The contribution of specific functional networks to individual variability

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INTRODUCTION

Individual differences in brain activity are a critical area of research in the struggle to understand the human brain. Recently, Miller et al. (2002) have used a whole-brain correlation technique to investigate inter-individual variability in fMRI results. The question that we sought to answer with this study was whether these whole-brain inter-individual differences in fMRI results could be localized to specific functional networks within the brain.

METHODS

• Participants
Twelve subjects (8 female, 4 male, mean age = 23.4) recruited from the local university community completed all aspects of the experiment.

• Overall Design
The experiment was a 2 x 3 design with principal factors of task [episodic memory and working memory] and experimental design [block, event-related genetic optimization, and event-related m-sequence]. Two runs consisting of 100 EPI volumes were completed for each condition. A total of twelve runs were completed. For the purposes of this investigation only data from the episodic memory condition with a genetically-optimized design was used. This enabled the examination of data that is a balance between statistical power and hemodynamic estimation efficiency. The Optimize Design toolbox by Wager & Nichols (2003) was used to generate this sequence.

• Memory Task
The episodic memory condition involved the recognition of words selected from an initial encoding session performed at the beginning of the experiment. For each run there were 25 novel and 25 previously encoded words. This generated a total of 50 words of each type across two runs.

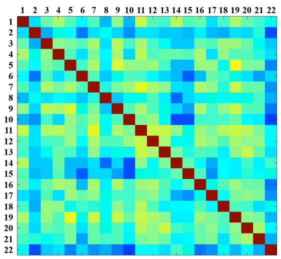
• Neuroimaging Analysis
Preprocessing steps included realignment of the functional images, normalization to a common atlas space (ICBM-152), and spatial smoothing of 8mm FWHM. First-level analysis was completed using the general linear model (GLM). Appropriate design matrices were constructed for each condition and estimated using restricted maximum likelihood (ReML).

• Analysis of Behavior
A signal detection approach was chosen for the analysis of memory performance. Responses were coded with regard to hits, misses, false alarms, and correct rejections. A hit was defined as correctly identifying an 'old' word from the encoding task. Measures of d-prime and criterion were then calculated, along with measures of reaction time.

• Independent Components Analysis
To investigate separable functional networks across the group we used an independent components analysis (ICA) approach. We used the MELODIC toolbox from the FSL software suite to perform a joint tensor-ICA decomposition of the entire dataset (Beckmann and Smith, 2005). This results in a three-way decomposition representing the different signals and artifacts present in the data in terms of their temporal, spatial and subject-dependent variations.

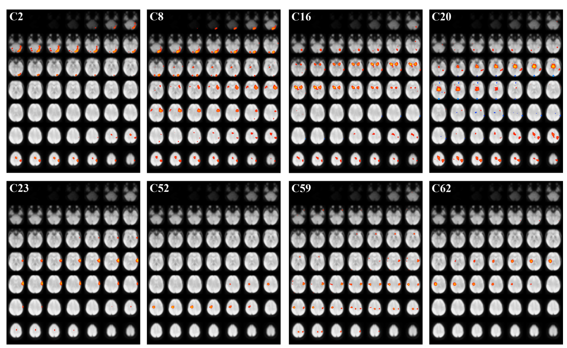
INTER-SUBJECT VARIABILITY

To quantify inter-individual variation across subjects we used the cross-correlation method of Miller et al. (2002). This involves turning the t-statistic results of the task > fixation contrast for each subject into a vector that can be correlated against the data vectors from other subjects. In turn, all subjects are correlated against all other subjects. The mean correlation value of each subject is taken as a measure of inter-subject distance.



The figure above shows the correlation matrix of values for each subject pair. We calculated the mean correlation value for each subject as a measure of inter-subject distance. We then correlated this value with the subject/session mode of each ICA component to identify those components whose variability was significantly related to the calculated inter-subject variability. The average inter-subject correlation was 0.43 (range of 0.16 to 0.62).

COMPONENT RELATIONSHIPS



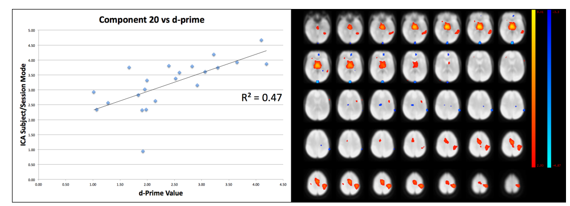
There were 146 components that resulted from the ICA analysis. An analysis of the component timecourses using the FSL FEAT toolbox revealed that only a subset of 56 components had activity that was significantly related to the task. The subject/session mode of 8 out of the 56 components was determined to be significantly correlated ($r = 0.36$ to 0.45, $p < 0.05$) with the inter-individual variability as quantified using the Miller approach. The spatial extent of these components is displayed in the above figure. The results support the hypothesis that separable functional networks within the brain are driving the whole-brain inter-individual differences in regional brain activity.

BEHAVIORAL RELEVANCE

Measure	Whole Brain	ICA-C2	ICA-C8	ICA-C16	ICA-C20	ICA-C23	ICA-C52	ICA-C59	ICA-C62
Hits	0.21	0.35	0.33	0.34	0.58	0.36	0.41	0.22	0.51
Misses	-0.09	-0.43	-0.29	-0.35	-0.57	-0.31	-0.23	-0.13	-0.36
False Alarms	0.01	-0.13	0.03	-0.14	-0.19	-0.44	-0.04	-0.06	-0.02
Correct Rejections	0.05	0.28	0.04	0.27	0.27	0.42	0.16	0.19	0.21
d-prime	0.17	0.46	0.21	0.46	0.68	0.60	0.23	0.16	0.38
Criterion	-0.11	-0.14	-0.15	-0.06	-0.16	0.17	-0.05	-0.01	-0.20

The above table shows the correlation values between measures of memory behavior, whole-brain inter-individual variability, and inter-individual variability in the significant ICA components. Cells are highlighted according to the significance threshold. Orange cells are significant at the $p < 0.05$ level while yellow cells are significant at the $p < 0.001$ level and survive multiple comparisons correction using the Bonferroni method.

Several of the ICA components that were significantly related to whole-brain inter-individual variability were also significantly related to memory performance. As shown in the above table, some ICA components possessed strong relationships with d-prime, a measure of memory sensitivity. This is in contrast to the relationship between d-prime and the whole-brain inter-individual differences, which showed a much weaker relationship ($r = 0.17$).



CONCLUSIONS

The variability in whole-brain correlations can indeed be localized to specific functional networks within the brain. Some of these networks/components are strongly related to observed inter-subject variability in memory performance. However, the multiple comparisons problem of correlating across such a high number of ICA components is an issue that must be resolved. New methods of component downselection must be devised for this approach to succeed. Alternatively, independent training/testing pairs of data could be used.

REFERENCES

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