Relationship between Gray Matter and Intelligence: Convergent Evidence from Voxel Based Morphometry and Stereology

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Introduction

How the brain supports intelligence can be explored by examining the effects on intelligence of focal brain lesions and by investigating which brain regions activate in healthy volunteers when intelligence is exercised, but it can also be examined by determining whether variations in the volume of any brain region correlate with individual differences in intelligence in healthy individuals. We applied two well-established brain image analysis techniques to high-resolution MR brain images from a group of healthy adults to investigate whether there exists a structural relationship between grey-matter and fluid intelligence.

Subjects and methods

To minimize the influences from the aging effect, the present study included 55 subjects (30F, 25M, age 40 ± 12 yrs) who were all under age 60. High-resolution T1-weighted images were acquired on a 1.5 T SIGNA MR imaging system (General Electric, Milwaukee, USA) with a 3D SPGR pulse sequence (TR/TE 34/9 msec, flip angle 30°, slice thickness 1.6 mm). The subjects were all right handed and underwent a battery of standard neuropsychology tests. The preliminary investigation reported in the present study focuses on analysis of the fluid intelligence as measured by Cattell's Culture Fair test and the Wechsler Adult Intelligence Scale-Revised (WAIS-R) test of Performance intelligence.

Optimized voxel-based morphometry [1] was carried out using Statistical Parametric Mapping (SPM 99, http://www.fil.ion.ucl.ac.uk/spm). Voxel-by-voxel regression analysis of grey matter concentration was performed taking total brain grey matter as a confound and Culture Fair scores, or WAIS-R Performance scores, in turn as covariates of interest, within the framework of the general linear model in SPM99. Analyses were performed both with and without including age as a nuisance variable. Results from analyses were thresholded at a p value of less than 0.05 (corrected for multiple comparisons), and after partialling out age or sex, were thresholded at $p < 0.0001$ (uncorrected).

The Cavalieri method of modern design stereology was applied in conjunction with point counting to estimate the volume of several sub-regions of frontal cortex [2]. We specifically estimated the prefrontal cortical subfield volumes using a previously established parcellation technique [3]. Total intracranial volumes were also estimated and used as a basis for normalising the regional brain volumes. The stereological volume estimates of the prefrontal subfields were correlated with neuropsychological measures of fluid intelligence (i.e., Culture Fair scores and WAIS-R Performance test) by performing a stepwise multiple regression analyses.

Results

Correlation of grey matter concentration with fluid intelligence

Optimised VBM analysis detected a cluster of grey matter in the medial region of frontal cortex (mainly left anterior cingulate gyrus and dorsomedial prefrontal cortex) that showed a significant positive correlation with Culture Fair scores ($p < 0.05$ corrected for the multiple comparisons) and remains after controlling for age ($p < 0.0001$, uncorrected for multiple comparison)(**Figure 1**, left panel). A significant positive correlation was also observed between grey matter concentration and WAIS-R performance scores for the same but smaller region of medial prefrontal cortex before controlling for age ($p < 0.0001$, uncorrected for multiple comparison, **Figure 1**, right panel). No negative relationships were observed for any of the above correlation analyses ($p > 0.05$).

Correlation of prefrontal subfield stereological volumes with fluid intelligence

Positive relationships between subfield volume estimates and fluid intelligence (i.e. Culture Fair scores and WAIS-R performance test) were revealed in medial prefrontal cortex (**Figure 2**). In particular, simple regression analysis showed that Culture Fair score was highly correlated with volume of left dorsomedial prefrontal cortex ($b = 0.50$, $p < 0.05$). After controlling for age, multiple regression analyses revealed significant correlations of prefrontal cortex subfield volumes (corrected for intracranial volumes) with Culture Fair scores in left dorsomedial ($b = 0.37$, $p < 0.05$) and left orbitomedial subfield ($b = 0.32$, $p < 0.05$). Similar findings were also observed for WAIS-R Performance scores in left orbitomedial prefrontal cortex after controlling for age and intracranial volume ($p < 0.05$).

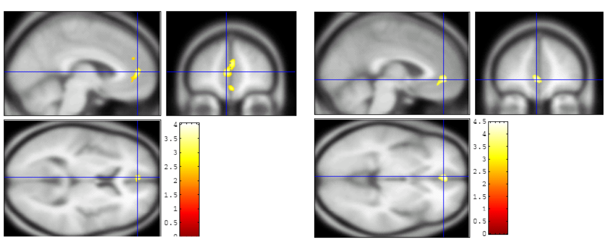

Figure 1. Statistical parametric maps superimposed on T1-weighted orthogonal images, showing a positive correlation between grey matter concentration and Culture Fair score after controlling for age (left panel) or WAIS-R performance score before controlling for age (right panel). The coloured bar to the right indicates the Z score level.

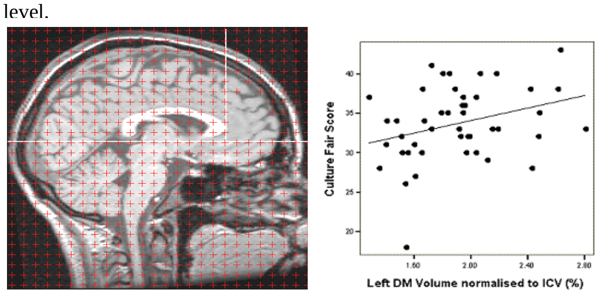

Figure 2. Stereological subfield analysis [3] for left dorsomedial (DM) prefrontal cortex (left panel) and multi-covariate regression analysis of prefrontal subfield volumes expressed as percentage fractions of intracranial volume (ICV) against Culture Fair Scores with fitted regression line ($\beta = 0.50$, $p < 0.05$)(right panel).

Discussion

Prefrontal cortex has been well recognized as the main region associate with higher order cognitive functions [4]. The present study has shown that both VBM and stereology converged in finding that the volume of this brain region was positively associated with fluid intelligence and that it was the only brain region to show such an association. The results are also broadly convergent with those of a structural imaging study of intelligence in a healthy paediatric population [5].

A major limitation of the present investigation was the relatively small size of the study group. A considerably larger group would have been needed to provide sufficient statistical power to examine whether there are sex differences in the way in which the volume of prefrontal (and possibly other brain structures) relate to different kinds of fluid intelligence. Future work, therefore, should examine a larger group of young healthy subjects of both sexes, perhaps between 20 and 30 years of age, on several different kinds of fluid intelligence test that load highly on general factor or "g" (minimally including visuospatial and verbal tests) as well as on crystallized intelligence tests with matching materials.

The convergent evidence we have obtained from VBM and stereology studies represents important methodological cross-validation of the significance of medial prefrontal cortex in fluid intelligence. We recommend that our findings are also cross-validated with functional neuroimaging studies performed on selected subjects using similar materials to determine to what degree activated sites and sites that show volume-intelligence correlations correspond.

References

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