An RDoC framework integrating structural MRI with cognitive Control and Working Memory

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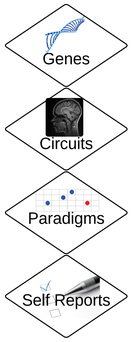
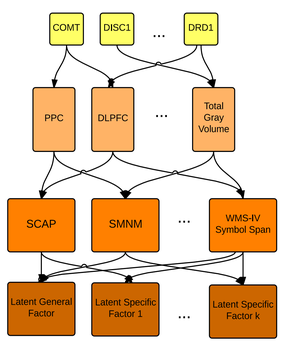
INTRODUCTION

The growth of biological psychiatry over the last 50 years has increased accessibility of measures at multiple levels from the genomic through neuroimaging of brain circuit structure and function to sophisticated assessment of cognitive and behavioral processes. The RDoC initiative aims to leverage our capacity to assess these underlying dimensions with the aim to provide stronger bases for biological psychiatry. Here, we identify structural MRI correlates of working memory (visual and spatial) and cognitive control (response inhibition) using Bayesian networks in 278 subjects with and without a DSM diagnoses.

Units of Analyses



Bayesian Network



METHODS

The CNP dataset consists of volunteers (healthy and patient) from the greater Los Angeles area who enrolled and completed diagnostic interviews, self-reports, cognitive exams, and contributed genetic data. Sample characteristics are listed in Table 1. Neuroimaging data (MRI, fMRI) were collected along with all personality, neurocognitive measures and genotyping listed in Table 2

Structural MRI data was processed using FreeSurfer, extracting cortical and subcortical measurements.

Hierarchical cluster analyses was used to identify redundant variables with numerous outcome measures generated by each neurocognitive task. Next, exploratory bifactor analysis was used to develop measurement models for each construct of interest, wherein the bifactor approach allows us to examine what a set of tasks share in common (general factor) and data-driven models for specific variance would allow us to examine relationships among neurocognitive variables that remain after accounting for the general factor. Composite measures of cognitive control and working memory were created using bifactor modeling, extracting "g" general factor measurements of visual and spatial working memory separately.

Structural MRI, demographic information, and measures of working memory, response inhibition, anhedonia (Chapman scales), and other dimensions of the Hopkins symptom checklist Finally, these measurements were integrated using a Bayesian network, where the most likely relationship spanning all dimensions were assessed without assuming given hierarchy or causality. This network was learned using the score-based method, connecting 44 nodes with 133 arcs, fit using the BIC for conditional Gaussian.

METHODS (Continued)

Bayesian network modeling is a method of inference where the joint frequency of data is explained via a product of marginal distributions (9). In this framework, multimodal observations such as behavior, self-report, and paradigms represent observations recorded on a single subject. In the Bayesian networks, nodes represent random variables, and an arrow defines a probabilistic connection (dependence) among the variables. Formally, if the variables are defined as discrete, then the joint probability distribution can be defined as the product of the local probability distributions.

Variable	ADHD	BP	Control	SZ
n	42.00	48.00	133.00	55.00
Age	32.53	35.49	31.34	36.03
Gender (% Male)	0.45	0.42	0.48	0.24
Education (years)	14.63	14.61	15.03	12.69
Somatization Score (Hopkins	0.35	0.66	0.22	0.63
Obsessive Compulsive (Hopkins)	1.18	1.18	0.50	1.05
Interpersonal Sensitivity (Hopkins)	0.75	1.11	0.40	0.94
Depression (Hopkins)	0.66	0.97	0.37	0.84
Anxiety (Hopkins)	0.44	0.75	0.21	0.84
Response Inhibition (g)	0.01	0.03	-0.28	0.37
Visual Working Memory (g)	0.18	0.11	0.28	-0.27
Spatial Working Memory (g)	0.18	0.12	0.37	-0.20
Chapman Perception Aberration	4.71	6.04	3.14	8.93
Chapman Social Anhedonia	13.40	16.46	9.62	15.14
Chapman Physical Anhedonia	13.59	15.83	11.47	17.41

Table 1: The following measures were used in a Bayesian network to identify the hierarchical relationship about structural MRI markers, demographic features, diagnosis, and working memory and cognitive control.

	WM	CC
Screening/Diagnosis/Clinical Rating Scales		
ADHD Self-Report Scale ASRS-V1.1	x	x
Adult ADHD Interview (module from K-SADS-PL)	x	x
Structured Clinical Interview for DSM-IV, Axis 1, Patient Version	x	x
Young Mania Rating Scale		x
Scale for Assessment of Negative Symptoms	x	
Scale for Assessment of Positive Symptoms	x	
Brief Psychiatric Rating Scale	x	
Personality/Temperament/Symptom Questionnaires		
The Temperament and Character Inventory		x
Eckblad and Chapman's Hypomanic Personality Scale		x
Akiskal's Bipolar II Scale		x
Barratt Impulsivity Scale		x
Eysenck's Impulsivity, Venturesome and Empathy Inventory		x
MPQ (Control: Impulsivity items)		x
The Dickman Scale of Functional vs Dysfunctional Impulsivity		x
Chapman Scales (Revised Physical Anhedonia; Revised Social Anhedonia; Perceptual Aberrations	x	
Neurocognitive Measures		
Verbal Memory and Manipulation Task	x	
Spatial Memory and Manipulation Task	x	
Verbal Working Memory Capacity Tasks	x	
Spatial Working Memory Capacity Tasks	x	
WMS-IV Symbol Span	x	
WMS-IV Digit Span	x	
WMS-IV Letter Number Sequencing (LNS)	x	
Stop-Signal Task		x
CNP CPT		x
Reversal Learning		x
Color Trails Test		x
Task Set Switching		x
Stroop Test		x
Attention Networks Task (Exec Center)		x
Delay Discounting		x
Balloon Analog Risk Task		x
NeuroImaging Measures		
Functional MRI (Functional Network Connectivity from ICA-derived brain networks [see text])	x	x
Structural MRI volumes: (total brain, total cortical, DLPFC, VLPFC, PPC, total grey/white cortical and subcortical, Ventrofronto-striatal, hippocampal, thalamic, globus pallidus)	x	x
Genotyping		
Omni Express	x	x

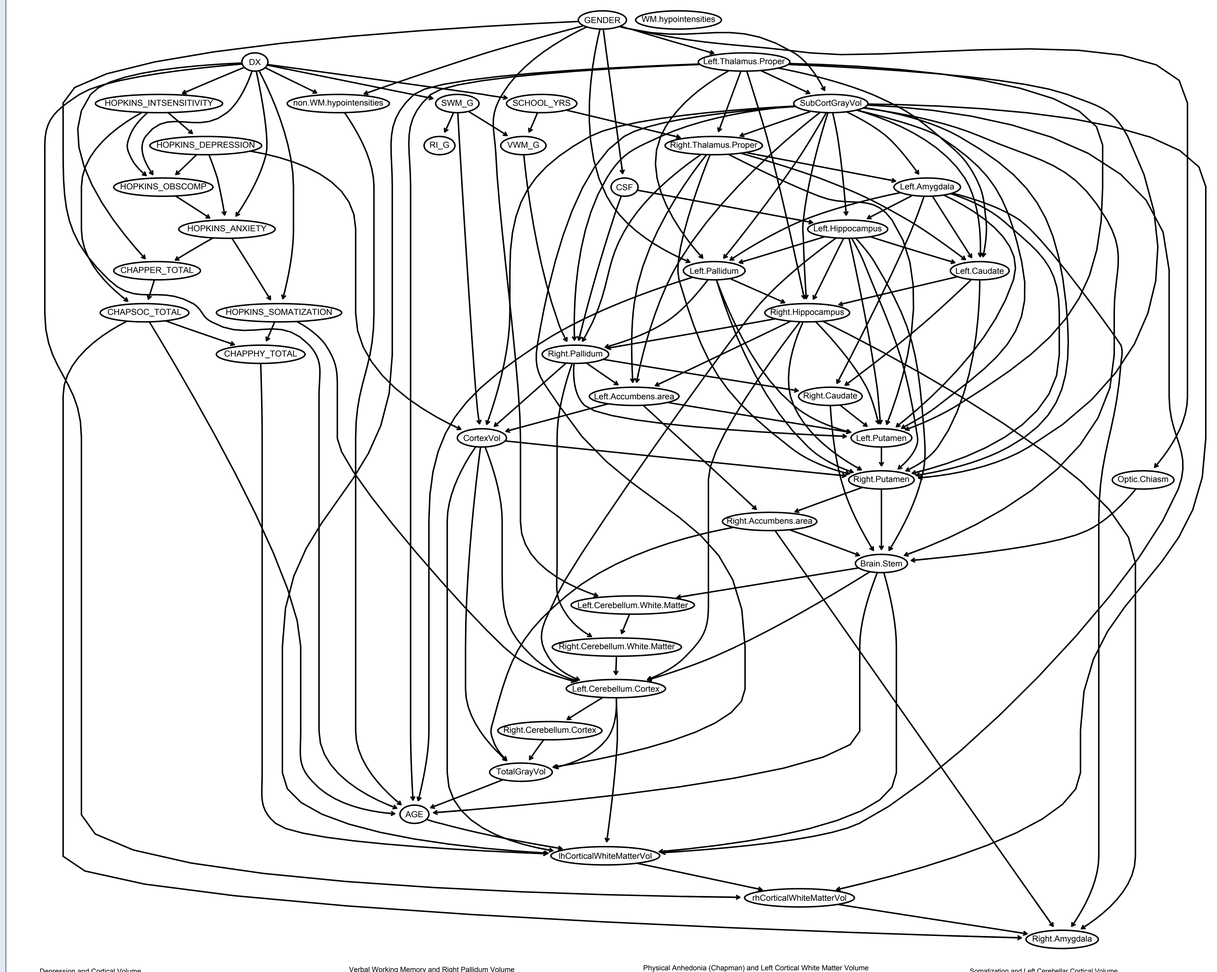
Table 2: Units of analyses available in the CNP data

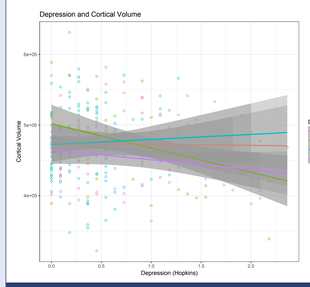
RESULTS

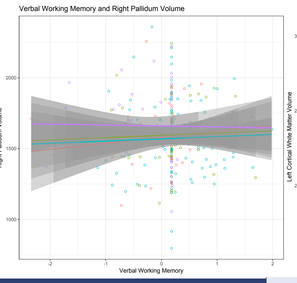
Homegeneous Item Parcels	G	F1	F2	F3	F4	F5	h2	u2	p2
Carelessness	0.51	0.47					0.52	0.48	0.48
Haphazardness	0.44	0.76					0.77	0.23	0.26
BlindActions	0.40	0.69					0.64	0.36	0.25
SeekFrighteningThings						0.68	0.50	0.50	0.07
Activities2						0.48	0.27	0.73	0.07
ThrillSeeking						0.61	0.40	0.60	0.05
Organization	0.38				0.34		0.28	0.72	0.53
Deliberation1	0.56				0.44		0.51	0.49	0.61
Deliberation2	0.58				0.41		0.54	0.46	0.60
Overspending	0.32		0.57				0.44	0.56	0.22
SpendVsSave	0.35		0.60				0.50	0.50	0.25
BuyingSpendingSprees	0.36		0.85				0.85	0.15	0.15
AvoidSnapDecisions	0.30			0.74			0.64	0.36	0.14
AvoidSimpleSnapDecisions	0.33			0.79			0.74	0.26	0.15
QuickDecisions	0.37			0.35			0.29	0.71	0.48

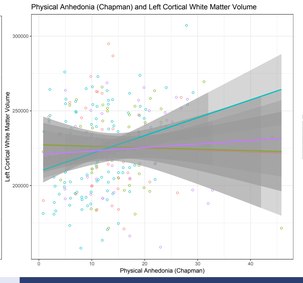
Table 3: Bifactor analyses of self-report parcels, yielding a single common dimension and 5 specific factors. h2 is communality, u2 is unique variance, and p2 is percent of common variance attributable to the general factor. Loadings < .30 not shown.

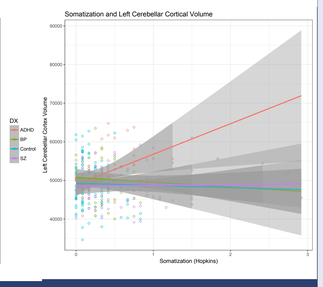
RESULTS











CONCLUSIONS

Our results suggest that Bayesian networks can be used to identify the dependencies between structural MRI measurements and observed changes in cognition and behavior. More broadly, diagnosis still modulates the relationship between symptom measures and structural MRI measures, suggesting that diagnosis may be capturing information not contained already in the structural and symptom based measures. Future work will include genotype and functional MRI measures to further assess the hierarchical structure spanning the RDoC framework.

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