Cortical measures and heritability in 326 identical and fraternal twins

Abstract No:

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Introduction:

Imaging genetics studies aim to find specific genes that influence brain structure and function. A first step in these studies is to examine morphometric measures that can be automatically computed from MRI, and rank them in terms of their heritability. Then, the most heritable measures can be explored more intensively using candidate gene or genome-wide association studies. Here we studied the heritability of cortical anatomy using a brain MRI dataset from 326 young adult monozygotic (MZ) and dizygotic (DZ) twins. As in a related MRI study of a large pedigree [7], we set out to evaluate and compare the intraclass correlation and the heritability of three measures - surface area, gray matter thickness and gray matter volume - obtained in 34 cortical regions of interest.

Methods:

We collected 3D structural brain MRI scans from 326 normal right handed young adult twins (age range: 22-25 years/160 MZ, 166 DZ). Scans were collected using a 4 Tesla Bruker Medspec whole body scanner at the Center for Magnetic Resonance (University of Queensland, Australia). Three-dimensional T1-weighted images were acquired with a magnetization prepared rapid gradient echo MP-RAGE sequence to resolve anatomy at high resolution. Acquisition parameters were: inversion time (TI)/repetition time (TR) /echo time (TE) = 1500/ 2500/3.83 msec; flip angle = 15^o; slice thickness = 0.9 mm with a 256x256x256 acquisition matrix. We used parcellated cortical gray matter volumes as our structural measures of interest. To compute these, we used the Freesurfer automated processing pipeline [1] for automated skull stripping, tissue classification, surface extraction, and cortical parcellation. This calculates volumes of individual gray matter parcellations in mm^3 and surface areas in mm^2. It also provides surface, volume statistics and geometric measures for 34 different regions of interest (ROIs). These consist of the surface area, gray matter volume, average thickness, mean curvature, curvedness and local foldedness for each of the parcellations [1].

For each ROI, the intraclass correlation (ICC) was computed in both MZ and DZ groups using an extension of the common Pearson correlation, based on restricted maximum likelihood methods (REML)[4]. The intraclass correlation measures the resemblance between twin pairs for a given phenotype. Corresponding p-values were also computed based on a permutation distribution [6].

Falconer's heritability estimate is defined as the difference in intraclass correlations between MZ and DZ twins:
h^2 = 2*(ICC_MZ-ICC_DZ); this estimates the variation in a measurement attributable to genetic differences among individuals [2].

Results:

Tables 1 and 2 show the ICC values for the MZ and DZ groups, respectively. Only three characteristics are reported as they gave greatest effect sizes. Non-significant values are bolded. As expected, ICC values were typically higher for MZ pairs than for DZ pairs; results were generally consistent across the three measures. Correlations were highest in the inferior parietal and temporal, pericalcarine, precentral, precuneus, superior frontal, temporal and parietal regions and in the insula in the MZ groups. The correlation values in the fusiform and insular cortices were similar for both types of twins. Heritability estimates (h^2) are displayed in Figure 1. Surface area measures are generally more heritable. Interestingly the pars opercularis and triangularis - components of Broca's language area - show a higher heritability on the left than the right side for the thickness average.
Overall, for all ROIs, heritability values were highest for the surface area measures. Cortical regions in the vicinity of the superior parietal, frontal, temporal and supramarginal regions showed high heritability.

Conclusions:

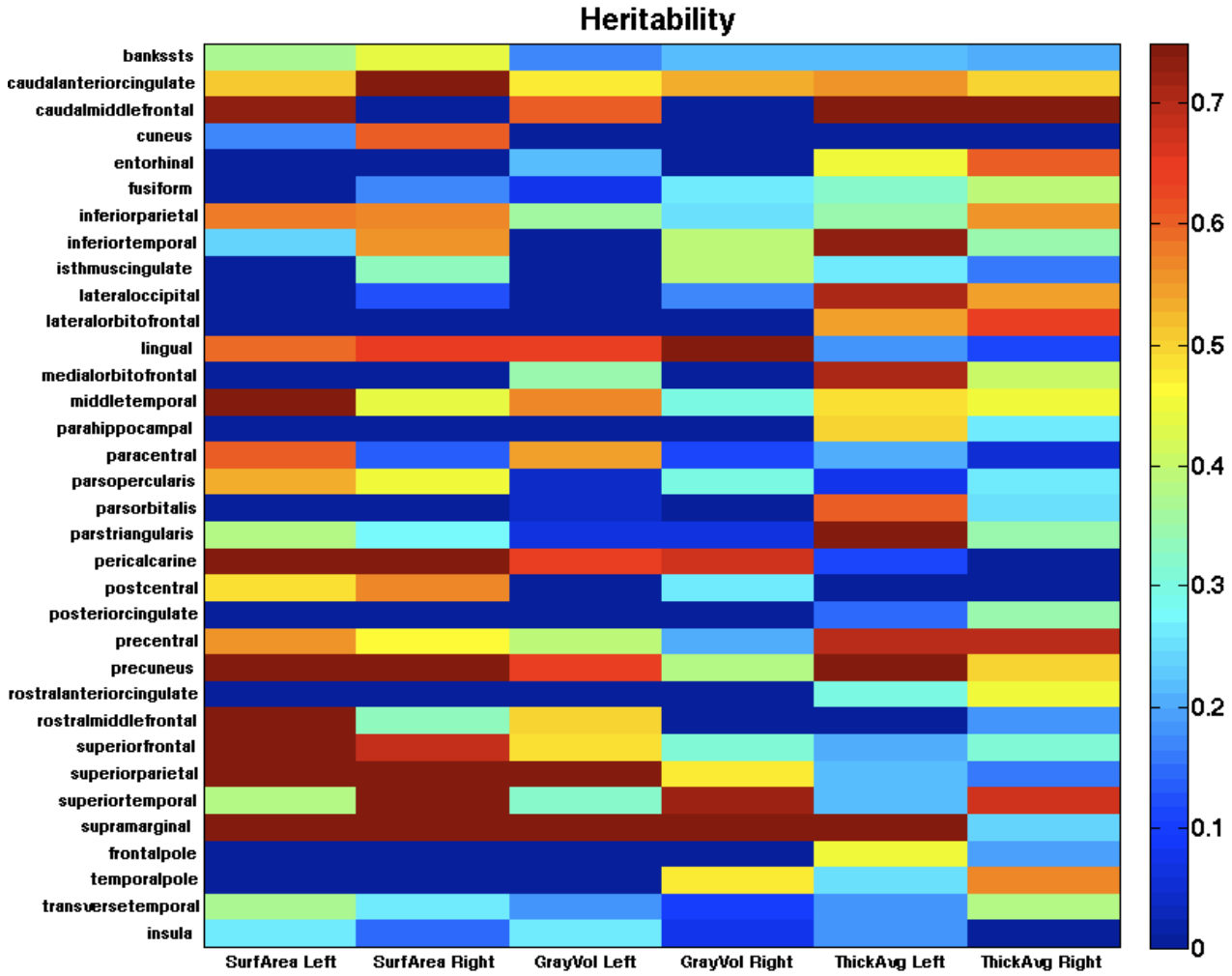
In our twin study of 34 cortical ROIs, our finding of high MZ correlations in frontal, temporal, superior parietal and supramarginal areas is consistent with a recent pediatric twin study [5]. However, as noted in [7], cortical thickness and surface area varied in terms of which measure was most sensitive to genetic influences. In particular, structural characteristics in language areas have been shown to be highly heritable, but heritability was high only for cortical thickness.

Our heritability measures for cortical thickness agree with the findings of [3]; we found a very high heritability bilaterally for the middle frontal and the lateral occipital cortices. In agreement with the

same study, Wernicke's area were more heritable than their left hemisphere counterparts and less heritable than regions containing Broca's area. These measures provide a ranked list of quantitative phenotypes to narrow the search for quantitative trait loci that influence brain structure.

Regions	Surface Area		Gray matter		Thickness Av	
	L	R	L	R	L	R
bankssts	0.41	0.42	0.40	0.35	0.42	0.21
caudalanteriorcingulate	0.42	0.55	0.34	0.48	0.52	0.34
caudalmiddlefrontal	0.60	0.31	0.57	0.31	0.61	0.62
cuneus	0.41	0.56	0.27	0.37	**0.002**	**0.08**
entorhinal	**0.026**	**0.051**	0.33	**0.15**	0.23	0.42
fusiform	0.39	0.55	0.35	0.53	0.45	0.36
inferiorparietal	0.56	0.62	0.53	0.54	0.51	0.45
inferiortemporal	0.36	0.36	0.30	0.35	0.53	0.35
isthmuscingulate	**0.16**	0.31	**0.17**	0.41	0.33	0.23
lateraloccipital	0.41	0.56	0.33	0.51	0.50	0.44
lateralorbitofrontal	0.33	0.43	0.32	0.43	0.60	0.43
lingual	0.59	0.65	0.61	0.60	0.53	0.51
medialorbitofrontal	0.22	0.28	0.36	0.26	0.51	0.40
middletemporal	0.65	0.56	0.58	0.53	0.44	0.32
parahippocampal	**0**	**0.032**	**0.11**	**0.10**	0.25	0.26
paracentral	0.55	0.49	0.48	0.43	0.44	0.55
parsopercularis	0.41	0.53	0.20	0.56	0.45	0.40
parsorbitalis	**0.12**	0.32	**0.13**	**0.18**	0.50	0.37
parstriangularis	0.49	0.49	0.30	0.37	0.50	0.34
pericalcarine	0.62	0.62	0.56	0.54	0.38	0.47
postcentral	0.54	0.60	0.36	0.50	0.34	0.40
posteriorcingulate	**0.061**	**0.11**	**0.037**	**0.08**	0.23	0.30
precentral	0.65	0.57	0.53	0.46	0.60	0.59
precuneus	0.56	0.62	0.50	0.49	0.72	0.61
rostralanteriorcingulate	**0**	**0**	**0.02**	**0.002**	0.32	0.36
rostralmiddlefrontal	0.73	0.60	0.59	0.44	0.43	0.44
superiorfrontal	0.79	0.78	0.66	0.69	0.51	0.54
superiorparietal	0.78	0.67	0.63	0.56	0.52	0.52
superiortemporal	0.54	0.59	0.56	0.56	0.40	0.42
supramarginal	0.59	0.57	0.59	0.54	0.62	0.49
frontalpole	**0**	**0.035**	**0**	0.097	0.35	0.34
temporalpole	**0**	**0.10**	**0.04**	0.37	**0.19**	0.40
transversetemporal	0.21	0.25	0.24	0.27	0.42	0.48
insula	0.54	0.57	0.52	0.58	0.42	0.22

Regions	Surface Area		Gray matter		Thickness Av	
	L	R	L	R	L	R
bankssts	0.22	0.22	0.32	0.25	0.31	**0.10**
caudalanteriorcingulate	**0.17**	**0.12**	**0.10**	0.21	0.24	**0.08**
caudalmiddlefrontal	0.23	0.33	0.26	0.39	**0.16**	**0.15**
cuneus	0.33	0.25	0.38	0.46	0.40	0.2
entorhinal	0.30	0.37	0.22	0.27	**0**	**0.12**
fusiform	0.41	0.47	0.32	0.39	0.29	**0.15**
inferiorparietal	0.27	0.33	0.35	0.41	0.33	**0.17**
inferiortemporal	0.24	**0.08**	0.30	**0.15**	**0.16**	**0.18**
isthmuscingulate	0.24	0.14	0.25	0.21	0.20	**0.15**
lateraloccipital	0.50	0.50	0.41	0.42	**0.15**	**0.17**
lateralorbitofrontal	0.34	0.45	0.38	0.43	0.33	**0.12**
lingual	0.30	0.32	0.30	0.22	0.44	0.45
medialorbitofrontal	0.33	0.32	0.19	0.32	**0.15**	0.20
middletemporal	0.23	0.34	0.30	0.38	0.20	**0.09**
parahippocampal	0.35	0.28	0.40	0.33	**0**	**0.13**
paracentral	0.24	0.42	0.22	0.38	0.34	0.52
parsopercularis	**0.15**	0.31	**0.17**	0.40	0.41	0.27
parsorbitalis	**0.14**	0.37	**0.11**	0.38	0.20	0.24
parstriangularis	0.30	0.35	0.26	0.33	**0.07**	**0.17**
pericalcarine	0.22	**0.18**	0.24	0.20	0.32	0.47
postcentral	0.29	0.32	0.36	0.37	0.45	0.53
posteriorcingulate	0.42	0.42	0.44	0.48	**0.17**	**0.13**
precentral	0.36	0.33	0.33	0.35	0.25	0.24
precuneus	**0.13**	**0.17**	**0.18**	0.30	0.22	0.35
rostralanteriorcingulate	0.31	0.50	0.27	0.48	**0.17**	**0.13**
rostralmiddlefrontal	0.32	0.43	0.34	0.45	0.44	0.35
superiorfrontal	0.32	0.43	0.41	0.53	0.41	0.38
superiorparietal	**0.07**	0.24	**0.14**	0.32	0.41	0.44
superiortemporal	0.34	**0.17**	0.40	0.19	0.2	0.08
supramarginal	**0.14**	**0.12**	**0.17**	**0.11**	**0.10**	0.36
frontalpole	0.50	0.63	0.50	0.73	**0.12**	0.24
temporalpole	**0.07**	**0.15**	**0.15**	**0.12**	**0.06**	**0.12**
transversetemporal	**0.02**	**0.11**	**0.14**	0.22	0.33	0.28
insula	0.41	0.50	0.39	0.54	0.33	0.33



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Categories

- Genetics (Genetics)
- Anatomical MRI (Imaging Techniques and Contrast Mechanism)
- Anatomical Studies (Neuroanatomy)