IQ in childhood and atherosclerosis in middle-age

IQ in childhood and atherosclerosis in middle-age: 40 year follow-up of the Newcastle Thousand Families Cohort Study

ABSTRACT

Objective: Carotid IMT is a known precursor to CHD and other relevant health outcomes such as stroke and cognitive impairment. In addition, higher childhood intelligence has been associated with lower risk of coronary heart disease events in later life, although the mechanisms of effect are unclear. We therefore examined the association between childhood intelligence and atherosclerosis using carotid IMT as a marker of the atherosclerotic process. **Approach:** Participants were 412 members of the Newcastle Thousand Families Study, a prospective cohort study of all 1142 births in the city of Newcastle in May and June 1947, who took an IQ test and English and arithmetic tests at age 11 years. Study members participated in a medical examination and lifestyle assessment at age 49-51 years during which intima-media thickness (IMT) was measured using ultrasound techniques.

Results: Individuals with higher childhood IQ score had a lower mean IMT in middle-age. A standard deviation higher score in childhood overall IQ was associated with a 0.053mm (95% CI -0.102, -0.004) lower IMT in men and a 0.039mm (95% CI -0.080, -0.002) lower IMT in women. Similar levels of association were found for the English and arithmetic tests. After adjustment for a range of covariates including education, the size of effect was undiminished in men but increased in women.

Conclusions: In the present study, higher childhood IQ scores were associated with a lower degree of atherosclerosis by middle-age.

Short Communication: Atherosclerosis

IQ in childhood and atherosclerosis in middle-age: 40 year follow-up of the Newcastle Thousand Families Cohort Study

Beverly A. Roberts[1], G. David Batty[1,2], Catharine R. Gale [1,3], Ian J. Deary[1], Louise Parker[4], and Mark S. Pearce[5]

[1] Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, Edinburgh, UK.

[2] Department of Epidemiology and Public Health, University College London, London, UK

[3] MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

[4] Departments of Medicine and Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada

[5] Institute of Health & Society, Newcastle University, Newcastle upon Tyne, UK

Correspondence to: Dr Beverly A. Roberts, Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ, UK.

beverly.roberts@ed.ac.uk. Tel: +44 (0) 131 650 9861. Fax: +44 (0) 131 651 1771.

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INTRODUCTION

Findings from extended follow-up of a series cohort studies initiated in childhood reveal an association between lower childhood IQ scores and raised coronary heart disease (CHD) events in middle- and older-age.[1-7] These effects do not appear to be due to reverse causality or confounding. Despite these concordant reports of the IQ-CHD association, explanations for it remain unclear. One suggestion is that established behavioural (smoking, diet, heavy alcohol intake, physical inactivity)[8-11] and cardiometabolic (obesity, metabolic syndrome)[12-14] CHD risk factors, which are also related to IQ, lie on the pathways linking IQ with CHD, although this appears to be only partially the case.[2]

Further insight into the mechanisms by which IQ is associated with CHD is limited by the use of clinical CHD outcomes, such as fatal and non-fatal myocardial infarction, which occur late in the natural history of the disease. Atherosclerosis, the most significant pathology giving rise to CHD, is characterised by a thickening of the artery wall.[15] The degree of atherosclerosis can be determined using a range of methods including carotid-wall intima-media thickness (IMT)[15] and ankle brachial index,[16] both of which offer predictive validity for coronary events[17,18] and other relevant outcomes such as stroke[19] and dementia[20]. In the only prospective study of which we are aware, IQ in early adulthood was inversely related to ankle brachial index,[21] a marker of atherosclerosis, but this was a study of men who were recruited from the US army, so raising concerns regarding the generalizability of the results. Accordingly, we used the Newcastle Thousand Families Study, a general population-based study of men and women to further examine the relationship between IQ between in childhood and IMT ascertained in middle-age.

MATERIAL AND METHODS

The Newcastle Thousand Families Study is a prospective birth cohort study of all 1142 children (583 males, 559 females) born in May and June 1947 to mothers then residing in the city of Newcastle upon Tyne, UK.[22,23] In 1958, the children sat the so-called ‘11-plus’ examination, a

standard IQ-type test widely used in English schools at that time for the purposes of educational selection from primary to secondary education.[24] The full range of tests taken included the Moray House Tests 57 & 58, the English and Arithmetic tests and the Mill Hill and Raven's Progressive Matrices.[24]

Further data collection included father's occupation which was used to derive social class based on the UK Registrar General's Standard Occupational Classification (categorised as professional, managerial, skilled, semi-skilled, unskilled), and birth weight (kg, standardised for gestational age and gender). All participants provided their informed consent. Of the 967 children alive and remaining in the city of Newcastle upon Tyne at age one year, 832 (86.0%) were traced at the age of 49-51 years.[22] Following approval the local research ethics committee, between October 1996 and December 1998, 412 (42.6%) study members completed both a health survey questionnaire and a clinical examination.[22-25] This subsample is representative of the complete group.[23] Also, we have previously shown that risk factor-disease associations do not fundamentally differ in people lost to follow-up vs. those included.[26]

Carotid artery IMT was measured bilaterally by B mode ultrasonography (7 MHz linear array, Acuson 128/XP-10) at three locations in the common and internal carotid arteries; an average was made of readings at the six sites.[26] Height, weight, waist and hip circumferences, percent body fat, serum insulin levels, plasma glucose concentrations, insulin resistance, insulin secretion, blood pressure, total cholesterol, triglyceride, and fibrinogen were all collected using standard protocols.[27-30] Data on highest level of education of the participant, occupational social class of the main wage earner of the household at age 49-51 years, and health-related behaviours (smoking status and history, including number of pack years of cigarettes smoked, and weekly alcohol intake) were collected by questionnaire.[17]

Correlation coefficients were used to examine the association between intima-media thickness and the covariates included in the regression models. Linear regression was used to examine the relation of a standard deviation increase (advantage) in childhood IQ with change in IMT in mm. Regression coefficients were initially unadjusted, then adjusted separately for individual

confounding and mediating variables. These analyses were completed for men and women separately and based on those participants with complete data with respect to childhood IQ and covariate data.

RESULTS

Of the 412 individuals who attended the screening examination and returned the questionnaires at the age 49-51 years, 278 (67.6%; 127 men, 151 women) had complete data relevant to these analyses. There was no marked nor statistically significant difference in mean childhood IQ and IMT between those with complete data and those excluded owing to missing data (mean childhood IQ, excluded 100.6 vs. included 100.4, p=0.12; mean IMT, excluded 0.80 vs. included 0.86, p=0.08).

In the group of 278 study members, the mean (standard deviation) IMT was 0.86mm (0.26) (men=0.90mm (0.29), women=0.82mm (0.23), p=0.003). In men, the following covariates were correlated with IMT at conventional levels of statistical significance: birth weight, body mass index, systolic blood pressure (BP), insulin resistance, total cholesterol, triglycerides, fibrinogen, waist/hip ratio, percent body fat, and adult social class (Table 1). In women, only waist/hip ratio and smoking in pack years were correlated with IMT.

In unadjusted regression analyses, IMT was negatively associated with overall performance in both men and women (Table 2). That is, a one-SD higher performance score in childhood was associated with a 0.053mm (95% CI -0.102, -0.004) lower IMT value in men and a 0.039mm (95% CI -0.080, -0.002) lower value in women. In temporal sequence, we then added potential explanatory variables individually and collectively to the multivariable model. In general, the relationship between increased childhood cognitive performance and lower IMT in both men and women remained. The regression analysis was also completed for the English and arithmetic tests. For both men and women the correlation between the English and arithmetic tests was 0.86 ($p<.0001$). For men, the correlation between overall performance and the English test was 0.94 ($p<.0001$), the correlation with the arithmetic test was 0.89 ($p<.0001$). For women the

correlation between overall performance and the English test was 0.94 (p<.0001), for the arithmetic test it was 0.87 (p<.0001). In general, the relationship remained similar for the English test for both men and women. However, the association was slightly stronger for both men and women for the arithmetic test.

The moderately positive correlation between IQ and education in both men (r=0.59, p<.0001) and women (r=0.58, p<.0001) in this cohort study raises concerns regarding collinearity. We therefore present two fully-adjusted models with and without controlling for education. The inverse association between childhood IQ and IMT was apparently robust to full adjustment with education in women although statistical significance was lost in men. Childhood IQ accounted for 2.4% of the variance in IMT in men and 2.5% in women in the fully adjusted model.

--Insert table 1 and 2 here--

DISCUSSION

In this prospective cohort study, having a higher overall childhood IQ, and higher scores on tests of English and arithmetic were significantly associated with lower IMT at age 50 in both men and women. On controlling for selected confounding or mediating variables, the strength of these associations were essentially unchanged in men but increased in women. To our knowledge, only one previous paper has examined the association between early life cognition and later life atherosclerosis.[21] In that study, the results, as discussed, were less generalisable than the present ones, the authors found that men with a higher intelligence score in early adulthood had more favorable levels of ankle brachial index.

The main strength of this study is the well characterized nature of the population, most notably the early life IQ scores. While this measurement of IQ would have pre-dated the onset of clinical cardiovascular disease events in our cohort members, the process of atherosclerosis can begin in childhood.[31] As such, the extent to which our study members would all have been atherosclerosis-free when their IQ was ascertained around four decades ago is moot. However, one limitation is that we do not have a repeat measurement of IQ in later life with which to test the possibility that the

influence of early life IQ on adult IMT could be mediated by later cognitive function, as well as some of the other risk factors. A second issue to consider is replication. It was not possible to repeat the study in an independent replication dataset as the 1000 Families in Newcastle Study is a closed birth cohort study, meaning the sample is not refreshed by new recruits over time. Datasets with information on both childhood cognition and later adult health are rare, but may provide opportunities for other research groups to examine the link between childhood intelligence and markers of subclinical atherosclerosis.

In conclusion, higher childhood IQ, in addition to being related to a lower risk of a CHD event, was also associated with the earlier stages of the disease process leading to CHD.

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DISCLOSURES

None.

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SIGNIFICANCE

This is only the second paper to examine the association between childhood intelligence and atherosclerosis in adulthood and the first to examine this in a population sample using intima-media thickness. It has shown that those of lower childhood intelligence may be at higher risk of atherosclerosis in adulthood. In this study there was a suggestion of partial mediation by intermediary risk factors, although, importantly, none of these appeared to completely account for the IQ-IMT association.

LEGENDS

Table 1: Regression coefficients (95% CI) for the relation of a SD change (continuous variables) and unit change (*categorical variables) in the covariates with intima-media thickness in $*10^{-3}$mm (unadjusted) (N=127 for men; N=151 for women).

Table 2: Regression coefficients (95% confidence interval) for the relation of a SD increase in childhood IQ with change in intima-media thickness ($*10^{-3}$mm) after adjustment for a range of covariates (N=127 for men; N=151 for women)