

Supplementary Materials

Image Acquisition:

An AGAR phantom was used to perform quality assurance of scanners across sites based on guidance and recommendations from the FBIRN initiative. Structural 3D T1-weighted images were acquired using an MPRAGE sequence (TR=2300ms, TE~3.0ms, TI=900 ms, 90 flip angle, FOV=256 x 240 mm, matrix=256 x 240, 1 mm isotropic voxels, 176 sagittal slices). Functional images sensitive to gradient-echo BOLD contrast were acquired using echo-planar imaging with the following parameters: (TR=2000ms, TE=30ms, 77o flip angle, FOV=220 x 220 mm, matrix=64 x 64, voxel size=3.4375 x 3.4375 x 4.0 mm, 32 axial-oblique slices approximately parallel with the anterior/posterior commissure with no interslice gap). A dual-echo gradient-echo scan was obtained to estimate magnetic field inhomogeneity (TR=500ms, Δ TE=2.46, 55o flip angle, with same FOV, resolution, and slice thickness as the BOLD scans).

Image Processing:

Pre-Processing - Brain volumes were extracted from full-head functional and structural images. Functional images were motion corrected (FSL's MCFLIRT) and high-pass filtered for frequencies below 200 s. Subjects with greater than 0.37 mm of mean relative frame-to-frame movement (representing greater than 3 standard deviations from the cohort mean) were excluded. Functional images were registered to each participant's MPRAGE using a rigid-body transformation (FSL's FLIRT). Functional images underwent B0 un-warping using the gradient-echo fieldmap estimates for each subject to correct for magnetic field inhomogeneity. Images were spatially smoothed with a Gaussian kernel (7mm FWHM, isotropic).

Modeling of subject-level fMRI data - Temporal autocorrelation of the fMRI time series was accounted for by pre-whitening (FSL's FILM). Activity associated with each event type was modeled by convolving a vector of expected neural activity with the 3 basis-function set of FMRIB's Linear Optimal Basis Sets (FLOBS). The first basis function represents a canonical hemodynamic response, while the other two effectively model delay and dispersion variability in the hemodynamic response, and are included to decrease error in first level GLM fit. However, only canonical response estimates were passed up to higher (group-level) analysis. For the encoding task, item-specific and relational encoding were modeled as separate event types, and non-response trials were also modeled as their own event. Item recognition had seven event types: hits and misses separately for "old" targets that underwent item-specific and relational encoding, correct rejections and false alarms for "new" foil items, and non-response trials. Analysis of response trials revealed that patients averaged at least 35 correct responses during item recognition, with the lowest number of correct responses occurring for one patient who had 19 correct responses following item-specific encoding. Response distributions were generally comparable for control subjects, who averaged at least 40 correct responses, with one control generating 25 correct responses, again following item-specific encoding. Associative recognition had three event types: hits (i.e., correctly identifying a "changed" or "unchanged" target pair), misses (i.e., incorrectly identifying a "changed" target pair as "unchanged" or vice versa), and non-response trials. Analysis of response trials revealed that controls averaged 19 correct responses, and patients averaged 18 correct responses, with the lowest number of correct responses occurring for one patient who had only 9 correct responses, and one control with only 8 correct

responses. It should be noted that, because of task design, there were only about half as many correct responses for the associative recognition as for the item recognition task, which may have reduced signal-to-noise (SNR) for detecting significant group fMRI differences in the associative recognition task. To better equate SNR, future studies may wish to double the number of associative recognition encoding and retrieval trials. However, because of time limitations, this was not possible in the current study.

Modeling of group-level fMRI data - We first examined *a priori* regions in prefrontal and medial temporal cortices, followed by exploratory whole-brain analyses. Regional analysis goals were two-fold: 1) to establish neural construct validity and, 2) to identify group differences. To establish construct validity, we ran contrasts to test for predicted activation within anatomically defined regions for the full sample (i.e., across the patient and control groups). Activated voxels within those regions were used as ROIs for subsequent one-sample and two-sample t-tests. Anatomical ROIs for the PFC were identified for the relational minus item encoding contrast for the full sample, with structural masks from the WFU_PictAtlas (Maldjian et al., 2003) used to restrict activated voxels to left and right DLPFC [Brodmann areas (BA) 9, 46, and 9/46] and VLPFC (BA 44, 45 and 47). MTL ROIs were identified for the hit minus miss contrast during item recognition and associative recognition for the full sample, and structural masks from the Harvard Oxford Atlas identified boundaries for left and right HI and PHG. Within these PFC and MTL ROIs, one-sample t-tests were performed to confirm that the predicted effect was robust in controls and to examine activation effects in the patient group, and two-sample t-tests were performed to test for between-group differences. Resulting z (Gaussianized t) statistic images were subjected to a voxelwise

threshold of $z > 2.3$, and a corrected cluster mass significance threshold of $p < 0.05$ based on Gaussian Random Field theory (Worsley, 2001) as implemented in FEAT.

Additionally, any effects outside of ROIs were explored using the FSL T1-image whole brain gray matter mask (values ≥ 100), using the same thresholding and cluster-correction procedures.

fMRI Site Differences:

Because this is a multi-site study, several metrics relevant to data quality were examined to determine if there were any site differences or site by group interactions. Absolute and relative movement, spatial smoothness, and a measure of temporal signal-to-noise (tSNR; Table 1), were entered into a two (group) by five (research site) by four (data quality variable) multi-variate analysis of variance (MANOVA). This revealed a main effect of site [$F(4,99)=6.9, p<.0001$], but no effect of group [$F(1,99)=0.3, p=.57$] or any group by site interactions [$F(4,99)=2.0, p=.10$]. Site differences were present for absolute motion [$F(4,104)=4.0, p<.005$], relative motion [$F(4,104)=2.8, p<.05$], and tSNR parameters [$F(4,104)=6.7, p<.0001$]. These site differences motivated our decision to include site as a covariate in the group-level GLM analyses.

Table 1: fMRI Image Quality at Participating Research Sites

	Baltimore	Davis	Minnesota	Rutgers	WashU
Sample Size	14 HC, 9 SZ	12 HC, 13 SZ	13 HC, 12 SZ	6 HC, 3 SZ	12 HC, 15 SZ
Absolute Motion	0.61 (.06)	0.36 (.04)	0.32 (.06)	0.46 (.06)	0.43 (.05)
Relative Motion	0.15 (.01)	0.10 (.01)	0.11 (.01)	0.11 (.01)	0.13 (.01)
Smoothness	10.3 (.16)	10.5 (.15)	10.2 (.11)	10.2 (.66)	10.4 (.17)
tSNR	188.7 (11.7)	243.6 (6.9)	241.9 (7.4)	195.7 (14.4)	221.3 (9.4)

note: HC = healthy controls, SZ = people with schizophrenia. Motion and smoothness measures are in mm. Values in parenthesis are SD. Absolute motion is computed relative to a fixed reference frame (middle time point of the run) and relative motion is computed from one frame to the next. Both are outputs of FSL's MCFLIRT tool for motion correction. Smoothness is the full-width half-maximum estimate of the spatial smoothness of the residuals from the first (subject) level GLM (obtained by converting the "resels" estimate from FSL's 'smoothest' function into units of mm). Temporal signal-to-noise (tSNR) for each run was obtained by first computing a spatial (voxel-wise) map of mean signal over time divided by the standard deviation of the residuals from the first level GLM. This tSNR map was then averaged over space using a weighted average according to the probability of gray matter at that voxel in MNI152 space. For all measures, values were averaged across the 3 runs for each subject and those subject-specific averages formed the basis for analysis of site and group effects (see main text for statistical analysis).

Table 2: Whole brain Activation During Relational Versus Item-specific Encoding in Healthy Comparison Subjects

Cluster	Voxels	Z-value	X	Y	Z	Location	BA
1	3,866	6.5	44	38	8	Right Middle Frontal Gyrus	46
		6.43	48	8	22	Right Inferior Frontal Gyrus	9
		6.38	26	4	56	Right Sub-Gyral	6
		4.44	36	22	-6	Right Insula	13
		3.24	44	18	-18	Right Inferior Frontal Gyrus	47
		2.4	20	10	66	Right Medial Frontal Gyrus	6
2	8,779	9.22	-46	6	24	Left Inferior Frontal Gyrus	44
		8.93	-24	6	52	Left Sub-Gyral	6
		7.78	-32	-2	54	LeftPrecentral Gyrus	6
		7.28	-44	34	10	Left Middle Frontal Gyrus	46
		7.02	-42	32	18	Left Middle Frontal Gyrus	46
3	23,213	6.61	-42	42	-4	Left Inferior Frontal Gyrus	10
		9.74	-40	-46	46	Left Inferior Parietal Lobule	40
		9.25	-52	-38	42	Left Inferior Parietal Lobule	40
		9.13	-52	-62	-6	Left Middle Occipital Gyrus	19
		9.06	-22	-66	44	Left Precuneus	7
		8.21	-10	-68	54	Left Precuneus	7
	8.09	50	-58	-12	Right Fusiform Gyrus	37	

note: BA = Brodmann Area; x, y and z coordinates are reported in Montreal Neurological Institute space. Significance threshold was set at $Z = 2.3$ ($p < .01$), cluster-corrected at $p < .05$ for the total number of whole-brain voxels.

Table 3: Whole-brain Activation During Relational Versus Item-specific Encoding in Patients with Schizophrenia

Cluster	Voxels	Z-value	X	Y	Z	Location	BA
1	4,797	7.13	-24	6	54	Left Sub-Gyral	6
		7.04	-50	8	26	Left Inferior Frontal Gyrus	9
		4.66	-48	30	30	Left Middle Frontal Gyrus	9
		4.48	-48	38	6	Left Inferior Frontal Gyrus	46
		4.44	-48	44	2	Left Inferior Frontal Gyrus	46
		4.13	-50	12	8	Left Precentral Gyrus	44
2	14,429	7.04	-52	-68	-8	Left Middle Occipital Gyrus	37
		7.02	-40	-46	46	Left Inferior Parietal Lobule	40
		6.57	-22	-68	46	Left Precuneus	7
		6.36	-36	-84	24	Left Middle Occipital Gyrus	19
		6.35	-34	-84	28	Left Superior Occipital Gyrus	19
		6.03	-10	-74	54	Left Precuneus	7

note: BA = Brodmann Area; x, y and z coordinates are reported in Montreal Neurological Institute space. Significance threshold was set at $Z = 2.3$ ($p < .01$), cluster-corrected at $p < .05$ for the total number of whole-brain voxels.

Table 4. Group Differences Between Patients With Schizophrenia and Healthy Comparison Subjects in Whole-brain Activation During Relational Versus Item-specific Encoding.

Cluster	Voxels	Z-value	X	Y	Z	Location	BA
1	540	3.34	20	-68	-26	Right Cerebellum	--
		3.3	16	-68	-26	Right Cerebellum	--
		3.27	12	-54	-38	Right Cerebellum	--
		3.19	40	-66	-26	Right Cerebellum	--
		3.03	8	-72	-34	Right Cerebellum	--
		2.99	12	-68	-32	Right Cerebellum	--

note: BA = Brodmann Area; x, y and z coordinates are reported in Montreal Neurological Institute space. Significance threshold was set at $Z = 2.3$ ($p < .01$), cluster-corrected at $p < .05$ for the total number of whole-brain voxels..

Table 5. Whole-brain Activation During Successful Item Recognition (Hits > Misses) Following Item-specific Encoding in Healthy Comparison Subjects.

Cluster	Voxels	Z-value	X	Y	Z	Location	BA
1	1,375	3.85	-18	68	6	Left Superior Frontal Gyrus	10
		3.69	-30	34	42	Left Middle Frontal Gyrus	8
		3.50	-12	70	10	Left Superior Frontal Gyrus	10
		3.46	-26	64	4	Left Superior Frontal Gyrus	10
		3.37	-22	66	0	Left Middle Frontal Gyrus	10
		3.26	-22	62	18	Left Superior Frontal Gyrus	10
2	1,002	4.03	-58	-50	40	Left Inferior Parietal Lobule	40
		3.92	-44	-70	44	Left Precuneus	19
		3.78	-38	-78	38	Left Superior Occipital Gyrus	19
		3.69	-52	-50	48	Left Inferior Parietal Lobule	40
		3.43	-40	-70	36	Left Precuneus	39
		3.33	-44	-54	32	Left Superior Temporal Gyrus	39
3	3,133	4.56	4	-70	34	Right Cuneus	7
		3.74	8	-76	48	Right Precuneus	7
		3.58	-10	-62	30	Right Precuneus	31
		3.35	14	-52	29	Right Precuneus	31
		3.34	14	-48	32	Right Precuneus	31
		3.34	12	-42	32	Right Precuneus	31

note: BA = Brodmann Area; x, y and z coordinates are reported in Montreal Neurological Institute space. Significance threshold was set at $Z = 2.3$ ($p < .01$), cluster-corrected at $p < .05$ for the total number of whole-brain voxels.

Table 6. Whole-brain Activation During Successful Item Recognition (Hits > Misses) Following Relational Encoding in Patients with Schizophrenia.

Cluster	Voxels	Z-value	X	Y	Z	Location	BA
1	1420	3.79	-22	7	-7	Left Putamen	--
		3.75	-26	4	-8	Left Putamen	--
		3.69	-18	6	-13	Left Subcallosal Gyrus	34
		3.38	-35	6	-16	Left Superior Temporal Gyrus	38
		3.24	-18	8	11	Left Putamen	--
		3.19	-14	-13	19	Left Caudate Body	--
2	1342	3.66	16	11	-7	Right Putamen	--
		3.63	31	0	9	Right Claustrum	--
		3.58	20	11	-9	Right Putamen	--
		3.46	25	-4	-13	Right Amygdala	--
		3.41	16	-8	-13	Right Parahippocampal Gyrus	28
		3.38	16	-4	-19	Right Uncus	34
3	1093	3.48	-5	-71	19	Left Cuneus	18
		3.29	-13	-58	36	Left Precuneus	7
		2.86	-3	-56	36	Left Precuneus	7
		2.85	6	-49	38	Right Precuneus	7
		2.76	-3	-78	11	Left Cuneus	17
		2.75	-9	-60	28	Left Precuneus	31

note: BA = Brodmann Area; x, y and z coordinates are reported in Montreal Neurological Institute space. Significance threshold was set at $Z = 2.3$ ($p < .01$), cluster-corrected at $p < .05$ for the total number of whole-brain voxels.

Table 7. Whole-brain Activation During Successful Item Recognition (Hits > Misses) Following Item-Specific Encoding in Patients with Schizophrenia.

Cluster	Voxels	Z-value	X	Y	Z	Location	BA
1	1028	3.37	-30	-72	42	Left Precuneus	19
		3.12	-54	-50	32	Left Supramarginal Gyrus	40
		3.11	-47	-51	47	Left Inferior Parietal Lobule	40
		2.99	-45	-55	45	Left Inferior Parietal Lobule	40
		2.94	-43	-64	37	Left Angular Gyrus	39
		2.92	-51	-54	28	Left Supramarginal Gyrus	40
2	1758	3.63	10	-79	36	Right Cuneus	19
		3.31	-1	-58	25	Left Cingulate Gyrus	31
		3.25	-1	-57	39	Left Precuneus	7
		3.2	1	-48	18	Right Posterior Cingulate	30
		3.18	-3	-73	49	Left Precuneus	7
		3.11	0	-81	36	Left Cuneus	19

note: BA = Brodmann Area; x, y and z coordinates are reported in Montreal Neurological Institute space. Significance threshold was set at $Z = 2.3$ ($p < .01$), cluster-corrected at $p < .05$ for the total number of whole-brain voxels.