured in early adulthood. Including these variables in models with the variable for intelligence did not change the effect of IQ on life span. The dummy variable denoting the source of the test score (i.e. AGCT or GCT) was never significant in the models (most significant probability = 0.19, but generally it was >0.8).

Co-twin control analyses

In the co-twin control model conditional on twin pairing, IQ was no longer associated with longevity (HR = 1.06, \( P = 0.84 \)). To explore whether the intra-pair similarity on GCT/AGCT was limiting our ability to detect an association, we then re-ran the analyses limiting the sample to only twin pairs for whom the within-pair difference on the IQ testing was greater than the mean intra-pair difference for the entire group (360 pairs). In this analysis, the effect of test scores on life span was stronger but still did not approach statistical significance (\( P = 0.59 \)).

In co-twin control models using the entire sample, smoking history (HR = 1.11, \( P = 0.10 \)), heavy alcohol use (HR = 1.39, \( P = 0.23 \)), BMI (HR = 0.88, \( P = 0.34 \)), and

<table>
<thead>
<tr>
<th>Risk variable</th>
<th>Monozygotic twins</th>
<th>Dizygotic twins</th>
<th>( \hat{h}^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rose Questionnaire (positive or negative)</td>
<td>0.074</td>
<td>-0.041</td>
<td>0.15</td>
</tr>
<tr>
<td>Rose questions (as a continuous variable)</td>
<td>0.30</td>
<td>-0.060</td>
<td>0.60</td>
</tr>
<tr>
<td>Vascular score</td>
<td>0.39</td>
<td>-0.049</td>
<td>0.78</td>
</tr>
<tr>
<td>Pack-years smoked</td>
<td>0.39</td>
<td>0.45</td>
<td>0.24</td>
</tr>
<tr>
<td>Heavy drinking</td>
<td>0.26</td>
<td>0.05</td>
<td>0.42</td>
</tr>
<tr>
<td>Test score</td>
<td>0.79</td>
<td>0.47</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Note: \( \hat{h}^2 \) = Falconer’s estimate of heritability. Risk variables are defined in legend of Table 1.

Figure 1. Kaplan Meier survival curves for four categorised levels of the AGCT/GCT test scores.

In co-twin control analyses, only the twin pairs in which one or both members of the pair were deceased were informative. In twin pairs where both members survive, no events (death) occur within-twin strata and they do not contribute information to the analysis. However, the reduced number of informative individuals did not seem to explain the lack of significant findings, as the proportional hazard regression coefficient also decreased between the independent analyses and the co-twin control analyses.

Discussion

In case-control analyses, higher IQ predicted longer life span through approximately age 80 years. It is striking that
the magnitude of the association between IQ and life span reported in the present study is close to that reported by a previous study, that is, a relative risk of 0.68 for a two-standard deviation change for men [3]. The presence of modifiable risk factors in midlife such as smoking, heavy alcohol use and vascular disease also impacted life span in predictable ways, but did not alter the association between IQ and longevity. In contrast, in co-twin control analyses where each twin was used as a matched control for his co-twin, neither the differences in IQ nor a modifiable risk factors had an appreciable effect on life span.

To our knowledge, this is the first study to investigate in twins the reported association between early life intellect and life span. The discrepant outcomes from our case-control and co-twin control analyses suggest that IQ alone may have little impact on longevity. Rather, higher scores on intelligence tests may reflect the combination of genetic predisposition and healthy early environment—contributing to a higher level of ‘fitness’ of both the brain and body that results in a longer life span [3]. We note, however, that these factors are largely shared in twin pairs, leading to reduced variation within pairs compared to biologically unrelated individuals. Although the within-twin pair differences in AGT/AGCT scores in our sample averaged about one-half of a standard deviation; we cannot exclude the possibility that this somewhat limited variability was insufficient to detect an impact on life span.

A few other twin studies have investigated whether the genetic influences on mortality are accounted for by the genetic influences on covariates such as smoking, BMI, heavy alcohol use and vigorous physical exercise [9, 10, 12]. Their findings suggest that there is little overlap between the genetic influences on smoking and BMI and mortality, but the findings for heavy alcohol use, physical activity and mortality are less clear-cut. It is noteworthy that these studies detected an association between these modifiable risk factors and mortality in co-twin control analyses, suggesting that limited within-twin pair variance does not explain our inability to find such an association in the present study. These previous studies suggest that multiple genetic and non-genetic factors contribute to life span. It is possible that analyses without the sort of genetic control provided by twins could result in over-interpretation of associations between IQ and life span. Our findings suggest that genetic and early life environmental factors contribute heavily to life span and when one controls these factors by using twins, the effect of intelligence is diminished. However, we acknowledge that, due to the within-twin pair similarity for many of these variables, the criteria for detecting differences is more stringent in the co-twin control design.

Limitations of our study include the right censoring of many of the veterans because they are still alive. It is possible that fewer censored individuals would alter the results somewhat; however, given that the co-twin control analyses typically did not approach significance, it is unlikely that this would alter the general conclusions. Another limitation is the use of self-reported risk factor information, which generally leads to an under-reporting of the risk factors. However, it seems unlikely that this would be limited to the veterans who lived longer and thus, would not explain our results.

Key points

- When twin pairs are analysed as individuals, modifiable risk factors affect longevity as expected.
- When twin pairs are analysed as individuals, higher intelligence in young adulthood is associated positively with longevity.
- When twin pairs are analysed as pairs, neither modifiable risk factors or intelligence is associated with longevity.
- Genetic factors and early childhood environment may weigh heavily on longevity.

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References

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