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Sibling Analysis of Adolescent Intelligence and Chronic Diseases in Older Adulthood

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PURPOSE: We examined whether associations of adolescent intelligence with chronic diseases in adulthood are explained by socioeconomic factors, health behaviors, or common sources of variance in intelligence and chronic disease risk.
METHODS: A prospective cohort study (Wisconsin Longitudinal Study) of high school graduates and their siblings with intelligence assessed in adolescence and chronic diseases reported in adulthood (n = 10,168; mean age 53.9 and n = 9051; mean age 64.8 in two follow-ups).
RESULTS: After adjustment for age and sex, greater intelligence was associated with lower risk of heart disease (odds ratio per 1 SD advantage in intelligence 0.93; 95% confidence interval 0.87−0.99), circulation problems (0.85; 0.79−0.92), stroke (0.80; 0.70−0.91), and diabetes (0.88; 0.81−0.95). Participants' risk of stroke and circulation problems also was predicted by their sibling's intelligence, suggesting potential common causes for intelligence and cerebrovascular diseases. Sibling analysis provided no support for shared family environment in explaining associations between intelligence and disease outcomes because between-families and within-siblings regression models were not different. Adjusting for common risk factors had little impact on these associations. In contrast, adjusting for adult socioeconomic status attenuated the associations by 25%−100% (66% on average).
CONCLUSIONS: Multiple mechanisms may link intelligence with occurrence of chronic diseases of major public health importance.
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KEY WORDS: Childhood, Chronic Disease, Health, Intelligence, IQ, Socioeconomic Status.

INTRODUCTION

Intelligence, measured using standard intelligence quotient (IQ)-type tests, is inversely associated with the risk of mortality (1–6) and with specific chronic health outcomes (1, 4–13), including cardiovascular disease (14–17), stroke (12), diabetes (18), some cancers (19), and respiratory diseases (20). However, evidence for the disease-specific associations is not entirely consistent, as the authors of some studies have reported no associations between intelligence and the aforementioned diseases (21–23), and the mechanisms underlying these associations are not well understood.

High intelligence may reduce disease risk indirectly through its association with better socioeconomic trajectories or more favorable health behaviors (6–8, 24–26). The few studies available on this issue suggest that this could be only a partial explanation for the intelligence−disease gradient. The issue is further complicated by the fact that indicators of socioeconomic status (SES) may function as proxy measures of intelligence, so that adjustment for SES may lead to overadjustment of the effects of intelligence (27–29).

There may also be common causes underlying cognitive development and health (1–7). Twin or sibling-pair comparisons would provide useful designs to examine this explanation (30), but apparently in only two studies have researchers conducted such analyses, with mixed findings. One suggested the association between intelligence and coronary heart disease mortality is not explained by shared family environment (31). In the other study, intelligence was not predictive of mortality within twin pairs (11), suggesting that shared genetic background or common environment might explain the IQ−mortality association. However, both of these studies were hampered by a small sample size (< 500 sibling pairs) and limited range of health outcomes.

We sought to examine the mechanisms linking intelligence and five chronic conditions that cause more than one-half of all deaths in the United States: heart disease,

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Selected Abbreviations and Acronyms

IQ = intelligence quotient (cognitive ability)
SES = socioeconomic status
WLS = Wisconsin Longitudinal Study
BMI = body mass index
CI = confidence interval
OR = odds ratio

stroke, obstructive pulmonary disease (bronchitis or emphysema), diabetes, and cancer (32). First, we assessed the role of common socioeconomic and behavioral risk factors in mediating the intelligence–disease associations. Second, we used sibling analysis to examine the potential contribution of shared family background or common causes in the associations between intelligence and disease risk.

METHODS

Participants

Data were from the ongoing Wisconsin Longitudinal Study (WLS; http://www.ssc.wisc.edu/wlsresearch) (33), a prospective cohort study of a random sample of 10,317 participants (5326 women, 4991 men) born between 1937 and 1940 followed since they graduated from Wisconsin high schools in 1957. After baseline data collection in 1957, survey responses were collected in 1964–1975–1992, and 2004. The WLS sample is broadly representative of white, non-Hispanic U.S. men and women who completed at least high school education. Among Americans ages 50 to 54 in 1990 and 1991, approximately 66% were non-Hispanic white persons who completed at least 12 years of schooling. It is estimated that about 75% of Wisconsin youth graduated from high school in the late 1950s; everyone in the primary WLS sample graduated from high school (33). In addition to the graduates, the WLS includes a sample of the graduates' siblings (one selected sibling per graduate for a subsample of graduates) (34).

The present study included all graduates and their siblings with data on adolescent IQ participating in the follow-up study in 1993–1994 (n = 10,168) or 2003–2005 (n = 9051). In sib-pair analyses, we included only sibling pairs who had no more than a 10-year age difference (85% of the eligible pairs), so that the comparisons would not be confounded by large age differences. These inclusion criteria resulted in 2420 sibling pairs with the necessary data for analysis using 1993–1994 survey, and 2900 pairs for the analysis with the 2003–2005 survey. Because of missing data, the number of participants varied slightly across models predicting different outcomes. Table 1 shows the descriptive statistics for the sample.

TABLE 1. Descriptive statistics

	Year 1993–1994	Year 2003–2005
Sample, graduate/sibling; %	67.5/32.5	68.5/31.5
Sex, men/women; %	46.4/53.6	45.6/54.4
Age	53.9 (3.9)	64.8 (3.8)
Intelligence percentile[a]	62.1 (25.7)	63.2 (25.4)
Heart disease, %/n	6.5/663	14.9/1286
Stroke, %/n	-	3.2/276
Circulation problems, %/n	5.9/598	9.8/805
Diabetes, %/n	4.3/438	11.8/1014
Cancer, %/n	3.8/388	10.9/943
Respiratory disease, %/n	6.7/682	6.7/552
Body mass index, kg/m^2	26.8 (4.6)	-
Physical activity, 0 to 3	1.6 (0.8)	-
Smoking, ex/current; %	37.5/17.4	-
Alcohol consumption[b]	0.6 (2.2)	-
Education, years	13.8 (2.3)	-
Occupational status[c]	50.7 (22.8)	-
Financial assets, log$_e$ dollars	11.8 (1.4)	-
n	10168	9051

Note: Values are means (and standard deviations) unless otherwise indicated.
[a]Henmon-Nelson test percentile rank based on national test takers.
[b]Number of times had five drinks or more at one time.
[c]1970 Duncan socioeconomic index (range, 2–6). An en-dash indicates no data collected.

Intelligence

Intelligence testing in adolescence was undertaken by the Wisconsin Testing Service which for many years routinely administered the Henmon-Nelson Test of Mental Ability (1954 revision) to all Wisconsin high school 11th graders. The Henmon-Nelson test is a 30-minute test consisting of 90 items in order of increasing difficulty. The test includes vocabulary, sentence completion, disarranged sentences, classification, logical selection, series completion, directions, analogies, anagrams, proverb interpretation, and arithmetic problems. The correlation between Henmon-Nelson and other IQ tests, such as Wechsler Adult Intelligence Scale, has been shown to be high, around r = 0.80 (35–37).

Disease Outcomes

The six disease items asked in the follow-up surveys included (i) heart disease (referred to as "heart trouble" in the first follow-up, and specified in the second follow-up as "a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems"), (ii) stroke (included only in the final follow-up phase), (iii) circulation problems, (iv) diabetes, (v) cancer, and (vi) respiratory disease (specified as "bronchitis or emphysema"). For each disease, the participants reported whether a medical professional had ever told them that they had the disease in question (yes/no).

Covariates

Health-related risk factors assessed in 1993–1994 included body mass index (calculated from self-reported weight in kg

divided by height in meters squared), current smoking (0 = never, 1 = ex-smoker, 2 = current smoker), physical activity (mean of frequency of moderate and vigorous physical activity per week), and heavy alcohol consumption (number of times five or more drinks consumed on one occasion during the last month). SES was assessed on the basis of education, occupational status (1970 Duncan Socioeconomic Index), and financial assets reported in 1993–1994. Less than 2% of the participants (including sibling sample) had not graduated from high school. The few missing values of covariate data were imputed with regression method by the use of all available data on other covariates. The proportion of imputed values was 2.5% for body mass index (BMI), 3.0% for physical activity, 1.6% for smoking, 0.3% for education, 3.0% for occupation, and 8.8% for financial assets. Missing values of covariates were not imputed when they were used as outcomes. Questions of alcohol consumption were administered only to a 79% subsample of graduates and siblings, so these data were not imputed,and alcohol consumption was analyzed separately only in the subsample.

Statistical Analysis

Multilevel logistic regression was used to take into account the nonindependence of sibling observations. The mediating role of covariates was determined by the percent reduction in the regression coefficient for intelligence after inclusion of these explanatory factors, using the formula: Attenuation $= 100 \times (\beta_{\text{age– and sex–adjusted}} - \beta_{\text{age–, sex– and explanatory factor–adjusted}})/\beta_{\text{age– and sex–adjusted}}$. In adjusting for SES as a mediating variable, we used factor analysis to create a composite score of SES, which accounted for 55% of the total variance.

In sibling analyses, we fitted models assessing between-families and within-siblings effects of intelligence by regressing each participant's disease risk against (i) the average intelligence of sibling-pairs and (ii) siblings' individual intelligence difference from the sibling-pair's mean intelligence (38). A negative between-families coefficient would indicate that siblings from high-intelligence families are, on average, healthier than siblings from low-intelligence families. This finding might reflect the effects of shared family environment and/or shared genes. A significant negative within-siblings coefficient, in turn, would indicate that among sibling-pairs, the sibling with greater intelligence is healthier than his/her sibling with lower intelligence (30). The total effect of intelligence is calculated as a weighted average of the within-siblings and between-families coefficients.

To address the issue of common cause of intelligence and disease risk in greater detail, we first examined whether a person's disease risk could be predicted by his/her sibling's intelligence. We then decomposed intelligence to: (i) shared intelligence factor, representing latent common causes of intelligence shared by sibling-pairs, and (ii) unique intelligence factor, representing intelligence variance unrelated to sibling's intelligence (residual of the shared intelligence factor; Fig. 1). In these models, each observation consisted of a sibling-pair, and coefficients were constrained to be equal for graduates and siblings. Intelligence and disease risk were adjusted for sex and age. If intelligence and chronic diseases share common genetic or environmental causes, then one should be able to predict a person's disease risk by sibling intelligence and by latent intelligence covariance shared by siblings. If there is no shared background, the associations between intelligence and disease should be observed only for individual's unique intelligence factor.

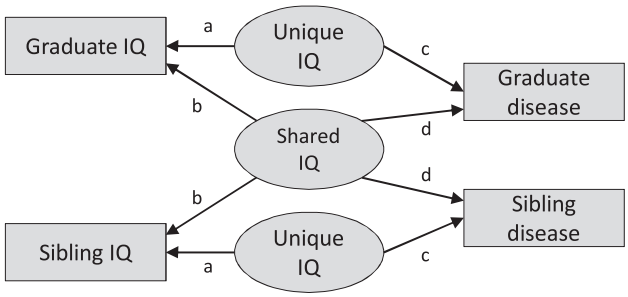

FIGURE 1. Structural equation model of siblings' shared and unique intelligence (IQ) predicting disease risk. Rectangles are observed variables; ovals are latent variables. Shared IQ represents latent common causes accounting for the covariance of siblings' IQ, and unique IQ is modeled as the residual of IQ variance not explained by shared intelligence. Paths marked with identical letters are constrained to be equal. IQ and disease risk are adjusted for sex and age (not shown).

All coefficients for intelligence are presented for standardized scale (mean = 0, SD = 1), and all models were adjusted for sex and age. There were no sex interaction effects in the main associations between intelligence and disease outcomes (all p-values $>.21$), justifying combined analyses for men and women. Statistical analysis was performed with STATA 11.0 (STATA Corp., College Station, TX) and MPlus 5 software.

RESULTS

In linear and logistic regression models adjusted for sex and age, greater intelligence predicted lower BMI (B, −0.17; 95% confidence interval [CI], −0.27, −0.08), greater physical activity (B, 0.08; 95% CI, = 0.06–0.09), lower alcohol consumption (B, −0.07; 95% CI, −0.12, −0.03), greater SES (B, 0.33; 95% CI, 0.32–0.35), and, compared with nonsmokers, nonsignificantly greater odds of being an

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TABLE 2. Predicting chronic diseases with adolescent intelligence in the total sample

Outcome	A	B	C	*n*
Year 1993–1994				
Heart disease	0.91* (0.83–0.99)	0.92* (0.84–1.00)	0.95 (0.86–1.05)	10,144
Circulation problems	0.79* (0.72–0.86)	0.81* (0.74–0.88)	0.89* (0.81–0.98)	10,130
Diabetes	0.84* (0.76–0.94)	0.88* (0.78–0.98)	0.98 (0.87–1.11)	10,136
Cancer	1.14* (1.02–1.26)	1.13* (1.02–1.26)	1.09 (0.96–1.22)	10,136
Respiratory disease	1.10* (1.01–1.19)	1.12* (1.03–1.22)	1.19* (1.09–1.30)	10,134
Year 2003–2005				
Heart disease	0.93* (0.87–0.99)	0.95 (0.88–1.01)	0.98 (0.91–1.06)	8628
Stroke	0.80* (0.70–0.91)	0.84* (0.73–0.96)	0.85* (0.74–0.99)	8623
Circulation problems	0.85* (0.79–0.92)	0.87* (0.80–0.94)	0.94 (0.86–1.03)	8192
Diabetes	0.88* (0.81–0.95)	0.91* (0.84–0.99)	1.04 (0.95–1.13)	8626
Cancer	1.07 (0.99–1.15)	1.07 (0.99–1.15)	1.01 (0.93–1.09)	8629
Respiratory disease	0.89* (0.81–0.98)	0.92 (0.83–1.02)	0.99 (0.88–1.10)	8223

Note: Values are odds ratios (and 95% confidence intervals) for standardized intelligence score (SD = 1) predicting health outcomes.
Model A adjusts for sex and age.
Model B adjusts for A and health behaviors (body mass index, physical activity, smoking) assessed in 1993–1994.
Model C adjusts for A and socioeconomic status (factor score of education, occupational status, and financial assets) assessed in 1993–1994.
*$p < .05$.

ex-smoker (odds ratio [OR], 1.04; 95% CI, 0.99−1.09) and significantly lower odds of being a current smoker (OR, 0.87; 95% CI, 0.82−0.92).

In a multivariate sample attrition analysis including participants with data available in 1992-1993, male sex (OR, 0.79; 95% CI, 0.71−0.89), age (OR, 1.03; 95% CI, 1.02−1.05), intelligence (OR, 0.84; 95% CI, 0.78−0.89), physical activity (OR, 0.91; 95% CI, 0.85−0.97), smoking (OR, 1.54; 95% CI, 1.34−1.77), SES (OR, 0.80; 95% CI, 0.73−0.87), and the total number of the five assessed chronic diseases (OR, 1.45; 95% CI, 1.33−1.57) but not BMI (OR, 0.99; 95% CI, 0.98−1.01) predicted dropout from the study between 1992–1993 and 2003–2005.

Multivariate Adjusted Analyses

Intelligence was associated with lower risk of heart disease, circulation problems, diabetes, and stroke (Table 2, model A). There was a positive association between intelligence and cancer risk in the first but not the second follow-up. High intelligence was associated with lower risk of respiratory disease in 1993–1994 but greater risk in 2003–2005. These results remained substantially the same in a subsample with complete data on all disease outcomes at both measurement times ($n = 7674$; data not shown). Adding health behaviors generally had little effect (model B). This was also the case when nonimputed covariate data were used (data not shown). Adjusting for alcohol consumption in the subsample of 6148–7556 participants had only marginal effects on the coefficients of intelligence (1.3% change at maximum).

When SES was adjusted for (model C), the inverse associations between intelligence and disease risk were considerably attenuated; by 44% and 71% for heart disease at the first and second follow-up, 48% and 60% for circulation problems, 88% and 100% for diabetes, 91% for respiratory disease at second follow-up, and 25% for stroke (an average of 66% calculated over all the inverse associations). When we adjusted for the three indicators one at a time in separate models, education attenuated the inverse associations the most (by 51% on average, range 29%−94%), whereas financial assets (23% on average, range 11%−34%) and occupational status (26% on average, range 0%−66%) had smaller effects.

Sibling Analyses

The standard deviation of intelligence between families was more than twice the standard deviation within siblings (0.91 and 0.41, respectively). In the sibling-pair sample, high intelligence was related to a lower risk of circulation problems, diabetes, and stroke but was not associated with cancer or respiratory disease (Table 3). The differences of between-families and within-siblings coefficients were not statistically significant for any of the disease outcomes, indicating that intelligence was similarly associated with health differences (or, at least, not significantly dissimilarly) between people from the same family and between people from different families.

High sibling intelligence was related to person's lower risk of circulation problems and stroke, but not other diseases (Table 4). Table 5 presents the odds ratios for common (latent) sources of intelligence variance shared by sibling-pairs and for unique intelligence variance not shared by sibling-pairs (Fig. 1). Shared intelligence latent factor accounted approximately 45% of the total variance of intelligence, and the overall fit of the structural equation models for all disease outcomes were good (Comparative Fit Index > 0.85, root mean square error of approximation

TABLE 3. Sibling-pair analysis of the association between adolescent intelligence and chronic diseases

Outcome	Total effect	Within siblings	Between families	*p*	*n*
Year 1993–1994					
Heart disease	1.00 (0.88–1.13)	1.01 (0.82–1.24)	0.99 (0.85–1.15)	.90	4818
Circulation problems	0.81* (0.71–0.91)	0.88* (0.67–0.90)	0.88 (0.71–1.09)	.31	4792
Diabetes	0.83* (0.71–0.98)	0.84 (0.64–1.10)	0.83 (0.68–1.02)	.96	4806
Cancer	1.11 (0.97–1.29)	1.01 (0.78–1.29)	1.17 (0.98–1.39)	.33	4808
Respiratory disease	1.04 (0.94–1.16)	0.97 (0.80–1.18)	1.08 (0.95–1.23)	.37	4800
Year 2003–2005					
Heart disease	0.95 (0.87–1.03)	0.95 (0.82–1.10)	0.95 (0.85–1.05)	.97	5254
Stroke	0.81* (0.68–0.97)	0.83 (0.61–1.13)	0.80* (0.64–1.00)	.85	5248
Circulation problems	0.87* (0.78–0.98)	0.81* (0.67–0.98)	0.91 (0.79–1.04)	.34	4438
Diabetes	0.90* (0.81–0.99)	0.88 (0.74–1.04)	0.92 (0.80–1.05)	.70	5252
Cancer	1.05 (0.96–1.15)	0.95 (0.81–1.12)	1.09 (0.98–1.22)	.17	5246
Respiratory disease	0.94 (0.82–1.07)	0.86 (0.68–1.08)	0.98 (0.84–1.15)	.32	4468

Note: Values are odds ratios (and 95% confidence intervals) of multilevel logistic regression models unless otherwise indicated. All models adjust for sex and age.
All regression coefficients are calculated for standardized intelligence scores (SD = 1).
The p-value indicates the difference of between-families vs within-siblings coefficients.
*$p < .05$.

<0.05 in all models; data not shown). In agreement with the results of sibling- intelligence models (Table 4), shared intelligence factor contributed to the risk of circulation problems and stroke. The partitioning these associations to two sources resulted in some associations being nonsignificant despite a significant total effect observed in the main analyses (cf. Tables 2 and 5).

DISCUSSION

Findings from the Wisconsin Longitudinal Study suggest that high intelligence is associated with a decreased risk of heart disease, stroke, circulation problems, and diabetes and an increased risk of cancer. No consistent evidence was found for respiratory disease. Multivariate analyses provided limited support for health behaviors in explaining these associations, whereas adjustment for a composite SES score consisting of education, occupational status, and financial assets substantially attenuated the inverse associations between intelligence and disease risk. Results from sibling analysis suggested that intelligence may share common causes with the risk of cerebrovascular diseases (stroke and circulation problems), although siblings' shared family environments do not explain associations between intelligence and disease outcomes.

There is consistent evidence of an inverse association between intelligence and heart disease (2, 12, 14, 16, 17, 23),

TABLE 4. Predicting person's disease risk with his/her sibling's intelligence

Outcome	Sibling intelligence	*n*
Year 1993–1994		
Heart disease	0.97 (0.89–1.06)	8852
Circulation problems	0.90* (0.83–0.98)	8836
Diabetes	0.94 (0.84–1.05)	8845
Cancer	1.08 (0.98–1.20)	8847
Respiratory disease	1.02 (0.94–1.10)	8843
Year 2003–2005		
Heart disease	0.94 (0.89–1.00)	9394
Stroke	0.82* (0.73–0.93)	9388
Circulation problems	0.92* (0.86–0.99)	8551
Diabetes	0.95 (0.88–1.02)	9388
Cancer	1.04 (0.97–1.11)	9397
Respiratory disease	0.94 (0.86–1.02)	8582

Note: Values are odds ratios (and 95% confidence intervals) of standardized sibling intelligence scores (SD = 1) in predicting participant's disease outcomes. All models adjust for sex and age.
*$p < .05$.

TABLE 5. Predicting disease risk with siblings' shared and unique intelligence variance

	Unique intelligence	Shared intelligence	
Outcome	OR	OR	*n*
Year 1993–1994			
Heart disease	0.96 (0.90–1.02)	0.99 (0.92–1.06)	4818
Circulation problems	0.93* (0.88–0.99)	0.90* (0.84–0.97)	4792
Diabetes	0.97 (0.91–1.04)	0.94 (0.87–1.02)	4806
Cancer	0.95 (0.88–1.04)	1.08 (0.99–1.17)	4808
Respiratory disease	1.01 (0.95–1.08)	1.02 (0.95–1.09)	4800
Year 2003–2005			
Heart disease	0.98 (0.94–1.03)	0.97 (0.92–1.03)	5254
Stroke	0.99 (0.91–1.07)	0.91* (0.85–0.99)	5248
Circulation problems	0.95 (0.90–1.01)	0.95 (0.90–1.01)	4438
Diabetes	0.95 (0.90–1.00)	0.96 (0.90–1.01)	5246
Cancer	1.01 (0.96–1.07)	1.02 (0.96–1.08)	5252
Respiratory disease	0.93 (0.87–0.99)	0.98 (0.91–1.05)	4468

Note: Values are standardized odds ratios (and 95% confidence intervals) of shared and unique latent intelligence factors from structural equation model presented in Figure 1. All models adjust for sex and age.
*$p < 0.05$.

and in most (12–20) but not all (23) previous investigations researchers have confirmed a similar association with stroke. Only one study seems to have associated intelligence with diabetes (18); at least three studies have reported no association with the onset of diabetes (21, 39, 40). One study has reported high intelligence to predict lower risk of respiratory disease mortality (20). Previous findings on cancer are unequivocal. Although the authors of some studies have demonstrated an association between high intelligence and lower risk of cancer mortality, including lung, stomach, and female breast cancers (19, 24, 41), other authors have found no evidence for such associations (22, 42–44) or found, as in the present study, even positive association between intelligence and some cancers (melanoma and other skin malignancies) (22).

We suggest that the positive association for cancer is more likely to represent the effect of intelligence on cancer detection rather than on cancer incidence. Analogously, some common cancers, such as prostate and female breast cancer, appear to be more prevalent in individuals with high compared with low SES (45–48). Individuals with high intelligence and high SES may be more likely to participate in screenings and thereby become aware of their condition, although some causal processes may also be at work, e.g., fertility history in the case of breast cancer.

The present results are in agreement with previous studies in which the authors demonstrated that SES, education in particular, substantially attenuates the intelligence–health associations, whereas common health risk factors, such as smoking, BMI, and physical activity have modest or negligible effects (4–6, 8–15, 24). Whether SES represents a true causal mediating factor of intelligence, however, remains an open question. SES, especially education, is strongly predicted by childhood and adolescent intelligence (29–49). Insofar as SES indicators function as proxy measures of intelligence (i.e., individual differences in cognitive ability not captured by the specific intelligence measures used in a specific study) rather than measures of individuals' social and economic circumstances (27, 28), adjusting intelligence for SES may lead to overadjustment. The results concerning SES as a mediator should therefore be interpreted with caution, and more detailed study designs need to be set up to address this issue in greater detail.

Our results extend previous findings of intelligence, stroke, and circulatory problems by demonstrating that intelligence may share common genetic or environmental causes with these disease outcomes; person's risk of stroke and circulation problems was predicted by sibling's intelligence and the sibling-pair's shared intelligence covariance. Because it is unlikely that the sibling's intelligence would affect a person's disease risk by influencing the person's behavior, shared causes underlying intelligence and risk of cerebrovascular diseases seem a more plausible explanation. Twin and adoption studies have shown sibling resemblance in intelligence to be mostly to the result of shared genes rather than shared environment (50–52). It is therefore plausible that the common causes underlying sibling resemblance in intelligence reflect mainly shared genetic background. If replicated, this finding has important implications in understanding the relationship between intelligence and cerebrovascular diseases. There was no evidence for common causes linking intelligence and other diseases.

Multilevel models demonstrated no significant differences between "between-families" and "within-sibling pairs" regression coefficients. This finding suggests that the association between intelligence and disease outcomes is not attributable to factors common to siblings from the same family, because such common factors cannot explain differences between siblings. For instance, advantages from early social circumstances affecting all siblings in the family cannot explain why adolescent intelligence is related to later chronic diseases. These findings do not, however, exclude the possibility that the intelligence–disease association might still be partially explained by early environmental factors specific to each individual. Furthermore, the contribution of adult mediating factors, shared developmental origins, and individual-specific effects are not necessarily mutually exclusive explanations for the association between intelligence and disease risk, because each of them may explain part of the total association between intelligence and morbidity, depending on the specific disease of interest.

There are some limitations that need to be considered when interpreting the results. First, the sample was not representative of the U.S. population because the participants were largely white individuals with greater-than-average education, which may limit the generalizability of the results. The higher education of the participants also implies greater intelligence and more restricted range of individual variation than would be observed in the general population. The sibling analysis was additionally restricted to a sample of individuals with a surviving sibling taking part in the study, which may have introduced further selection bias. Second, the study was not fully genetically informative, so we could not separate genetic and environmental effects. Twin studies would be informative in this respect. Third, data on common health risk factors were collected only in one point in time, several risk factors specific to each chronic disease were not available, and data on chronic diseases were based on self-reports of diseases diagnosed by medical professionals. Studies comparing self-reports and medical records have shown self-reports of chronic diseases to be generally reliable (53–56). Nevertheless, these data are subject to potential bias because intelligence may influence not only disease risk but also opportunities and interest in maintaining health and seeking medical consultation (10). This could attenuate the intelligence–disease associations, or even

create spurious associations between intelligence and some diseases, e.g., cancer.

In summary, our findings confirm that adolescent intelligence is related to several chronic diseases in midlife and early old age and suggest that the mechanisms explaining these associations are in part disease-specific. Socioeconomic circumstances and common causes of intelligence and disease risk seem particularly important in explaining the health effect of intelligence.

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REFERENCES

1. Batty GD, Deary IJ, Gottfredson LS. Premorbid (early life) IQ and later mortality risk: Systematic review. Ann Epidemiol. 2007;17:278–288.
2. Batty GD, Gale CR, Mortensen LH, Langenberg C, Shipley MJ, Deary IJ. Pre-morbid intelligence, the metabolic syndrome and mortality: The Vietnam Experience Study. Diabetologia. 2008;51:436–443.
3. Hemmingsson T, Melin B, Allebeck P, Lundberg I. The association between cognitive ability measured at ages 18–20 and mortality during 30 years of follow-up—a prospective observational study among Swedish males born 1949–51. Int J Epidemiol. 2006;35:665–670.
4. Jokela M, Batty GD, Deary IJ, Gale CR, Kivimäki M. Low childhood IQ and early adult mortality: The role of explanatory factors in the 1958 British Birth Cohort. Pediatrics. 2009;124:E380–E388.
5. Whalley LJ, Deary IJ. Longitudinal cohort study of childhood IQ and survival up to age 76. Br Med J. 2001;322:819–822.
6. Jokela M, Elovainio M, Singh-Manoux A, Kivimäki M. IQ, socioeconomic status, and early death: The US National Longitudinal Survey of Youth. Psychosom Med. 2009;71:322–328.
7. Gottfredson LS, Deary IJ. Intelligence predicts health and longevity, but why? Curr Dir Psychol Sci. 2004;13:1–4.
8. Batty GD, Shipley MJ, Mortensen LH, Boyle SH, Barefoot J, Gronbaek M, et al. IQ in late adolescence/early adulthood, risk factors in middle age and later all-cause mortality in men: The Vietnam Experience Study. J Epidemiol Community Health. 2008;62:522–531.
9. Deary IJ, Batty GD, Pattie A, Gale CR. More Intelligent, more dependable children live longer: A 55-year longitudinal study of a representative sample of the Scottish nation. Psychol Sci. 2008;19:874–880.
10. Gottfredson LS. Intelligence: Is it the epidemiologists' elusive "Fundamental cause" of social class inequalities in health? J Personality Social Psychol. 2004;86:174–199.
11. Holsinger T, Helms M, Plassman B. Intelligence in early adulthood and life span up to 65 years later in male elderly twins. Age Ageing. 2007;36:286–291.
12. Lawlor DA, Batty GD, Clark H, McIntyre S, Leon DA. Association of childhood intelligence with risk of coronary heart disease and stroke: Findings from the Aberdeen Children of the 1950s cohort study. Eur J Epidemiol. 2008;23:695–706.
13. Martin LT, Kubzansky LD. Childhood cognitive performance and risk of mortality: A prospective cohort study of gifted individuals. Am J Epidemiol. 2005;162:887–890.
14. Batty GD, Shipley MJ, Dundas R, Macintyre S, Der G, Mortensen LH, et al. Does IQ explain socio-economic differentials in total and cardiovascular disease mortality? Comparison with the explanatory power of traditional cardiovascular disease risk factors in the Vietnam Experience Study. Eur Heart J. 2009;30:1903–1909.
15. Batty GD, Shipley MJ, Mortensen LH, Gale CR, Deary IJ. IQ in late adolescence/early adulthood, risk factors in middle-age and later coronary heart disease mortality in men: the Vietnam Experience Study. Eur J Cardiovasc Prev Rehabil. 2008;15:359–361.
16. Hart CL, Taylor MD, Smith GD, Whalley LJ, Starr JM, Hole DJ, et al. Childhood IQ and cardiovascular disease in adulthood: prospective observational study linking the Scottish Mental Survey 1932 and the Midspan studies. Social Sci Med. 2004;59:2131–2138.
17. Hemmingsson T, von Essen J, Melin B, Allebeck P, Lundberg I. The association between cognitive ability measured at ages 18–20 and coronary heart disease in middle age among men: A prospective study using the Swedish 1969 conscription cohort. Social Sci Med. 2007;65:1410–1419.
18. Olsson GM, Hulting AL, Montgomery SM. Cognitive function in children and subsequent type 2 diabetes. Diabetes Care. 2008;31:514–516.
19. Batty GD, Mortensen LH, Gale CR, Shipley MJ, Roberts BA, Deary IJ. IQ in late adolescence/early adulthood, risk factors in middle age, and later cancer mortality in men: The Vietnam Experience Study. Psychooncology. 2009;18:1122–1126.
20. Shipley BA, Der G, Taylor MD, Deary IJ. Cognition and mortality from the major causes of death: the Health and Lifestyle Survey. J Psychosom Res. 2008;65:143–152.
21. Batty GD, Deary IJ, Schoon I, Gale CR. Mental ability across childhood in relation to risk factors for premature mortality in adult life: the 1970 British Cohort Study. Journal of Epidemiol Community Health. 2007;61:997–1003.
22. Batty GD, Wennerstad KM, Smith GD, Gunnell D, Deary IJ, Tynelius P, et al. IQ in early adulthood and later cancer risk: cohort study of one million Swedish men. Ann Oncol. 2007;18:21–28.
23. Batty GD, Mortensen EL, Andersen AMN, Osler M. Childhood intelligence in relation to adult coronary heart disease and stroke risk: evidence from a Danish birth cohort study. Pediatr Perinat Epidemiol. 2005;19:452–459.
24. Kuh D, Shah I, Richards M, Mishra G, Wadsworth M, Hardy R. Do childhood cognitive ability or smoking behaviour explain the influence of lifetime socio-economic conditions on premature adult mortality in a British post war birth cohort? Soc Sci Med. 2009;68:1565–1573.
25. Jokela M, Singh-Manoux A, Ferrie JE, Gimeno D, Akbaraly TN, Shipley MJ, et al. The association of cognitive performance with mental health and physical functioning strengthens with age: The Whitehall II cohort study. Psychol Med. 2010;40:837–845.
26. Link BG, Phelan JC, Miech R, Westin EL. The resources that matter: Fundamental social causes of health disparities and the challenge of intelligence. J Health Soc Behav. 2008;49:72–91.

27. Rowe DC, Vesterdal WJ, Rodgers JL. Herrnstein's syllogism: Genetic and shared environmental influences on IQ, education, and income. Intelligence. 1998;26:405–423.
28. Bartels M, Rietveld MJH, Van Baal GCM, Boomsma DI. Heritability of educational achievement in 12-year-olds and the overlap with cognitive ability. Twin Res. 2002;5:544–553.
29. Deary IJ, Strand S, Smith P, Fernandes C. Intelligence and educational achievement. Intelligence. 2007;35:13–21.
30. Lahey BB, D'Onofrio B. All in the family: Comparing siblings to test causal hypotheses regarding environmental influences on behavior. Curr Dir Psychol Sci. 2010;19:319–323.
31. Silventoinen K, Modig-Wennerstad K, Tynelius P, Rasmussen F. Association between intelligence and coronary heart disease mortality: a population-based cohort study of 682361 Swedish men. Eur J Cardiovasc Prev Rehabil. 2007;14:555–560.
32. Kung HC, Hoyert DL, Xu JQ, Murphy SL. Deaths: Final data for 2005. National Vital Statistics Report, Vol. 56, No. 10. Hyattsville, MD: National Center for Health Statistics; 2008.
33. Wollmering E, ed. Wisconsin Longitudinal Study Handbook (12.10.07). 2007.
34. Hauser RM, Sewell WH, Clarridge BR. The Influence of Family Structure on Socioeconomic Achievement: A Progress Report. Madison, WI: Center for Demography and Ecology, University of Wisconsin-Madison; 1982.
35. Kling JO, Davis WE, Knost EK. Henmon-Nelson IQ scores as predictors of WAIS full scale IQ in alcoholics. J Clin Psychol. 1978;34:1001–1002.
36. Klett WG, Watson CG, Hoffman PT. The Henmon-Nelson and Slosson tests as predictors of WAIS-R IQ. J Clin Psychol. 1986;42:343–347.
37. Watson CG, Klett WG, Kucala T, Nixon C, Schaefer A, Gasser B. Prediction of the WAIS scores from the 1973 Henmon-Nelson revision. J Clin Psychol. 1981;37:840–842.
38. Carlin JB, Gurrin LC, Sterne JAC, Morley R, Dwyer T. Regression models for twin studies: a critical review. International J Epidemiol. 2005; 34:1089–1099.
39. Batty GD, Deary IJ, Macintyre S. Childhood IQ in relation to risk factors for premature mortality in middle-aged persons: The Aberdeen Children of the 1950s study. J Epidemiol Community Health. 2007;61:241–247.
40. Paile-Hyvarinen M, Kajantie E, Raikkonen K, Henriksson M, Leskinen JT, Laaksonen I, et al. Intellectual ability in early adulthood and type 2 diabetes in later life. Acta Diabetol. 2009;46:249–252.
41. Deary IJ, Whalley LJ, Starr J. IQ at age 11 and longevity: Results from a follow-up of the Scottish Mental Survey 1932. In: Christen Y, ed. Brain and Longevity: Perspectives in Longevity. Berlin: Springer; 2003. p. 153–164.
42. Hart CL, Taylor MD, Smith GD, Whalley LJ, Starr JM, Hole DJ, et al. Childhood IQ, social class, deprivation, and their relationships with mortality and morbidity risk in later life: Prospective observational study linking the Scottish Mental Survey 1932 and the Midspan studies. Psychosom Med. 2003;65:877–883.
43. Batty GD, Wennerstad KM, Smith GD, Gunnell D, Deary IJ, Tynelius P, et al. IQ in Early Adulthood and Mortality By Middle Age Cohort Study of 1 Million Swedish Men. Epidemiology. 2009;20:100–109.
44. Leon DA, Lawlor DA, Clark H, Batty GD, Macintyre S. The association of childhood intelligence with mortality risk from adolescence to middle age: Findings from the Aberdeen Children of the 1950s cohort study. Intelligence. 2009;37:520–528.
45. Liu LH, Cozen N, Bernstein L, Ross RK, Deapen D. Changing relationship between socioeconsmic status and prostate cancer incidence. J Natl Cancer Inst. 2001;93:705–709.
46. Cheng I, Witte JS, McClure LA, Shema SJ, Cockburn MG, John EM, et al. Socioeconomic status and prostate cancer incidence and mortality rates among the diverse population of California. Cancer Causes Control. 2009;20:1431–1440.
47. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. Cancer Causes & Control. 2001;12:703–711.
48. Robert SA, Strombom I, Trentham-Dietz A, Hampton JM, McElroy JA, Newcomb PA, et al. Socioeconomic risk factors for breast cancer - Distinguishing individual- and community-level effects. Epidemiology. 2004;15:442–450.
49. Strenze T. Intelligence and socioeconomic success: A meta-analytic review of longitudinal research. Intelligence4. 2007;35:401–426.
50. Hoekstra RA, Bartels M, Boomsma DI. Longitudinal genetic study of verbal and nonverbal IQ from early childhood to young adulthood. Learning Individual Differences. 2007;17:97–114.
51. Deary IJ, Johnson W, Houlihan LM. Genetic foundations of human intelligence. Hum Genet. 2009;126:215–232.
52. Bouchard TJ, McGue M. Genetic and environmental influences on human psychological differences. J Neurobiol. 2003;54:4–45.
53. Beckett M, Weinstein M, Goldman N, Lin YH. Do health interview surveys yield reliable data on chronic illness among older respondents? Am J Epidemiol. 2000;151:315–323.
54. Merkin SS, Cavanaugh K, Longenecker JC, Fink NE, Levey AS, Powe NR. Agreement of self-reported comorbid conditions with medical and physician reports varied by disease among end-stage renal disease patients. J Clin Epidemiol. 2007;60:634–642.
55. Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. J Clin Epidemiol. 2004;57:1096–1103.
56. Haapanen N, Miilunpalo S, Pasanen M, Oja P, Vuori I. Agreement between questionnaire data and medical records of chronic diseases in middle-aged and elderly Finnish men and women. Am J Epidemiol. 1997;145:762–769.