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Beyond a bigger brain: Multivariable structural brain imaging and intelligence

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A B S T R A C T

People with larger brains tend to score higher on tests of general intelligence (*g*). It is unclear, however, how much variance in intelligence other brain measurements would account for if included together with brain volume in a multivariable model. We examined a large sample of individuals in their seventies ($n = 672$) who were administered a comprehensive cognitive test battery. Using structural equation modelling, we related six common magnetic resonance imaging-derived brain variables that represent normal and abnormal features—brain volume, cortical thickness, white matter structure, white matter hyperintensity load, iron deposits, and microbleeds—to *g* and to fluid intelligence. As expected, brain volume accounted for the largest portion of variance (~12%, depending on modelling choices). Adding the additional variables, especially cortical thickness (+~5%) and white matter hyperintensity load (+~2%), increased the predictive value of the model. Depending on modelling choices, all neuroimaging variables together accounted for 18–21% of the variance in intelligence. These results reveal which structural brain imaging measures relate to *g* over and above the largest contributor, total brain volume. They raise questions regarding which other neuroimaging measures might account for even more of the variance in intelligence.

1. Introduction

Half or more of the variance in human intelligence test performance is accounted for by the general factor of cognitive ability, or *g* (Gignac & Watkins, 2013; Jensen, 1998). An extensive literature shows the importance of *g* for many educational, occupational, and health outcomes (Deary, 2012). Despite this, relatively little is known about the biological basis of *g* (see Deary, Penke, & Johnson, 2010, and Luders, Narr, Thompson, & Toga, 2009, for overviews). Here, we focus on what structural magnetic resonance imaging (MRI)-derived brain variables can contribute with respect to accounting for variance in *g*. We

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model several structural brain measures together to provide a reliable estimate of the association between brain structure and *g* at age 73.

The best-replicated neuroanatomical predictor of *g* is total brain volume (TBV; Galton, 1888; Gignac, Vernon, & Wickett, 2003; McDaniel, 2005; Pietschnig, Penke, Wicherts, Zeiler, & Voracek, 2014; Rushton & Ankney, 2009). Since TBV is associated with the overall number of neurons (e.g. Pakkenberg & Gundersen, 1997), it is plausible that larger brains allow for more complex, distributed cognitive processing. Initial brain imaging studies found widely-divergent estimates of the TBV-*g* correlation (Yeo, Turkheimer, Raz, & Bigler, 1987, found a correlation of $r = .07$, whereas Willerman, Shultz, Rutledge, & Bigler, 1991, found correlations as high as $r = .51$ in men). In a recent meta-analysis of 148 samples (total $N = 8036$, including the participants from the present study), Pietschnig et al. (2014) calculated an overall correlation between TBV and cognitive ability of $r = .24$ (~6% shared variance; note that some studies included observed and some included latent estimates of cognitive ability — the correlation may have been larger had all studies used latent *g*). In a sample of twins, Posthuma et al. (2002) showed that TBV and cognitive ability are genetically, as well as phenotypically, correlated.

A number of finer-grained MRI measures have also been associated with intelligence. For instance, measures of cortical thickness from regions across the brain have shown moderately-sized positive correlations with cognitive ability, potentially because they represent the density and arrangement of neurons in brain regions vital for cognition, such as prefrontal areas (e.g. Narr et al., 2007). Measures of the networks that support information transfer within the brain have also shown predictive validity for cognitive ability; in the same sample analyzed in the present study, a general factor of brain white matter tract structure measured by diffusion tensor MRI accounted for about 10% of the variance in *g* (Penke, Muñoz Maniega et al., 2012). Measures of damage to the white matter tracts, such as volume of white matter hyperintensities (WMH; Valdés Hernández et al., 2013), number of microbleeds (Cordonnier, Al-Shahi Salman, & Wardlaw, 2007; Werring et al., 2004), and number of iron deposits (Penke, Valdés Hernández et al., 2012) have also shown modest predictive validity for cognitive ability at age about 73. In a review of the literature on individual differences, Lubinski (2000) noted that the "biological phenomena [linked to g] are in no way mutually exclusive and can be complementary to one another" (p. 418). Thus, modelling these additional brain metrics alongside TBV will improve our understanding of whether they relate to general intelligence beyond brute brain size.

To our knowledge, no studies to date have included all of these structural brain variables together in a single model to assess their incremental predictive validity for intelligence. It is thus unclear whether they would each account for separate portions of variance, or whether the finer-grained variables would account for little after more global measures such as total brain volume are included. In the present study, we ask two questions. First, what is the best estimate of the percentage variance in *g* accounted for by the above brain measures when they are modelled together? Second, which brain imaging parameters have significant associations with *g* beyond total brain volume?

2. Method

2.1. Participants

Participants were members of the Lothian Birth Cohort 1936 (LBC1936; Deary et al., 2007; Deary, Gow, Pattie, & Starr, 2012), a sample of White European, community-dwelling older individuals. Most took part, at approximately 11 years of age, in the 1947 Scottish Mental Survey (Scottish Council for Research in Education, 1949). In Wave 1 of the LBC1936 study, 1091 of these individuals were followed-up when they were aged approximately 70 years old in 2004–07. In Wave 2, 886 (418 females) took part at age approximately 73 years, 700 of whom underwent brain MRI (Wardlaw et al., 2011). The data used in the present study come from Wave 2. Of the 700 who underwent brain MRI, 28 participants were removed from the current sample either based on quality control of the imaging data, or for scoring less than 24 on the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975), a commonly-used screening instrument for possible dementia. A total of 672 individuals (319 female, 47.5%) therefore provided data for the present study. These individuals had an average age of 72.49 years (SD = 0.71) and had an average of 10.8 years of education (SD = 1.1 years). Written informed consent was obtained from all participants before their inclusion in the study, and the study was approved by the Multi-Centre Research Ethics Committee for Scotland (MREC/01/0/56) and the Lothian Research Ethics Committee (LREC/2003/2/29).

2.2. Measures

2.2.1. Cognitive ability

The LBC1936 participants were administered fifteen cognitive tests at Wave 2. Three subtests were included from the Wechsler Memory Scale, 3rd Edition (WMS-III; Wechsler, 1998a): Logical Memory (immediate and delayed), Verbal Paired Associates (first and second recall), and Spatial Span (forwards and backwards). For this age group, the mean test–retest reliability coefficient of these subtests is .86 (Wechsler, 1998a). Six subtests were included from the UK version of the Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III^{UK}; Wechsler, 1998b): Digit Symbol Coding, Digit Span Backwards, Block Design, Letter–Number Sequencing, Matrix Reasoning, and Symbol Search (mean test–retest reliability estimate = .83; Wechsler, 1998b). The participants completed the National Adult Reading Test (NART; Nelson & Willison, 1991) and the Wechsler Test of Adult Reading (WTAR; Holdnack, 2001). Both these reading tests have reliability coefficients > .87 (Kreutzer, DeLuca, & Caplan, 2011). A measure of verbal fluency (using the letters C, F, and L; Lezak, 2004; test–retest reliability = .74; Tombaugh, Kozak, & Rees, 1999) was administered. The participants completed three elementary cognitive assessments of processing speed: Simple Reaction Time, Choice Reaction Time (both described in detail by Deary, Der, & Ford, 2001), and visual Inspection Time (Deary et al., 2007). These three measures have estimated reliability coefficients of .62, .92, and .81, respectively (Deary, Johnson, & Starr, 2010).

Here, we assessed the extent to which MRI variables predict both overall *g*, and 'fluid' *g*. All of the above measures were included in the overall *g*-factor of intelligence. In the alternative