

Functional and structural neuroimaging predictors of normative variance in cognition

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E-Poster

Introduction:

Functional and structural MRI predictors of cognition have been broadly identified for many domains including reading (Smallwood 2013, He 2013), language (Chiarello 2012, Deng 2016), motor skills (Kahn 2016, Stillman 2013), and working memory (Keller 2015, Banich 2015). But the synthesis of these findings across cognitive domains has been limited by many factors – notably, inter-study differences in statistical methodology or testing with a single neuroimaging modality and/or a single cognitive domain. To address these limitations, we recruited a normative sample of healthy adults who underwent cognitive assessment with a clinically validated neuropsychological test battery spanning multiple cognitive domains. Participants also underwent two neuroimaging sessions with T1-weighted anatomic MRI, diffusion tensor imaging (DTI), resting-state functional MRI (rs-fMRI), and task-based fMRI with tasks directly or conceptually replicated the neuropsychological instruments. Using this comprehensive dataset, we evaluated each MRI modalities' ability to predict normative variance across cognitive domains.

Methods:

47 adults (25 female, mean(sd) age =31(10) years) completed neuropsychological and neuroimaging sessions. MRI data were acquired with a Philips 3T Achieva X-series MRI scanner at UAMS with these parameters; T1-weighted MRI: MPRAGE (TR/TE/FA=min/min/90°, final resolution=1x1x1mm³); rs-fMRI: EPI (TR/TE/FA=2000ms/30ms/90°, final resolution 3x3x3 mm³); DTI scans: EPI (TR/TE/FA = 6228ms/70.68ms/90°, final resolution 2x2x2 mm³, with 32 gradients of b=800 s/mm² and 2 b=0 images). Structural, functional, and DTI data underwent standard preprocessing as described elsewhere (James 2016a, Ou 2015).

After preprocessing, we extracted cortical thickness and normalized volumes for regions of interest (ROIs) from FreeSurfer's cortical and subcortical atlases (Fischl 2002, Fischl 2004). Correlation matrices of rs-fMRI functional connectivity (rs-FC) were derived using our task- and rs-fMRI derived 200ROI atlas (James, 2016b). Mean fractional anisotropy (FA) were derived for 48 ROIs and 20 tracts using FSL's respective atlases (Desikan, 2006).

For each modality, linear regression with 1000 bootstraps used that modality's features (i.e. ROI thickness or volume, mean ROI or tract

FA, or pairwise ROI-ROI rs-FC) to predict performance on each cognitive instrument. All analyses included age as a covariate. Table 1 depicts the maximum variance (R^2) explained by each modality's features for each cognitive instrument.

Results:

rs-FC strongly predicted cognition, explaining 24-58% variance in performance across all neurocognitive instruments. Structural MRI measures (whether cortical thickness, regional volume, or white matter FA) were generally weaker predictors of cognition, explaining 10-44% of variance. Sub-analyses by cognitive domain show that resting-state connectivity was the best predictor (i.e. explained the most variance) of "higher-order" cognitions, including all instruments measuring working memory and executive function. In contrast, structural MRI features generally outperformed functional MRI features when predicting simpler cognitions, including instruments measuring visuospatial awareness, motor behavior, and language.

Cognitive Domain	Neurocognitive test instrument	Maximum Percent Variance Explained (R^2)				
		Cortical thickness	Volume (normed)	FA ROI	FA Tract	Resting Connectivity
Motor	Finger Tapping, Right Hand	0.233	0.441 *	0.234	0.223	0.550 **
Motor	Finger Tapping, Left Hand	0.199	0.422 *	0.238	0.155	0.588 **
Motor	Pegboard Speed, Right Hand	0.149	0.253	0.395 **	0.297	0.331 *
Motor	Pegboard Speed, Left Hand	0.172	0.199	0.258	0.265 *	0.309 **
Motor	D-KEFS Trails, Cond. V Speed	0.210	0.261	0.431 **	0.225	0.326 *
Visuospatial	Judgment of Line Orientation Test	0.327	0.375	0.401 **	0.397 *	0.332
Language	Boston Naming Task	0.422 **	0.318	0.251	0.170	0.378 *
Language	Verbal Fluency (COWAT, Letters)	0.283	0.360	0.448 **	0.304	0.377 *
Language	Verbal Fluency (COWAT, Categories)	0.333 *	0.322	0.179	0.166	0.341 **
Learning	Brief Visuospatial Memory Test, Revised	0.279	0.272	0.335	0.396 **	0.395 *
Learning	Verbal Paired Associates I	0.133	0.413 **	0.108	0.085	0.294 *
Learning	California Verbal Learning Test, Total 1-5	0.132	0.102	0.183 *	0.115	0.235 **
Working Memory	D-KEFS Spatial Span Forward	0.284 *	0.215	0.181	0.162	0.393 **
Working Memory	D-KEFS Spatial Span, Reverse	0.230	0.171	0.299 *	0.205	0.383 **
Working Memory	D-KEFS Digit Span, Forward	0.363 *	0.360	0.342	0.198	0.432 **
Working Memory	D-KEFS Digit Span, Backward	0.320 *	0.272	0.222	0.197	0.374 **
Working Memory	D-KEFS Digit Span, Sequencing	0.174 *	0.109	0.191	0.102	0.287 **
Executive Function	Test of Everyday Attention, Cond. IV	0.214	0.345 *	0.271	0.254	0.446 **
Executive Function	Booklet, Errors	0.384 *	0.347	0.383	0.354	0.476 **
Executive Function	D-KEFS Color-Word (Stroop), Interference	0.209	0.216	0.252 *	0.234	0.459 **
Executive Function	D-KEFS Trails, Cond. IV Speed	0.227	0.170	0.237	0.296 *	0.359 **

** = strongest predictor of cognition across all modalities

* = second strongest predictor of cognition across all modalities

Table 1. Percent Variance in Cognition Explained by Neuroimaging Modality.

Conclusions:

We have previously shown that resting-state functional connectivity can predict higher-order cognition (James, 2016). Our findings were independently replicated by Siegel et al. (2016), who demonstrated in stroke survivors that resting-state functional connectivity most strongly predicted stroke-related deficits of higher-order cognition but lesion location most strongly predicted deficits of motor or visual ability. Our findings suggest that these dissociations also exist among healthy comparison subjects, providing further insight into the neural encoding of normative variance in cognition.

Higher Cognitive Functions:

Executive Function ²

Imaging Methods:

Anatomical MRI
BOLD fMRI
Diffusion MRI

Modeling and Analysis Methods:

Task-Independent and Resting-State Analysis ¹

Poster Session:

Poster Session - Monday

Keywords:

ADULTS
Cognition
Computational Neuroscience
FUNCTIONAL MRI
NORMAL HUMAN
STRUCTURAL MRI
WHITE MATTER IMAGING - DTI, HARDI, DSI, ETC
Other - Individual Differences

^{1|2}Indicates the priority used for review

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Please indicate which methods were used in your research:

Functional MRI
Structural MRI
Diffusion MRI
Neuropsychological testing

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

AFNI
Brain Voyager
FSL
Free Surfer

Provide references in author date format

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