Structural Brain Asymmetry and General Intelligence in 73-Year-Olds

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Introduction

Higher general intelligence is associated with educational and occupational successes (Schmidt & Hunter, 1998; Strenze, 2007). Since performance is positively correlated across multiple cognitive tasks, a measure of general intelligence can be estimated using factor analysis (Spearman, 1904; Carroll, 1993). Investigating correlates of general intelligence could provide a better understanding of individual differences in mental ability, and aid identification of people with specific environmental circumstances and medical and neuropsychological disorders that might put them at risk of lower general intelligence.

Anatomical asymmetry, a measure of developmental instability across species (van Dongen, 2006), has been reported to be negatively associated with general intelligence. As two sides of a bilateral feature (for example the hands or face) represent independent replicates of the same developmental events, asymmetrical bilateral features indicate minor developmental errors (Hoyme, 1993). Anatomical asymmetry is linked to cognitive performance. For example, more symmetrical children have faster reaction times (Hope et al., 2015). Correlation sizes between combined anatomical asymmetry measures (e.g. asymmetries in the widths of wrists, ankles, or elbows, or lengths of fingers) and general intelligence tend to be small to modest (e.g. Furlow et al., 1997, N = 112, r = -.21; Bates, 2007, N = 164, r = -.29). And some studies report no correlation between anatomical asymmetry and general intelligence (Johnson, Segal & Bouchard Jr., 2008, N = 263, r = .01).

Some brain asymmetries might also be markers of developmental instability. However, this is not straightforward, since some functions are specialised in each of the two hemispheres, resulting in some hemispheric asymmetries being positively associated with specific cognitive abilities. For example, Plessen et al. (2014) report that right > left asymmetry in posterior brain regions is positively associated with visuospatial abilities. However, other structural brain asymmetries have negative associations with specific cognitive abilities. For example, greater rightward asymmetry of the fusiform gyrus is associated with increased severity of social cognition deficits in autistic spectrum disorder (N = 128, Dougherty, Evans, Katuwal & Michael, 2016). Moreover, there is some evidence to suggest that overall cortical asymmetry measures are associated with general intelligence. Yeo et al. (2016, N = 244) reported a small negative association (r = -.15) between cortical surface area asymmetry and general intelligence (a latent factor derived from a factor analysis on seven cognitive tests) in young adults.

The parieto-frontal integration theory of intelligence (P-FIT; Jung & Haier, 2007) proposes that cognitive processes rely most heavily on frontoparietal brain regions. In Yeo et al.'s

(2016) study, when frontoparietal and non-frontoparietal regions were separated, the association between surface area asymmetry and general intelligence was only found for frontoparietal regions. The authors interpreted this result as being consistent with the P-FIT. However, their study is not decisive, because they did not report whether the association was significantly larger in frontoparietal than non-frontoparietal regions.

Debate surrounds the specific nature of non-genetic environmental factors that affect general intelligence, although evidence suggests that they have substantial effects during early life (Petrill et al., 2004). For example, shorter gestational time and lower parental socioeconomic status (SES) are reliably associated with lower general intelligence in childhood and adulthood (Davis et al., 2011; Eide, Oyen, Skjaerven & Bjerkedal., 2007; Larson et al., 2015; Hackman & Farah, 2009). Furthermore, evidence suggests that associations between anatomical asymmetry and cognitive functioning are established in childhood. For example, bodily symmetry increases in childhood (Hope et al., 2013a) and facial asymmetry in older adults is negatively associated with childhood SES (Hope et al., 2013b).

The current study aimed to replicate Yeo et al.'s (2016) method with a sample of older adults, while also adding additional brain parameters and providing a methodological alternative for brain asymmetry calculation. Whereas Yeo et al. (2016) focused on the association between brain surface area asymmetry and general intelligence, the current study focused on three measures of brain cortical asymmetry: surface area, volume and thickness. For any associations between brain asymmetry and general intelligence, the role of childhood SES was investigated. Another aim of the current study was to investigate whether cortical asymmetry in P-FIT brain regions is more strongly associated with general intelligence than cortical asymmetry in non-P-FIT brain regions. Furthermore, the current study compared two methods of calculating cortical asymmetry: in the first method, individual regions contribute equally to the overall asymmetry score (used by Yeo et al., 2016); in the second method, the calculation of cortical asymmetry is proportional to the size of the region.

The brain's cortex is not the only part of the brain in which asymmetry can be measured. Some studies have reported associations between specific white matter tract fractional anisotropy asymmetries and specific cognitive abilities. For example, Lebel and Beaulieu (2009; N = 183) found a significant correlation between leftward lateralization of fractional anisotropy of the arcuate fasciculus and scores on the Peabody Picture Vocabulary Test (PPVT-III; r = .32; Dunn, 1977). Such findings suggest that associations between brain asymmetry and general intelligence are not restricted to grey matter measures. There is an association between intelligence and global white matter fractional anisotropy (Penke et al.,

2012). However, the association between asymmetry in global white matter fractional anisotropy and general intelligence has not been tested before. Therefore, a further aim of the present study was to investigate the relationship between global white matter fractional anisotropy asymmetry across multiple tracts and general intelligence.

2. Method

2.1. Participants

Participants were members of the Lothian Birth Cohort 1936 (LBC1936, see Deary et al., 2007; Deary, Gow, Pattie & Starr, 2012; Taylor, Pattie & Deary, 2018). The current study uses Wave 2 of data collection (collected between 2007 and 2011, Age *M* = 72.9 years, *SD* = 0.71), which was the first wave at which brain MRI scans were collected. Of those participants who completed cognitive testing at recruitment (Wave 1; N = 1091), 731 participants agreed to brain scanning at Wave 2. All participants were scanned in the same scanner in the same clinic.

After image processing, MRI data from 636 participants (336 males, 300 females, Age: *M* = 72.7 years, *SD* = 0.73) were available, and are the subject of this report. Depending on cognitive test, data from *N* = 624-636 was available (see Table 1). For the white matter fractional anisotropy analysis, after diffusion MRI processing, data from 556-664 participants were available depending on the tract of interest (see Supplementary Table 1).

An additional analysis was also run that excluded participants who had strokes or visible abnormalities in MRI images (e.g. cists); for this, the *N* = 530. The result of this analysis was very similar to that of the full analysis, and is presented in Supplementary Table 2.

Ethical permission for the LBC1936 study was obtained from the Multi-Centre Research Ethics Committee for Scotland (MREC/01/0/56), the Lothian Research Ethics Committee (LREC/2003/2/29) and the Scotland A Research Ethics Committee (07/MRE00/58). All participants gave written consent before cognitive and MRI measurements were collected.

2.2. Measures

2.2.1. Cognitive tests. The participants completed a wide-ranging selection of cognitive tests, of which 13 were selected for use in the current study. All tests were individually administered and all participants were tested in the same location, using the same equipment and instructions. Based on previous analyses of this battery of cognitive tests (e.g. Ritchie et al., 2016), these tests were grouped into four cognitive domains, modelled in a confirmatory factor analysis-based hierarchical model with a second-order general factor

(general intelligence): Visuospatial Skills, Crystallised Ability, Verbal Memory and Processing Speed.

Visuospatial Skills consisted of two subtests from the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997a): Matrix Reasoning and Block Design. It also included the Spatial Span (average of forward and backward) subtest from the Wechsler Memory Scale-III (WMS-III; Wechsler, 1997b).

Crystallised Ability was measured by two tests involving the participant reading a list of irregular words out loud: the National Adult Reading Test (NART; Nelson & Willison, 1991) and the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001). A test of Phonemic Verbal Fluency (Lezak, 2004) was also included.

Verbal Memory was measured using two subtests from the WMS-III: Verbal Paired Associates (total from immediate and delayed tests) and Logical Memory (total from immediate and delayed tests). It also included the Digit Span Backwards subtest from the WAIS-III.

Processing Speed was measured by two pencil and paper tests from the WAIS-III: Symbol Search and Digit-Symbol Substitution. Furthermore, two computerised instruments were used: Inspection Time (Deary et al., 2004); and Four-Choice Reaction Time (Deary, Der & Ford, 2001).

2.2.2. Childhood SES measures. The childhood SES data were collected when participants were recruited as members of the LBC1936, at a mean age of 70 years. The four measures relate to when participants were about 11 years old. These measures are: number of people per room in their house; type of toilet (indoor or outdoor) which is indicative of the size and quality of a house in the 1930s (indoor toilet was scored as higher SES; Dedman, Gunnell, Davey Smith & Frankel, 2001); number of people sharing a toilet; and father's social class. Father's social class was measured using the UK's 1951 Classification of Occupations (General Register Office, 1956; Knight, 1967). This was compiled for use in connection with the 1951 Census of England, Wales and Scotland and generally coincided with the middle of the father's career. It is reported on a 5-point scale ranging from 1 = professional to 5 = unskilled.

2.2.3. MRI protocol. For full details of the MRI protocol, see Wardlaw et al. (2011). In brief, MRI data was collected in the Brain Research Imaging Centre, University of Edinburgh, using a GE Signa LX 1.5T clinical scanner (General Electric, Milwaukee, WI). Image acquisition comprised whole brain T2-weighted, T2*-weighted and FLAIR-weighted axial

scans, and a high-resolution T1-weighted volume sequence in the coronal plane. Single-shot, spin-echo, echo-planar, and diffusion-weighted volumes (b = 1000 s/mm^2) were acquired in 64 non-collinear directions along with seven T2-weighted volumes (b = 0 s/mm^2). Seventy-two adjacent 2 mm thick axial slices acquired with a field of view of 256 x 256 mm and a matrix size of 128 x 128, giving a resolution of 2 × 2 × 2 mm^3. Repetition and echo times were 16.5 seconds and 95.5 milliseconds, respectively. Total image acquisition took approximately 70 minutes.

Methods for cortical reconstruction and volumetric segmentation were performed with the FreeSurfer image analysis suite (http://surfer.nmr.mgh.harvard.edu/). This FreeSurfer parcellation yields 34 paired measures across the two hemispheres based on the Desikan-Killiany atlas (Desikan et al., 2006). It was used to acquire a left and right measure for 34 regions for surface area, volume and thickness (for descriptive statistics, see Supplementary Table 3). The resultant parcellations were then visually inspected and manual editing rectified issues with skull stripping, tissue identification or ROI boundary identification. Thirty-two participants were excluded at this stage due to infarct, poor quality scan, general brain tissue identification failure, or major parcellation failure.

2.3. Tractography protocol.

In the current study, bilateral anterior thalamic radiations, cingulum bundles, and arcuate, uncinate, and inferior longitudinal fasciculi were used (Figure 1); the splenium and genu of the corpus callosum were also identified from this protocol but were not used in the current analysis as they are not separable for left and right hemispheres.

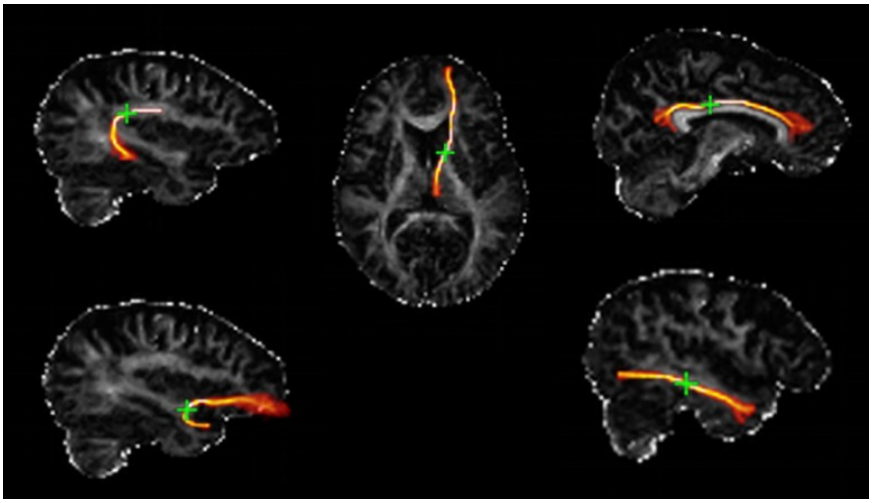

Figure 1. White matter tracts, segmented using probabilistic neighbourhood tractography overlaid on fractional anisotropy maps for a representative participant. Tracts are shown in orange and seed points are indicated by a green cross. Top (left to right): arcuate, anterior thalamic radiations, bilateral cingulum cingulate gyri. Bottom (left to right): uncinate, inferior longitudinal fasciculi (adapted from Ritchie et al., 2015).

For full details of the tractography protocol, see Clayden et al. (2011) and Bastin et al. (2010). In brief, data were pre-processed to extract the brain, remove bulk participant motion and eddy current-induced distortions, and estimate water diffusion tensor parameters using FLS tools (FMRIB, Oxford UK; Smith et al. 2004). Brain connectivity data were created using the BedpostX/ProbTrackX tractography algorithm (Behrens et al. 2007) with its default parameters of a 2-fiber model and 5000 streamlines to reconstruct tracts of interest. For each participant, the seed point producing the best match tract to a reference for each of the 10 pathways was determined using probabilistic neighbourhood tractography, implemented in the TractoR package (Clayden et al. 2011), with the resulting tractography mask applied to each participant's mean diffusivity and fractional anisotropy volumes. Tract-averaged values (weighted by the connection probability) were calculated from these masks and used in all subsequent analyses. The image analysts were blind to the characteristics of each participant.

All analyses were conducted in R (version 3.2.5; R Core Team, 2016). The lavaan package (Rosseel, 2012) was used to estimate structural equation models. The following fit indices were considered: chi-squared (χ^2), Comparative Fit Index (CFI), Tucker Lewis Index (TLI), Root Mean Square Error of Approximation (RMSEA) and Root Mean Square Residual (SRMR). Hu and Bentler's (1999) criteria for acceptable model fit were as follows: CFI > .95, TLI > .95, RMSEA < .06, SRMR < .08. Using these criteria, all models were estimated using full information maximum likelihood.

2.4. Statistical Analysis

2.5. Calculation of asymmetry

Two methods were used for calculating asymmetry. The first was that described by Yeo et al. (2016, p. 95). This method aimed to calculate asymmetry for each of the four measures: cortical surface area, cortical volume, cortical thickness and white matter fractional anisotropy parameters with each region/tract contributing equally to the overall asymmetry score. Yeo et al. (2016) explain that this modelled measure of equal contribution is typical for aggregate measures based on body features (e.g. Furlow et al., 1997; Bates, 2007). The procedure involved the following steps:

1. For each participant, directional asymmetries were calculated for each region/tract (the right value was subtracted from the left; see Supplementary Figure 1);
2. The mean directional asymmetry for each region/tract was found across the whole sample;
3. The values in Step 2 were subtracted from the values in Step 1, providing a measure of deviance from the sample mean for each region/tract for each participant;

4. The absolute values of the values in Step 3 were taken, providing a non-directional measure of asymmetry;
5. These values were divided by the average of each participant's left and right hemisphere values for the relevant region/tract, ensuring that each region/tract contributed equally to the overall asymmetry score.
    - This method treats each parcellation of the brain as an equal unit of interest.
    - This step was used by Yeo et al. (2016) since regions vary in size (e.g. in this sample, the total surface area of the superior frontal region is 12,730.15 mm^2 whereas the total surface area of the entorhinal region is 722.90 mm^2). Absolute asymmetry scores for each cortical region are given in Supplementary Table 4.
6. The values for all regions/tracts were averaged for each participant, providing an overall asymmetry score for each participant;
7. In separate analyses, testing the P-FIT theory (Jung & Haier, 2007), separate asymmetry scores (using the procedure above) were found for each participant for P-FIT and non-P-FIT regions (see Supplementary Figures 2 and 3).
    - P-FIT regions: caudal middle frontal, frontal pole, fusiform, inferior parietal, lateral orbitofrontal, medial orbitofrontal, rostral middle frontal, superior frontal, superior parietal and supramarginal.
    - Non-P-FIT regions: bank superior temporal sulcus, caudal anterior cingulate, cuneus, entorhinal, inferior temporal, insula, isthmus cingulate, lateral occipital, lingual, middle temporal, parahippocampal, paracentral, pars opercularis, pars orbitalis, pars triangularis, pericalcarine, postcentral, posterior cingulate, precentral, precuneus, rostral anterior cingulate, superior temporal, temporal pole and transverse temporal.

Although it might be valid for body-part asymmetry scores to make equal contributions to overall asymmetry scores, the same might not be the case for the brain. It might not be appropriate to allow, for example, the entorhinal cortex (722.90 mm^2) to contribute as much to the overall asymmetry measure as the much larger superior frontal region (12,730.15 mm^2). Allowing an equal contribution of regions could result in a substantially larger asymmetry score than is representative of the entire cortex. It is possible that proportional asymmetry provides a more representative index of hemispheric asymmetry. Thus, our second method for calculating asymmetry scores involved each region contributing proportionally to the asymmetry score, depending on their size. For this method, for each measure (cortical surface area, volume and thickness), the total right hemisphere value was subtracted from the left.

3. Results

All models reported in this section had acceptable fit, according to the criteria in the Methods section (see Supplementary Table 5).

3.1. Cognitive descriptive statistics

Descriptive statistics for all 13 cognitive tests are presented in Table 1 for the 636 participants who completed cognitive tests and MRI scanning.

Table 1. Descriptive statistics for cognitive tests (all completed at age 73).

Cognitive domain	Test	*N*	*M* (*SD*)
Visuospatial Skills	Matrix Reasoning	634	13.52 (4.93)
	Block Design	634	34.38 (10.01)
	Spatial Span	634	14.79 (2.72)
Crystallised Ability	NART	634	34.66 (8.10)
	WTAR	634	41.27 (6.94)
	Phonemic Verbal Fluency	635	43.55 (12.78)
Verbal Memory	Verbal Paired Associates	623	27.57 (9.48)
	Logical Memory	635	75.03 (17.84)
	Digit span backwards	636	7.88 (2.31)
Processing Speed	Symbol Search	634	24.88 (6.05)
	Digit-Symbol Substitution	634	56.68 (11.79)
	Inspection Time	624	111.78 (10.95)
	Four-Choice Reaction Time (s)	635	0.64 (0.08)

Tests for measurement invariance were performed (see Widaman, Ferrer & Conger, 2010). For general intelligence, strong measurement invariance for males and females could not be assumed ($p < .001$ for the difference between the model with strong invariance and one with only configural invariance). Therefore, the latent factor of general intelligence could not be treated the same across the sexes (see Supplementary Tables 6 and 7). Consequently, sex differences were not investigated in the models that included the latent factor of general intelligence.

3.2. Model of general intelligence

A hierarchical confirmatory factor analysis model was estimated for general intelligence (see Supplementary Figure 4). Each test loaded highly on the relevant domain, and all domains had high loadings on general intelligence (see Figure 3). In this model, the residual variance of the path from general intelligence to Verbal Memory was near-zero and was estimated as negative (β = -1.41), indicating that all variance in Verbal Memory was shared with general intelligence. To allow the model to converge on within-bounds estimates, the variance of Verbal Memory was fixed at zero. Covariance paths were added between NART and WTAR and between Verbal Paired Associates and Logical Memory, as these tests are similar and share method variance not incorporated by the rest of the model. All paths were statistically significant at the $p < .001$ level (see Supplementary Table 8).

3.3. Regional cortical asymmetry and associations with intelligence

Descriptive statistics for the left and right hemisphere surface area, volume, and thickness are presented in Supplementary Table 3. First, simple directional asymmetries (left minus right) were computed for each cortical region for each participant (see Supplementary Figure 1). To evaluate the extent and significance of these directional asymmetries, one-sample *t*-tests were conducted, comparing each asymmetry value to zero. Then, the absolute asymmetries of the 34 cortical regions were calculated (see Figure 2 and Supplementary Table 4).

β-weights of paths from the absolute asymmetry of the 34 cortical regions to general intelligence are presented in Supplementary Table 9. To summarise, for surface area asymmetry, the precuneus (β = .13, p = .007), rostral anterior cingulate (β = .13, p = .004) and transverse temporal (β = .09, p = .047) regions were positively associated with general intelligence. For cortical volume, asymmetry in the inferior temporal region was positively associated with general intelligence (β = .10, p = .034). For thickness asymmetry, there were no significant associations between any of the 34 cortical regions and general intelligence.

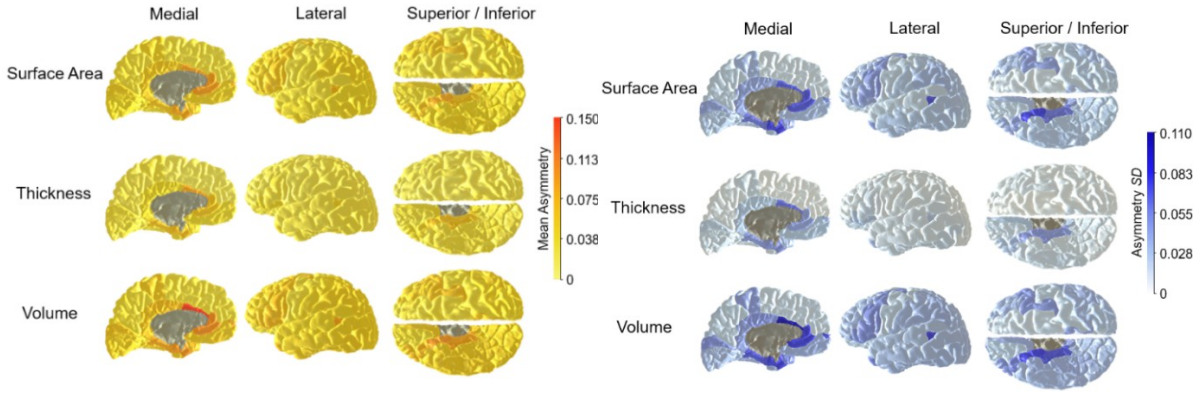

Figure 2. Brain heatmaps illustrating the absolute asymmetry of the 34 cortical regions: Means (left) and standard deviations (right).

3.3.1. Equal regional contribution analysis: general intelligence model

An equal regional contribution analysis was conducted, as in Yeo et al. (2016). Collapsing across the 34 cortical regions, values of overall asymmetry were calculated for surface area, volume and thickness. Surface area asymmetry was strongly correlated with volume asymmetry (r = .72, p < .001), and volume asymmetry was modestly correlated with thickness asymmetry (r = .28, p <.001). But, as was also found by Koelkebeck et al. (2014), there was no significant correlation between surface area asymmetry and thickness asymmetry (r = .04, p = .377).

A structural equation model was estimated to test the association between global cortical asymmetry and general intelligence (see Figure 3). The three cortical asymmetry measures (surface area, volume and thickness) were free to correlate with each other. This model revealed a small negative association between cortical thickness asymmetry and general intelligence (β = -.18, SE = .05, p < .001). There was no association between surface area asymmetry and general intelligence (β = -.03, SE = .07, p = .678), or between volume asymmetry and general intelligence (β = .07, SE = .07, p = .286).

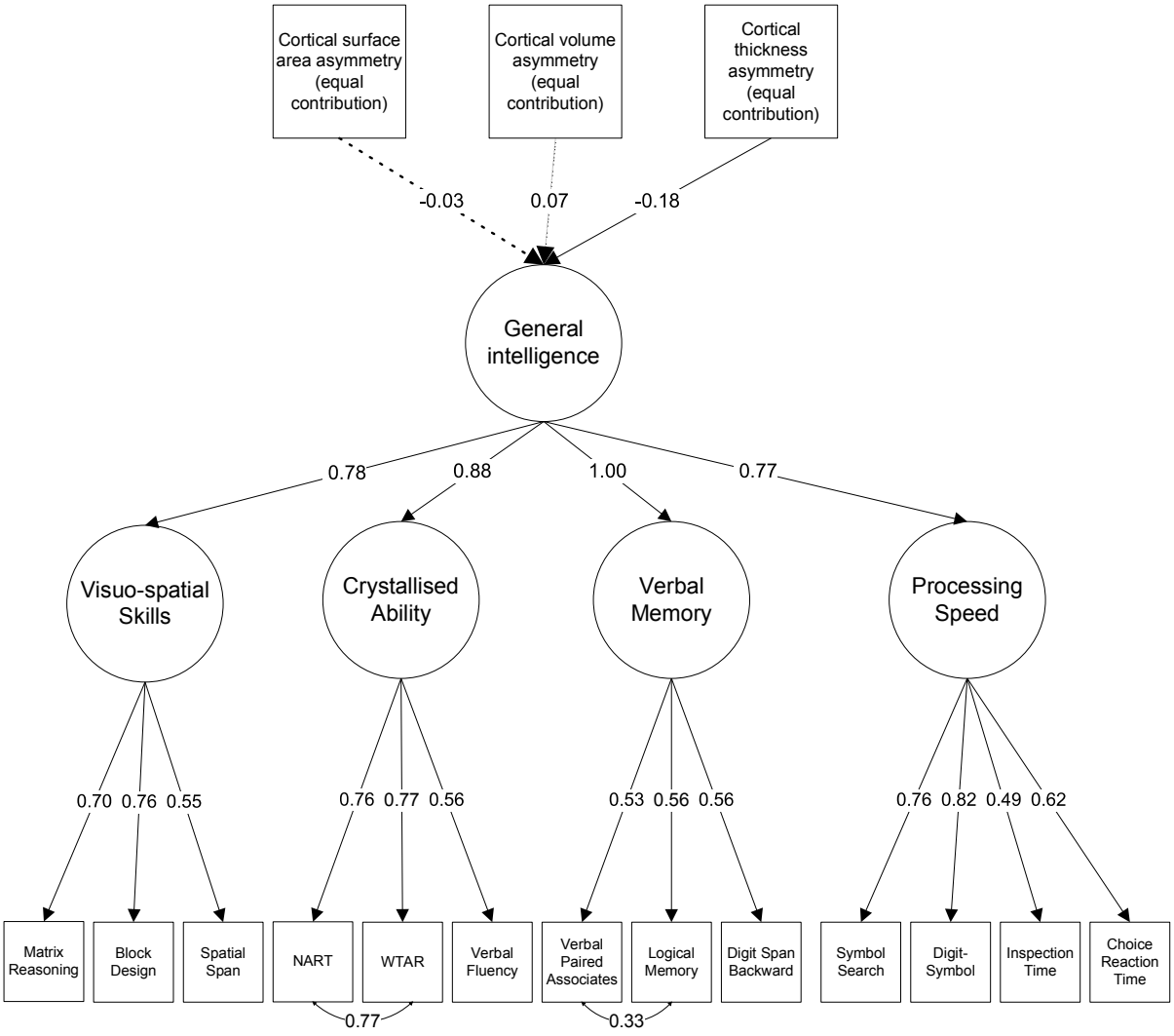

Figure 3. Simplified model estimating the association between cortical surface area asymmetry, volume asymmetry and thickness asymmetry (for equal-contribution asymmetry values) and general intelligence. Non-significant paths are illustrated with dotted lines.

Differences in effect sizes were analysed to investigate whether the association between thickness asymmetry and general intelligence was significantly different from the association between surface area asymmetry and/or volume asymmetry and general intelligence. As shown in Table 2, there were significant differences between the original, no constraints model (Model i) and models where equality constraints were placed on surface area asymmetry and thickness asymmetry (Model ii, p =.003) and volume asymmetry and thickness asymmetry (Model iii, p = .002). The no-constraint model had better model fit than the constrained models (e.g. AIC: Model i = 32939, Model ii = 32946, Model iii = 32947). Therefore, the effect size of the association between thickness asymmetry and general intelligence was significantly different to the associations between surface area asymmetry and general intelligence, and volume asymmetry and general intelligence. Thus, in this

sample, global thickness asymmetry was significantly more strongly related to general intelligence than was global surface area asymmetry or global volume asymmetry.

Table 2. Tests for differences in general intelligence effect sizes between cortical thickness asymmetry and i) surface area asymmetry and ii) volume asymmetry.

Model	Model constraints	χ^2	*df*	AIC	BIC	Model of comparison	$\Delta\chi^2$	Δ *df*	Δ *p*
i	None	224.57	96	32939	33089	-	-	-	-
ii	Thickness asymmetry and surface area asymmetry	233.41	97	32946	33092	i	8.84	1	.003**
iii	Thickness asymmetry and volume asymmetry	234.00	97	32947	33092	i	9.43	1	.002**

3.3.2. Equal regional contribution analysis: Childhood SES mediation model

As global cortical thickness asymmetry was significantly negatively related to general intelligence, a new model was estimated to test whether thickness asymmetry mediated the association between childhood SES and general intelligence (see Figure 4 and Supplementary Table 10). Father's occupational class, type of toilet and number of people sharing a toilet loaded significantly ($p < .001$) on the latent factor of childhood SES. The residual variance of the path from the number of people per room to childhood SES was estimated as negative ($\beta = -.153$), indicating all variance was shared with childhood SES. Therefore, as discussed above, its residual variance was set to zero. A covariance path was added between type of toilet and number of people sharing a toilet, since these variables shared significant covariance not accounted for by the paths in the rest of the model.

The bivariate association between SES and general intelligence was $\beta = -.29$, $p < .001$. Whereas cortical thickness asymmetry was significantly associated with general intelligence ($\beta = -.18$), it was non-significantly associated with childhood SES ($\beta = -.06$, $p = .154$). The mediation model indicated that the SES-general intelligence association was not significantly mediated by cortical thickness asymmetry (attenuation 3.81%, $p = .205$, from $\beta = -0.30$ to $\beta = -.29$).

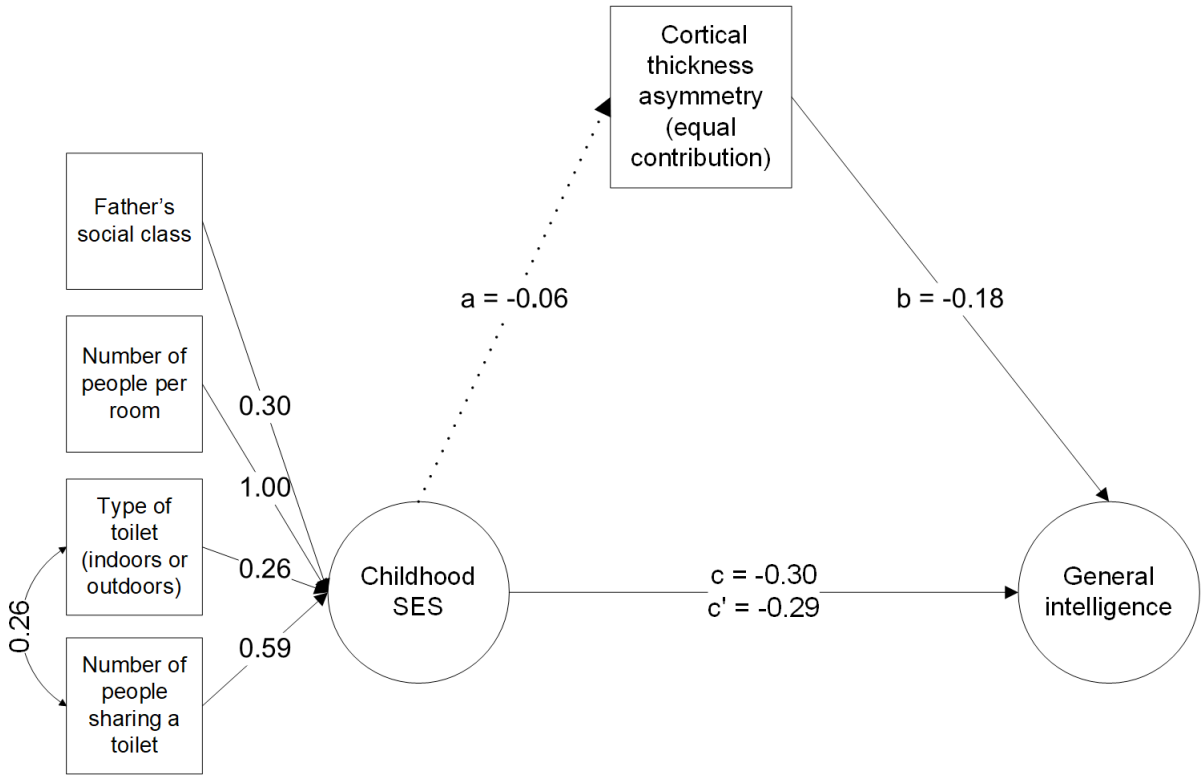

Figure 4. Simplified mediation model estimating the mediation of thickness asymmetry on the association between childhood SES and general intelligence. See also Figure 3 and Supplementary Table 10.

3.3.3. Equal regional contribution analysis: P-FIT versus non-Non-P-FIT asymmetry

Another aim of the present study was to investigate whether P-FIT asymmetry is more strongly related to general intelligence than non-P-FIT asymmetry, as was reported by Yeo et al. (2016). Separate values were calculated for P-FIT and non-P-FIT asymmetry. P-FIT and non-P-FIT asymmetry was moderately positively correlated on all three measures: surface area asymmetry $r = .29$, $p < .001$; volume asymmetry $r = .24$, $p < .001$; thickness asymmetry $r = .29$, $p < .001$. A new general intelligence model was estimated to include separate surface area asymmetry, volume asymmetry, and thickness asymmetry scores for P-FIT and non-P-FIT regions (see Table 3).

Table 3. *β*-values, *SE*s and *p*-values of paths from measures of cortical asymmetry to general intelligence for all regions, P-FIT and non-P-FIT regions.

	All regions	P-FIT	Non-P-FIT
Surface area asymmetry	-.03 (.07), *p* = .678	-.112 (.063), *p* = .076	.057 (.066), *p* = .389
Volume asymmetry	.07 (.07), *p* = .286)	.038 (.064), *p* = .549	.047 (.067), *p* = .483
Thickness asymmetry	-.18 (.05), *p* <.001	-.068 (.050), *p* = .173	-.131 (.049), *p* = .008

Importantly, we next tested formally whether P-FIT asymmetry was more strongly related to general intelligence than non-P-FIT asymmetry for cortical surface area, volume or thickness. To do this, equality constraints were placed on the P-FIT and non-P-FIT asymmetry scores for each measure in turn. For example, in Model B equality constraints were placed on P-FIT surface area asymmetry and non-P-FIT surface area asymmetry. These constrained models were compared to the original, freely-estimated, model (Model A). For each comparison, the critical *p*-value was > .05 (see Table 4). Therefore, P-FIT asymmetry was not more strongly related to general intelligence than non-P-FIT asymmetry for cortical surface area, volume or thickness.

Table 4. Equality constraint comparisons between P-FIT and non-P-FIT models. Δ values refer to the difference tests between models.

Model	Model constraints	χ^2	*df*	AIC	BIC	Model of comparison	Δ χ^2	Δ *df*	Δ *p*
A	None	261.86	132	21793	21956	-	-	-	-
B	P-FIT and non-P-FIT surface area asymmetry	264.70	133	21793	21952	A	2.84	1	.092
C	P-FIT and non-P-FIT volume asymmetry	261.88	133	21791	21949	A	0.02	1	.896
D	P-FIT and non-P-FIT thickness asymmetry	262.90	133	21792	21950	A	1.04	1	.308

3.4. Proportional regional contribution analysis

To investigate how similar equal and proportional region contribution methods for calculating asymmetry are, correlations were conducted. The correlations were between the two overall asymmetry scores (equal and proportional) for each of the 636 participants. There was no significant correlation between equal and proportional asymmetries for surface area: *r* = -.009 (*p* = .82). There were significant correlations for volume, *r* = .099 (*p* = .01), and thickness, *r* = .274 (*p* < .001). However, these correlations (particularly for volume) are weak. The weakness (and, in the case of surface area, non-significance) of these correlations highlights that these two methods of calculating cortical asymmetry result in very different outcomes.

Using the method of calculating asymmetry where each region contributed proportionally to the overall asymmetry score, there were no significant associations between any measures of cortical asymmetry and general intelligence (see Figure 5). As in the equal regional contribution analysis, the three cortical asymmetry measures (surface area, volume and thickness) were allowed to correlate with each other. For all paths, $p > .3$ and $SE = .046$.

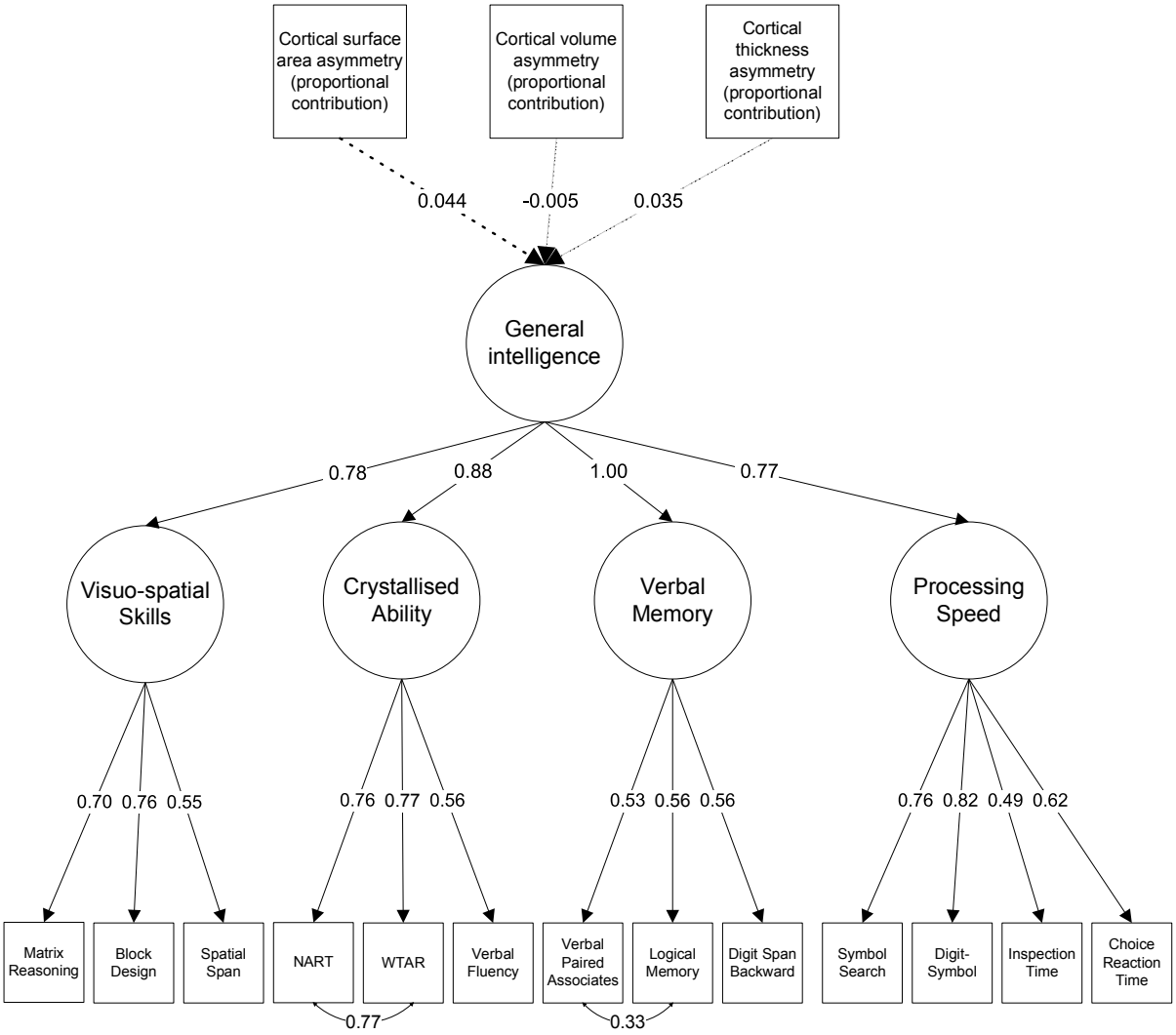

Figure 5. Simplified model estimating the association between cortical surface area asymmetry, volume asymmetry and thickness asymmetry (for proportional asymmetry scores) and general intelligence. Non-significant paths are illustrated with dotted lines.

3.5. White matter fractional anisotropy asymmetry model

White matter fractional anisotropy asymmetry scores were calculated so that each tract contributed equally. Directional asymmetries were calculated by subtracting the right white matter tract fractional anisotropy value from the left. No absolute asymmetries were individually associated with general intelligence (all β-values < .08, all p-values > .05; see Supplementary Table 1). A structural equation model was estimated to test the association

between global white matter fractional anisotropy asymmetry and general intelligence (see Supplementary Figure 5). The association was small and non-significant (β = .03, *SE* = .05, p = .512). Therefore, there was no evidence that combined white matter fractional anisotropy asymmetry was significantly associated with general intelligence.

4. Discussion

The association between brain asymmetry and general intelligence was estimated in a sample of older adults. Both regional and global measurements were used for grey matter (cortical volume, surface area and cortical thickness) and white matter fractional anisotropy, and general intelligence was estimated from a wide variety of tests covering several cognitive domains. The method of calculating asymmetry made a difference to the results: there was an association between cortical thickness asymmetry and intelligence when regions contributed equally to the estimation of cortical asymmetry, but there were no such associations when the contribution of each region was proportional to its size. Cortical volume and surface area showed no significant relations to intelligence in any analysis (all p-values > .3). It is important for future research to carefully consider and justify whether equal or proportional methods are used for calculating cortical asymmetry.

Using the method where regions contributed equally to the total asymmetry score, as in Yeo et al. (2016), asymmetry in global cortical thickness was significantly negatively associated with general intelligence. This association was modest (r = -.18), as expected from similar asymmetry-cognitive associations reported by Yeo et al. (2016) and in other previous studies (e.g. Furlow et al.; 1997; Bates, 2007). The novel aspects of our study are that the association between thickness asymmetry and cognition was investigated using a latent measure of general intelligence, we used multiple cortical metrics alongside an index of white matter microstructure, and tested these hypotheses in a sample of older adults. An exploratory analysis of a previous study suggests a positive association between cortical thickness asymmetry and working memory and vocabulary performance in young adults (N = 100, Plessen et al., 2014). However, like most previous studies, our finding suggested that higher bodily and brain asymmetry is linked to negative cognitive outcomes (e.g. Bates, 2007; Hope et al., 2013). Further investigation is required, as there are age-related differences in both cortical thickness asymmetry (Thambisetty et al., 2010) and general intelligence (MacDonald, Li & Bäckman, 2009) that might affect associations between these variables in samples of different ages.

There was no association between global cortical surface area asymmetry (calculated with equal regional contributions) and general intelligence. This result appears to be inconsistent

with Yeo et al. (2016; *N* = 244), who reported a significant negative association (*r* = -.15), despite using the same methods for cortical asymmetry calculation and a full-scale IQ measure. Differences in findings could be due to sample sizes, or could be age-related. Yeo et al. (2016) used a sample of 18-33 year olds, whereas the current study sampled a narrower age range of approximately 73-years-old. It is possible that age-related changes in surface area (Dotson et al., 2016; Plessen et al., 2014) could affect associations between its asymmetry and general intelligence.

In addition, there was no significant association between cortical volume asymmetry and general intelligence. Cortical volume is essentially the product of cortical thickness and cortical surface area and, in this sample, surface area and volume were more phenotypically similar than surface area and thickness (Cox et al., 2018). Therefore, because there was no association between surface area asymmetry and general intelligence, it follows that there was no association between volume asymmetry and general intelligence. Previous studies have not investigated a link between overall volume asymmetry and general intelligence. Instead, they focused on specific regions and specific populations (e.g. Woolard & Heckers, 2012; Dougherty et al, 2016). Future research should investigate whether cortical volume asymmetry is associated with general intelligence in healthy young adults.

P-FIT asymmetry was not more strongly associated with general intelligence than non-P-FIT asymmetry in 73-year-olds for cortical surface area, volume or thickness. Therefore, our findings do not support Yeo et al.'s (2016) suggestion that frontoparietal surface area asymmetry predicted general intelligence whereas non-frontoparietal surface area asymmetry did not. This discrepancy could, once again, be explained by age differences: frontoparietal integrity decreases more rapidly than non-frontoparietal integrity after 60 years old (e.g. Rönnlund, Sundström & Nilsson, 2015), and this could, in turn, affect associations between frontoparietal regions and general intelligence. Regarding the P-FIT theory, frontoparietal asymmetry does not appear to be a marker of the biological basis of general intelligence in older adults. It is possible that frontoparietal regions become less specialised for cognitive abilities in older age (see Campbell, Grady, Ng & Hasher, 2012), making the P-FIT less meaningful in older adults. This uncertainty provides motivation for future studies to test the P-FIT separately in older adults.

Cortical thickness asymmetry was not associated with childhood SES, providing evidence against the hypothesis that asymmetry is a significant mediator of the association between childhood SES and general intelligence. However, the participants in this study might not be representative of 73-year-olds in the general population, because they are a selective sample, who were self-motivated to participate in this research. Due to the nature of the

sample selection, the effect size may have been attenuated, as there are fewer people with low SES backgrounds compared to the general population. The sample size may not have been large enough to reliably estimate the likely modest association between childhood SES and thickness asymmetry. As brain asymmetry in older age may be affected by multiple environmental factors, future research using more representative samples should investigate whether childhood cortical asymmetry is associated with childhood SES.

There are differences between asymmetry for individual regions found in this study and in previous studies. For example, Wang et al. (2007) found significant directional asymmetry in the posterior cingulate in a sample of young adults. However, in the current study, there was no directional asymmetry in the posterior cingulate. Furthermore, unlike the current study, Yeo et al. (2016) found significant associations between surface area asymmetry to general intelligence in the frontal pole, caudal middle frontal, fusiform, isthmus cingulate and lingual regions. Unlike Yeo et al. (2016), the current study found significant associations from surface area asymmetry to general intelligence in the precuneus and rostral anterior cingulate regions. As the same methods were used, these findings suggest that the association between surface area asymmetry and general intelligence might change on a regional basis with age, though it could equally be that these findings are false positives or are the consequence of overfitting to the specific samples in question. To aid interpretation of these differences, future studies with longitudinal data could characterise region-based age-related changes in cortical surface area asymmetry, and also in volume and thickness. This would be especially worthwhile in large samples covering a wide age range.

Regional and global white matter tract fractional anisotropy asymmetries were not associated with general intelligence in 73-year-olds. It may therefore be the case that white matter fractional anisotropy asymmetry is not associated with cognitive performance. However, future research should investigate this association in younger adults. Alternatively, it could be more appropriate to investigate associations between white matter asymmetry in specific tracts and cognitive abilities relevant to them, as effects might be undetectable or negated when white matter tract asymmetry is combined. There are also other features of white matter tracts that could be investigated – for example, number of streamlines, which is a proxy measure for volume. It is also notable that our regional and global metrics were based upon a limited number of white matter pathways – these were selected due to our ability to reliably identify and measure their microstructure, but they comprise a relatively low proportion of the brain's overall white matter connective tissue.

The current study had a large sample size (N = 636) compared to other studies of intelligence and brain asymmetry, and a comprehensive battery of cognitive tests. The MRI

scans were completed in the same scanner at the sample clinic. The association between cortical thickness asymmetry and general intelligence was highly significant, and would survive Bonferroni correction across 166 tests. Both a strength and a limitation of the current study was the narrow age range of the sample. Whereas this enables stronger conclusions about effects in 73-year-olds, and mitigates the possibly-confounding effects of within-sample chronological age, it does not allow exploration of age-related differences, a factor which—as noted above—may moderate asymmetry-intelligence associations, yielding different results from those of previous work on asymmetry.

5. Conclusion

When regional measures contributed equally to structural brain asymmetry scores, brain cortical thickness asymmetry was negatively associated (β = -.18) with general intelligence in 73-year-olds. There were no associations between general intelligence and cortical surface area, cortical volume, or white matter fractional anisotropy asymmetries. Thickness asymmetry was not associated with childhood SES which did not mediate the association between childhood SES and general intelligence. There was no difference in the intelligence-cortical asymmetry association between P-FIT and non-P-FIT regions. These findings differ from Yeo et al. (2016), who found that there was a negative association between surface area asymmetry and intelligence, and that asymmetry of frontoparietal regions, but not asymmetry of non-frontoparietal regions was associated with intelligence. In contrast, when regional measures contributed proportionally to cortical hemispheric asymmetry metrics, there were no associations between cortical surface area, cortical volume or cortical thickness and general intelligence in 73-year-olds. This study raises questions about how structural brain asymmetry should be measured, and motivates future research to consider how best to characterise brain asymmetry.

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Supplementary Material for:

Structural Brain Asymmetry and General Intelligence in 73-Year-Olds

Supplementary tables

Supplementary Table 1: Descriptive statistics of separate white matter tract fractional anisotropy absolute asymmetries, and their β-weights to general intelligence. All β-weights were non-significant ($p > .05$).

White matter tract	*N* (Left)	*N* (Right)	*M* (*SD*)	β-weight to general intelligence
Arcuate	639	580	.01 (.01)	-.04
Anterior thalamic radiations	556	643	.01 (.003)	.02
Bilateral cingulum cingulate gyri	641	650	.11 (.09)	.001
Uncinate	567	628	.14 (.11)	-.05
Inferior longitudinal fasciculi	628	664	.11 (.09)	.08

Supplementary Table 2: Results from models that excluded MRI abnormalities.

	Surface area	Volume	Thickness
Equal contributions	β = 0.008, *SE* = 0.07, *p* = .914	β = 0.12, *SE* = 0.08, *p* = .125	β = -0.19, *SE* = 0.05, *p* < .001
Proportional contributions	β = 0.08, *SE* = 0.05, *p* = .115	β = 0.003, *SE* = 0.05, *p* = .945	β = -0.007, *SE* = 0.05, *p* = .893

Supplementary Table 3: Means and *SD*s for left and right hemispheres for cortical surface area, volume and thickness.

Cortical region	Surface area (mm^2)		Volume (mm^3)		Thickness (mm)	
	Left *M* (*SD*)	Right *M* (*SD*)	Left *M* (*SD*)	Right *M* (*SD*)	Left *M* (*SD*)	Right *M* (*SD*)
Banks of the superior temporal sulcus	887.07 (176.45)	815.68 (123.70)	1967.44 (433.66)	1922.69 (364.69)	2.13 (0.21)	2.27 (0.21)
Caudal anterior cingulate	573.26 (111.15)	670.79 (132.19)	1421.54 (414.88)	1674.57 (455.69)	2.34 (0.40)	2.25 (0.34)
Caudal middle frontal	2057.80 (321.87)	1931.41 (315.62)	5300.53 (898.39)	5010.71 (905.37)	2.29 (0.17)	2.28 (0.17)

Cuneus	1359.04	1413.75	2576.17	2703.91	1.74	1.75
	(201.45)	(199.53)	(443.63)	(454.17)	(0.14)	(0.15)
Entorhinal	384.15	338.75	1772.26	1672.95	2.99	3.16
	(74.77)	(79.03)	(416.12)	(401.35)	(0.48)	(0.50)
Frontal pole	219.70	294.80	788.58	1024.96	2.63	2.55
	(36.98)	(46.55)	(163.89)	(206.90)	(0.32)	(0.29)
Fusiform	2915.61	2818.91	8493.70	8154.62	2.38	2.38
	(407.09)	(382.98)	(1382.68)	(1277.06)	(0.19)	(0.19)
Inferior parietal	4096.06	4809.82	11002.15	13002.18	2.30	2.33
	(407.09)	(629.75)	(1382.68)	(1737.65)	(0.16)	(0.16)
Inferior temporal	2936.59	2777.45	9652.79	9322.60	2.61	2.64
	(407.09)	(405.39)	(1522.56)	(1444.17)	(0.20)	(0.21)
Insula	2030.83	2039.06	6518.68	6544.72	2.92	2.93
	(222.96)	(274.90)	(769.15)	(1444.17)	(0.19)	(0.19)
Isthmus cingulate	952.04	876.92	2410.87	2215.81	2.40	2.37
	(154.60)	(136.97)	(370.86)	(356.94)	(0.22)	(0.23)
Lateral occipital	4477.62	4321.30	10484.21	10624.96	2.08	2.17
	(543.53)	(523.59)	(1463.77)	(1475.80)	(0.15)	(0.16)
Lateral orbitofrontal	2237.17	2224.81	6542.66	6418.76	2.50	2.49
	(310.14)	(301.89)	(767.42)	(758.56)	(0.19)	(0.19)
Lingual	2729.36	2780.27	5675.67	5809.54	1.85	1.87
	(368.50)	(363.12)	(825.43)	(852.18)	(0.13)	(0.13)
Medial orbitofrontal	1685.51	1618.71	4910.28	4652.62	2.52	2.40
	(246.22)	(233.80)	(692.77)	(618.61)	(0.21)	(0.23)
Middle temporal	2746.85	3027.31	8929.82	10148.88	2.55	2.63
	(387.81)	(392.31)	(1368.09)	(1440.48)	(0.19)	(0.18)
Parahippocampal	641.80	613.79	1733.77	1589.82	2.16	2.10
	(107.99)	(93.26)	(375.98)	(312.77)	(0.37)	(0.32)
Paracentral	1229.38	1394.31	3030.94	3348.18	2.18	2.15
	(165.29)	(185.61)	(486.50)	(534.99)	(0.17)	(0.17)
Pars opercularis	1477.65	1254.60	3965.81	3337.00	2.29	2.31
	(221.72)	(194.24)	(661.38)	(564.48)	(0.15)	(0.15)
Pars orbitalis	579.37	701.70	1866.44	2248.28	2.44	2.46
	(77.76)	(99.09)	(275.13)	(341.98)	(0.22)	(0.22)
Pars triangularis	1146.92	1325.72	2909.65	3444.06	2.16	2.20
	(164.90)	(213.49)	(468.49)	(602.54)	(0.16)	(0.16)
Pericalcarine	1226.20	1357.73	1772.91	1972.25	1.50	1.49
	(215.37)	(231.18)	(351.02)	(379.21)	(0.14)	(0.14)
Postcentral	3982.52	3847.40	8427.31	7972.79	1.85	1.83
	(437.97)	(459.67)	(1062.01)	(1110.17)	(0.12)	(0.13)
Posterior cingulate	1023.76	1026.73	2666.34	2661.67	2.38	2.35
	(134.74)	(148.89)	(437.03)	(426.33)	(0.22)	(0.21)
Precentral	4530.40	4549.54	11252.33	11168.51	2.25	2.23
	(478.86)	(490.06)	(1301.43)	(1325.42)	(0.17)	(0.17)
Precuneus	3367.85	3520.62	8219.03	8415.09	2.15	2.14
	(399.04)	(443.47)	(1042.23)	(1073.91)	(0.15)	(0.14)
Rostral anterior cingulate	697.66	563.16	2274.40	1819.22	2.79	2.76
	(157.11)	(130.26)	(495.03)	(453.10)	(0.30)	(0.34)
Rostral middle frontal	4891.62	5150.11	12467.16	13065.35	2.15	2.14
	(672.51)	(756.24)	(1633.68)	(1789.28)	(0.14)	(0.14)
Superior frontal	6460.72	6269.43	18961.67	18241.14	2.45	2.42
	(735.87)	(739.08)	(2122.46)	(2112.27)	(0.15)	(0.14)
Superior parietal	5031.29	5051.21	11619.40	11612.34	2.01	2.00
	(574.64)	(585.32)	(1620.43)	(1669.89)	(0.18)	(0.16)
Superior temporal	3482.51	3319.09	9564.62	9420.31	2.30	2.36

	(401.16)	(356.92)	(1331.14)	(1316.02)	(0.18)	0.19)
Supramarginal	3542.61	3398.46	9331.00	8931.64	2.29	2.31
	(485.35)	(481.25)	(1251.36)	(1280.49)	(0.15)	(0.16)
Temporal pole	499.79	446.34	2515.83	2315.12	3.36	3.48
	(61.05)	(63.81)	(442.25)	(433.92)	(0.35)	(0.37)
Transverse	423.04	316.11	1000.71	779.84	2.12	2.19
temporal	(69.75)	(52.58)	(179.54)	(158.22)	(0.22)	(0.24)

Supplementary Table 4: Descriptive statistics for absolute cortical asymmetries (surface area, volume and thickness) for specific brain regions.

	Surface area asymmetry	Volume asymmetry	Thickness asymmetry
	M (*SD*)	*M* (*SD*)	*M* (*SD*)
Bank superior temporal sulcus	.07 (.07)	.09 (.07)	.04 (.03)
Caudal anterior cingulate	.09 (.07)	.15 (.11)	.08 (.06)
Caudal middle frontal	.06 (.05)	.06 (.05)	.02 (.02)
Cuneus	.05 (.04)	.06 (.05)	.03 (.03)
Entorhinal	.08 (.08)	.10 (.08)	.06 (.05)
Frontal pole	.07 (.06)	.09 (.07)	.05 (.04)
Fusiform	.04 (.03)	.05 (.04)	.03 (.02)
Inferior parietal	.04 (.03)	.04 (.04)	.02 (.02)
Inferior temporal	.04 (.03)	.05 (.04)	.03 (.02)
Insula	.05 (.03)	.04 (.03)	.02 (.02)
Isthmus cingulate	.05 (.04)	.06 (.05)	.04 (.03)
Lateral occipital	.04 (.03)	.04 (.04)	.02 (.02)
Lateral orbitofrontal	.03 (.02)	.03 (.03)	.03 (.02)
Lingual	.04 (.03)	.05 (.04)	.03 (.02)
Medial orbitofrontal	.05 (.04)	.05 (.04)	.03 (.03)
Middle temporal	.04 (.03)	.05 (.04)	.02 (.02)
Parahippocampal	.06 (.06)	.09 (.07)	.06 (.05)
Paracentral	.05 (.04)	.06 (.05)	.03 (.02)
Pars opercularis	.06 (.05)	.09 (.07)	.06 (.05)

Pars orbitalis	.05 (.04)	.06 (.05)	.02 (.02)
Pars triangularis	.06 (.05)	.06 (.05)	.04 (.03)
Pericalcarine	.05 (.04)	.07 (.05)	.03 (.02)
Postcentral	.03 (.03)	.06 (.05)	.03 (.03)
Posterior cingulate	.05 (.04)	.04 (.04)	.02 (.02)
Precentral	.03 (.02)	.06 (.05)	.04 (.03)
Precuneus	.03 (.02)	.03 (.03)	.02 (.02)
Rostral anterior cingulate	.09 (.07)	.03 (.02)	.02 (.02)
Rostral middle frontal	.05 (.03)	.10 (.08)	.06 (.05)
Superior frontal	.03 (.02)	.05 (.03)	.02 (.02)
Superior parietal	.03 (.03)	.03 (.02)	.02 (.01)
Superior temporal	.03 (.02)	.04 (.03)	.02 (.02)
Supramarginal	.05 (.04)	.04 (.03)	.02 (.02)
Temporal pole	.06 (.05)	.05 (.04)	.02 (.02)
Transverse temporal	.06 (.05)	.07 (.06)	.04 (.03)

Supplementary Table 5: Absolute fit indices for the four theoretical models estimated in the current study.

Model	χ^2	*df*	CFI	TLI	RMSEA	SRMR
General intelligence model	267.63	135	0.96	0.95	0.06	0.05
Equal-contribution cortical asymmetry and general intelligence model	224.57	96	0.96	0.95	0.05	0.05
Mediation model (including childhood SES)	294.69	129	0.97	0.95	0.05	0.06

Proportional contribution cortical asymmetry and general intelligence model	213.98	96	0.96	0.96	0.05	0.04
White matter fractional anisotropy asymmetry and general intelligence model	191.82	192	0.96	0.95	0.05	0.05

Supplementary Table 6: Male-female measurement invariance tests (configural, weak and strong) for the general intelligence model.

Model number	Model description	χ^2	*df*	AIC	BIC	Model of comparison	**Δ** χ^2	**Δ** *df*	**Δ** *p*
1	Configural invariance	237.33	120	45390	45777	-	-	-	-
2	Weak invariance (equal loadings)	258.29	132	45387	45721	1	20.96	12	.051
3	Strong invariance (equal loadings and equal intercepts)	313.14	140	45425	45725	1	54.86	8	<.001

Supplementary Table 7: Sex differences in cognitive tests.

Cognitive domain	Test	*N*	Overall *M* (*SD*)	M_{male} (*SD*)	M_{female} (*SD*)	Sex difference *p*	Sex difference *d*
Visuospatial Skills	Matrix Reasoning	634	13.52 (4.93)	14.00 (4.92)	12.98 (4.90)	.009	.21
	Block Design	634	34.38 (10.01)	35.56 (10.71)	33.07 (9.00)	.002	.25

	Spatial Span	634	14.79 (2.72)	15.09 (2.83)	14.45 (2.56)	.003	.24
Crystallised Ability	NART	634	34.66 (8.10)	33.67 (8.52)	35.77 (7.46)	.001	-.26
	WTAR	634	41.27 (6.94)	40.59 (7.70)	42.03 (5.89)	.008	-.21
	Phonemic Verbal Fluency	635	43.55 (12.78)	42.55 (13.43)	44.68 (11.93)	.035	-.17
Verbal Memory	Verbal Paired Associates	623	27.57 (9.48)	25.95 (9.77)	29.36 (8.84)	<.001	-.36
	Logical Memory	635	75.03 (17.84)	73.49 (18.59)	76.76 (16.83)	.020	-.18
	Digit span backwards	636	7.88 (2.31)	7.74 (2.36)	8.04 (2.23)	.095	-.13
Processing Speed	Symbol Search	634	24.88 (6.05)	24.59 (6.25)	25.20 (5.82)	.204	-.10
	Digit-Symbol Substitution	634	56.68 (11.79)	54.53 (11.88)	59.09 (11.23)	< .001	-.39
	Inspection Time	624	111.78 (10.95)	112.73 (11.38)	110.70 (10.34)	.020	.19
	Four-Choice Reaction Time	635	0.64 (0.08)	0.65 (0.09)	0.64 (0.08)	.280	-.09

Participants performed above WAIS-III and WMS-III manual norms for 70-74 year olds on all tests, apart from the Symbol Search test, where they performed at average (Wechsler, 1997a, 1997b). This indicates that they are not a representative sample of the general population. *t*-tests revealed significant sex differences in 10 of the 13 cognitive tests (see

Table 2). Generally, the sex differences found here are consistent with those reported in previous research (e.g. Delgado & Prieto, 1996; Krueger & Salthouse, 2010; Lowe, Mayfield & Reynolds, 2003). Males tended to perform better at visuospatial tasks and females tended to perform better at vocabulary-based tasks.

Supplementary Table 8: Path *β*-weight values, *SE*s, *p*-values and residual variances for the general intelligence model. *** < .001.

Cognitive domain	Domain *β* (*SE*)	*p*	Domain residual variances	Test	Test β (*SE*)	*p*	Test residual variance
Visuo-spatial	.78 (.03)	***	0.39	Matrix Reasoning	.70 (.03)	***	.50
				Block Design	.76 (.03)	***	.43
				Spatial Span	.55 (.04)	***	.70
Crystallised	.88 (.04)	***	0.23	NART	.76 (.03)	***	.42
				WTAR	.77 (.03)	***	.40
				Phonemic Verbal Fluency	.56 (.04)	***	.69
Verbal memory	1.00 (.00)	-	0.00	Verbal Paired Associates	.53 (.04)	***	.72
				Logical Memory	.56 (.03)	***	.69
				Digit span backward	.56 (.03)	***	.69
Speed	.77 (.03)	***	0.41	Symbol Search	.76 (.02)	***	.42
				Digit-Symbol Substitution	.82 (.02)	***	.32
				Inspection Time	.49 (.04)	***	.76
				Four-Choice Reaction Time	.62 (.03)	***	.62

Supplementary Table 9: Path *β*-weight values for individual cortical regions and general intelligence. Unless otherwise specified, $p > .05$. Significant *β*-weights are in boldface text.

	Surface area Asymmetry	Volume asymmetry	Thickness asymmetry
Banks of the superior temporal sulcus	.01	.07	.002
Caudal anterior cingulate	.07	.02	-.07
Caudal middle frontal	-.02	.04	-.007
Cuneus	-.04	-.06	-.02
Entorhinal	.02	.01	-.04
Frontal pole	-.07	-.07	-.04
Fusiform	-.09	-.05	.02
Inferior parietal	-.02	.02	.02
Inferior temporal	.06	**.10** ***p* = .034**	-.005
Insula	-.05	-.04	-.01
Isthmus cingulate	-.02	-.02	-.06
Lateral occipital	-.002	.06	-.04
Lateral orbitofrontal	-.06	-.07	-.03
Lingual	-.05	-.06	-.02
Medial orbitofrontal	.02	.001	-.04
Middle temporal	.02	.05	.03
Parahippocampal	.04	.02	-.02
Paracentral	.06	.06	-.009
Pars opercularis	.01	.02	-.04
Pars orbitalis	-.07	-.02	-.05
Pars triangularis	.07	.08	.04
Pericalcarine	-.08	-.03	-.09
Postcentral	-.07	-.01	-.007

Posterior cingulate	-.08	-.09	.02
Precentral	-.07	-.07	.02
Precuneus	**.13** ***p* = .007**	-.01	-.06
Rostral anterior cingulate	**.13** ***p* = .004**	.08	-.03
Rostral middle frontal	.04	-.01	-.04
Superior frontal	.08	.09	.005
Superior parietal	-.02	-.03	-.03
Superior temporal	.002	-.07	-.07
Supramarginal	-.02	-.04	.03
Temporal pole	-.02	-.06	-.02
Transverse temporal	**.09** ***p* = .047**	.09	.04

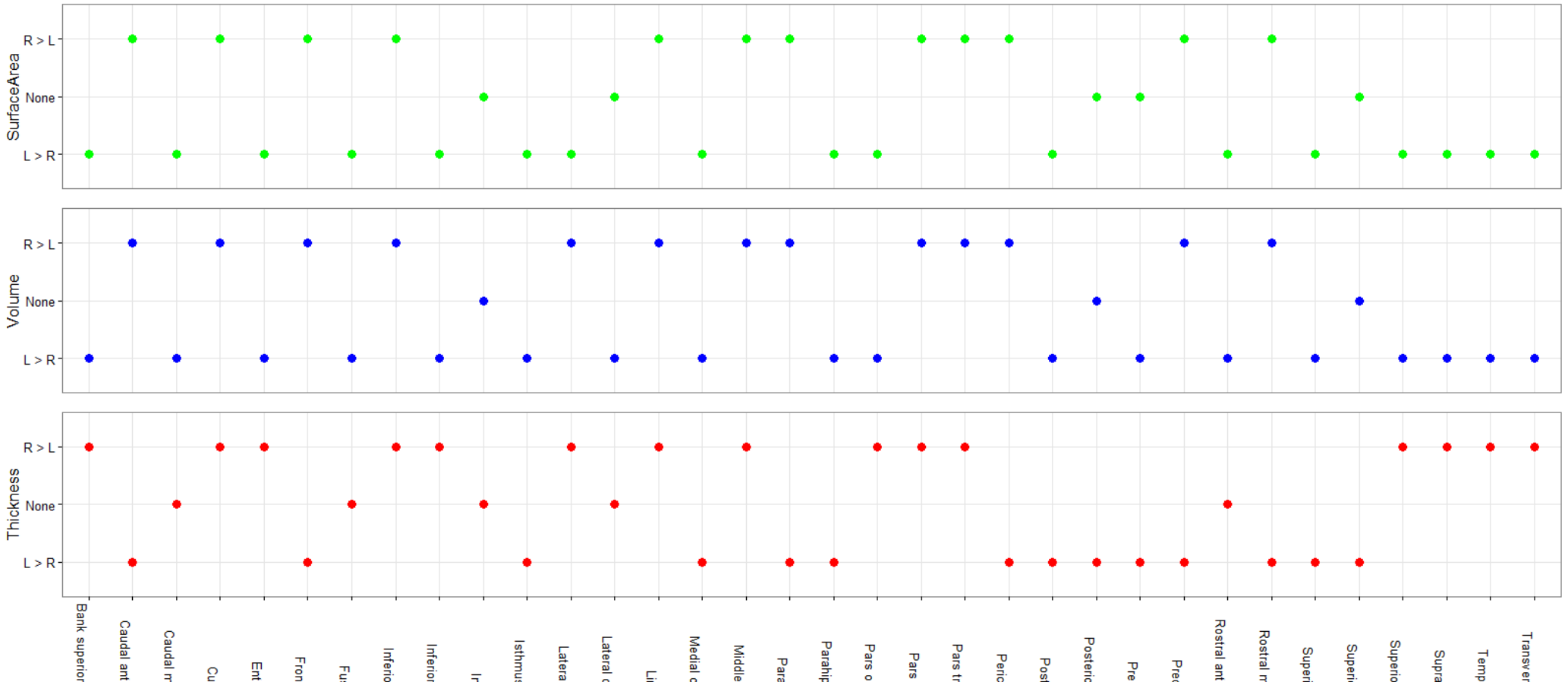
Supplementary Table 10: Descriptive statistics, path *β*-weight values, *SE*s, *p*-values and residual variances for the childhood SES latent factor in the exploratory mediation model.

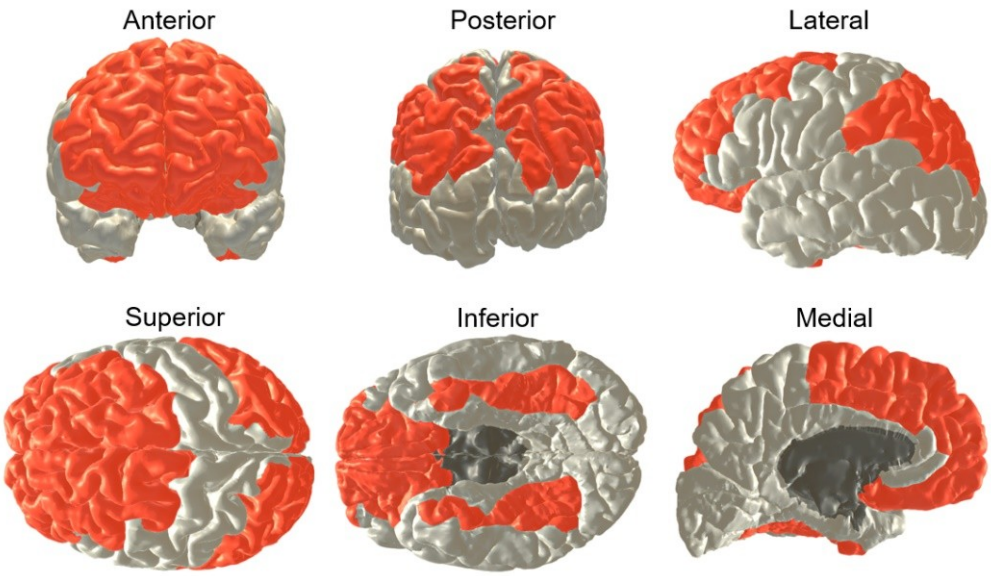
	N	*M* (*SD*)	β (*SE*)	*p*	Residual variance
Father's social class	584	2.92 (0.91)	.30 (.04)	<.001	.90
Number of people per room	630	1.34 (0.74)	1.00 (.00)	-	.00
Toilet type	632	1.11 (0.32)	.26 (.04)	<.001	.92
Number of people sharing a toilet	627	5.28 (2.54)	.59 (.03)	<.001	.62

Supplementary figures

BRAIN ASYMMETRY AND GENERAL INTELLIGENCE

Supplementary Figure 1: Summary of directional asymmetries for cortical surface area, volume and thickness of cortical regions.





Supplementary Figure 3: Illustration of P-FIT (red) and non-P-FIT (grey) regions.

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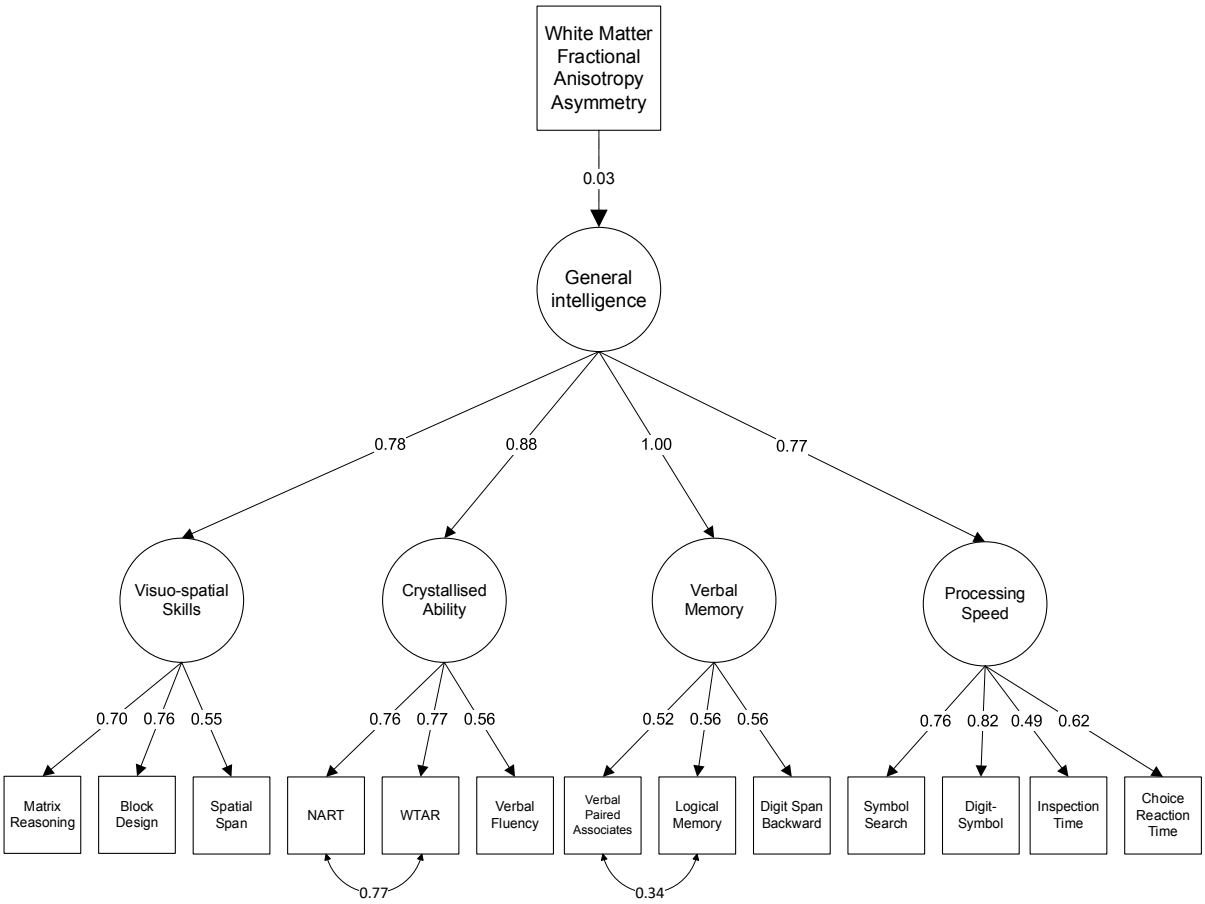
Supplementary Figure 4: Simplified model of general intelligence. For full details, including *SE*s, residual variances and *p*-values, see Appendix 1.



Supplementary Figure 5. Simplified diagram of model estimating the association between white matter fractional anisotropy asymmetry and general intelligence. Non-significant paths are illustrated with dotted lines. Residual variances for each variable are not shown.

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