SUPPLEMENTAL MATERIAL

for McTeague et al., Identification of Common Neural Circuit Disruptions in Cognitive Control Across Psychiatric Disorders. Am J Psychiatry (doi: 10.1176/appi.ajp.2017.16040400)

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CONTENTS

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Supplementary Methods

Peak Coordinate Extraction. Peak coordinates and participant descriptive information were extracted from each paper separately by a minimum of two doctoral-level researchers (LM, JH, DC, AE, YJ) with expertise in psychiatric neuroimaging. In the case of discrepancies one to three additional doctoral-level coders re-entered those articles. Each discrepancy resulting from more than straightforward entry error was reviewed to establish consensus.

Activation Likelihood Estimation (ALE) Meta-analysis. The revised ALE algorithm, implemented in MATLAB, was used to identify areas of convergence of reported coordinates for patient/control differences in activation during cognitive control tasks higher than expected under a random spatial association (28-29). ALE models activation as 3-dimensional Gaussian probability distributions centered on the reported peak coordinate, capturing the spatial uncertainty associated with each focus. The probability distributions for all foci of a given experiment were aggregated as a “modeled activation map” (30). The union of all modeled activation maps then resulted in voxelwise ALE scores, which were tested against an analytically derived null-distribution that reflects a random spatial association between experiments with a fixed within-experiment distribution of foci (30). Hereby, random-effects inference was applied, which assesses above-chance convergence between experiments. The observed ALE scores were tested against the expectation on the ALE scores under the null distribution of random spatial association across experiments. The resulting nonparametric p values were then thresholded at a cluster-level familywise-error-corrected threshold of $p < .05$ (cluster-forming threshold at voxel-level $P < .005$) and transformed into z scores for

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display. To avoid results dominated by one or two individual experiments and to have sufficient power to detect moderately sized effects, ALE analyses were limited to those contrasts with at least 20 experiments (31).

Supplementary Results

Final Selected Experiment Set. The final set of experiments submitted to meta-analysis consisted of 283 experiments from 251 articles (Figure 1; Table S1) for a total of 11,221 participants (5,728 control and 5,493 patient participants). The vast majority of experiments (n=260) utilized functional magnetic resonance imaging (fMRI) followed by 21 positron emission tomography experiments and one each using arterial spin labeling and single-photon emission computerized tomography. See Figure S3 for analyses limited to fMRI and PET. Experiments were published between 1996 and May 2015 with less than 5% published in the first five years, 23% in the next five years, 40% in the subsequent five years and finally 32% between 2011 and spring 2015.

For the small subset of articles that included multiple patient groups completing the same experimental paradigm (seven papers included more than one patient group) each patient versus control comparison was included as a separate experiment. Articles with results of multiple tasks probing cognitive control in the same participants were included as separate experiments in the meta-analysis (i.e., eight articles included two tasks; four articles included three tasks).

Experiments were selected to capture lifespan patterns and thus included participants ranging from childhood (youngest experiment group mean age=11.2 years) through older adulthood (oldest experiment group mean age=73.3 years). The majority of experiments represented adulthood (n=248; 18-50 years; participant mean

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age=34.12 years), followed by childhood/adolescence (n=27; <18 years; mean age=15.41 years) and very few with older adults (n=8; >50 years; mean age=58.03 years). See Figure S5 for analyses limited to adults and S6 for adults and children/adolescents separately. Furthermore, most experiments included medicated (n=193) versus unmedicated (n=60) patients while the information was lacking for 30 experiments. See Figure S7 for analyses by current medication status. Poorer behavioral performance on the scanner task by patients relative to control participants was reported in 135 experiments, no differences in 146 experiments, and not reported or assessed for 2 experiments. See Figure S8 for analyses by performance status. Baseline experiments of interventional studies (e.g., drug administration, treatment) otherwise meeting criteria were included.

The psychotic disorders category comprised 139 experiments almost exclusively of schizophrenia (n=135) in addition to mixed schizophrenia/schizoaffective (n=2), schizoaffective (n=1) and delusional disorders (n=1). The more heterogeneous non-psychotic disorders category comprised 144 experiments of unipolar depressive disorders (major depression n=24; dysthymia n=2; mixed depression/dysthymia n=1), anxiety disorders (obsessive compulsive disorder (OCD) n=25; posttraumatic stress disorder (PTSD) n=6; social anxiety disorder n=1); bipolar disorders n=49; and substance use disorders (mixed substance abuse and/or dependence disorders n=35: stimulant n=11; alcohol n=9; cannabis n=6; polysubstance n=4; opiate n=3; cocaine n=2). Across disorders, patient participants included those with first episode and chronic disorder manifestations, as well as interepisode expressions in the case of chronic bipolar and psychotic disorders (8/139 and 24/50 psychotic and bipolar disorder

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experiments respectively included interepisode patient samples). Reports of comorbidity were inconsistent across studies precluding quantification. Exclusion criteria also provided incomplete information about comorbidity as exclusion was often limited to substance abuse (in the case of non-substance use disorder studies) or psychotic symptoms or disorders (in the case of non-psychotic disorder studies) with no information pertaining to other disorders. In summary, the meta-analysis included a highly diverse sample of diagnostic presentations from across the major categories of Axis I psychopathology.

In the following paragraphs, we report on a series of chi-square tests of the distributions of experiments by 1) task domain (across diagnosis), 2) diagnostic grouping (across domain), and 3) task domain by diagnostic grouping.

In addition to the diversity in diagnoses, included experiments represented an array of cognitive control tasks corresponding to an array of performance domains (cf. Table S1). The representation of experiments (across diagnoses) varied by domain, $X^2(8)= 200.3$, $p<.001$.This was due to greater representation of experiments of working memory (n=100), response inhibition (n=42), recognition memory (n=37), and conflict monitoring (n=31), relative to experiments of verbal fluency (n=17), set shifting (n=15), response selection (n=12), performance monitoring (n=11) and a ninth set of 18 diverse experiments that did not cohere into any of these specific domains. Notably, the predominance of working memory experiments in relation to other domains (38%) is striking and could suggest a bias among investigators to hypothesize its critical role in psychiatric dysfunction. However, whole-brain meta-analyses of cognitive control in healthy samples have revealed a similar over-representation of working memory

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experiments (26) suggesting broader supposition in cognitive neuroscience of its foundational role in adaptive as well as maladaptive cognitive function. While these findings suggest that a broader sampling of tasks is warranted in future psychiatric neuroimaging studies, the parallel distribution of tasks in the current meta-analysis of patients to meta-analysis of healthy samples, underscores the relevance of these findings to the broader literature on intact cognitive functioning.

Experiments investigating psychotic (n=139) and non-psychotic disorder samples (n=144) were equally represented across domains, $X^2(2)= 0.09$, ns. However, the distribution of experiments (across domains) varied dramatically by more refined diagnostic category, $X^2(4)= 155.15$, $p<.001$. This was largely due to schizophrenia spectrum disorders (51%) far exceeding all other groups in representation, pairwise X^2 comparisons of schizophrenia to each group, *ps<.05*. Unfortunately, it was not possible to determine the sample correspondence between this dataset and that of found by Goodkind and colleagues (9) in their sample of whole brain VBM experiments, given the lack of indications to that end in the papers. Nevertheless, the breakdown by diagnosis is very similar, $X^2(4)= 5.89$, ns. The relative proportion of the respective samples is as follows (% of cognitive control experiments; % of VBM experiments): psychotic disorders (51%; 43%), bipolar disorders (18%; 14%), anxiety disorders (11%; 23%), depressive disorders (10%; 13%), substance use disorders (12%; 10%). While not an exhaustive representation of the extant literature, these findings do suggest that additional structural neuroimaging as well as functional neuroimaging of cognitive task activation is warranted in non-psychotic disorders.

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Finally, the distribution of tasks across the nine task domains varied by diagnosis, $X^2(32)= 78.25$, p<.001, due to the greater representation of schizophrenia spectrum samples relative to each of the other disorders specific to experiments of performance monitoring, verbal fluency, recognition, and working memory, *ps*<.05. The non-psychotic disorder groups showed no differences in distributions of experiments by domain, with the exception of verbal fluency, which had a higher proportion of bipolar disorder experiments than the other non-psychotic disorders. The wide distribution across cognitive domains by disorder is evident in Table S2, which shows the proportion of experiments within each diagnostic group corresponding to each task domain.

While the meta-analytic approach may impose limitations by the breadth of published literature, it also productively highlights a number of implied conceptual and methodological biases in psychiatric and cognitive neuroscience research. This was especially pronounced in examining lifespan effects. In the case of older adults, even with the very lenient threshold of categorizing all participants over 50 years as elderly, we could only identify eight eligible experiments, i.e., less than 3% of the included set. With a global average life expectancy of 71 years and 79 years in the United States (WHO; http://www.who.int/gho/mortality_burden_disease/life_tables/en/), there is a dearth of neuroimaging data to guide understanding of cognitive control and psychopathology in aging samples. In the case of children and young adults less than 18 years, we identified 27 eligible experiments, less than 10% of the experiment set. In turn, 53% of the total experiments were samples with mean ages between 30 and 40 years. Relatedly, schizophrenia spectrum disorders far exceeded other disorder classes. Anxiety and to some extent unipolar depression have shown more modest

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neuropsychological deficits than other disorders while more significant deficits have characterized bipolar and substance use disorders, yet the parallel functional imaging corpus is nonetheless limited. Finally, working memory was by far the best-represented task domain, a bias also represented in work with healthy samples (26).

Voxelwise Analyses by Cognitive Domain and Disorder Class. The primary questions of interest were focused on multiple-demand or general cognitive processing, and naturally, performance of most tasks involves a synergy of cognitive processes that spans domains. Nonetheless, to assess the contribution of different domains to the overall convergence, domain-specific analyses were performed for domains with contrasts from more than 20 experiments and thus adequate power to detect convergence (i.e., working memory (n=100), response inhibition (n=42), recognition memory (n=37), conflict monitoring (n=31). Patient hypoactivation was observed during working memory in right anterior insula/ventrolateral prefrontal cortex and vermis of the cerebellum, and during response inhibition in the right anterior insula/ventrolateral prefrontal cortex and right claustrum. Patient hyperactivation was evident during working memory in ventromedial prefrontal cortex. Other domains did not show significant regions of hyper- or hypoactivation (Figure S12). Overall, these data suggest that the broad array of cognitive demands evoked by a heterogeneous array of tasks contributed to the transdiagnostic convergence evident in the multiple-demand network abnormalities observed here. Again, ALE analyses were also run for each disorder by domain for the two contrasts with more than 20 experiments and thus adequate power to detect convergence (i.e., working memory experiments on schizophrenia (n=54) and recognition memory experiments on schizophrenia (n=27)). Schizophrenia spectrum

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disorders showed patient hypoactivation in right insula/ventrolateral prefrontal cortex during working memory (Figure S13) and no whole-brain activations converged for recognition memory tasks. All other comparisons included only one to 16 experiments.

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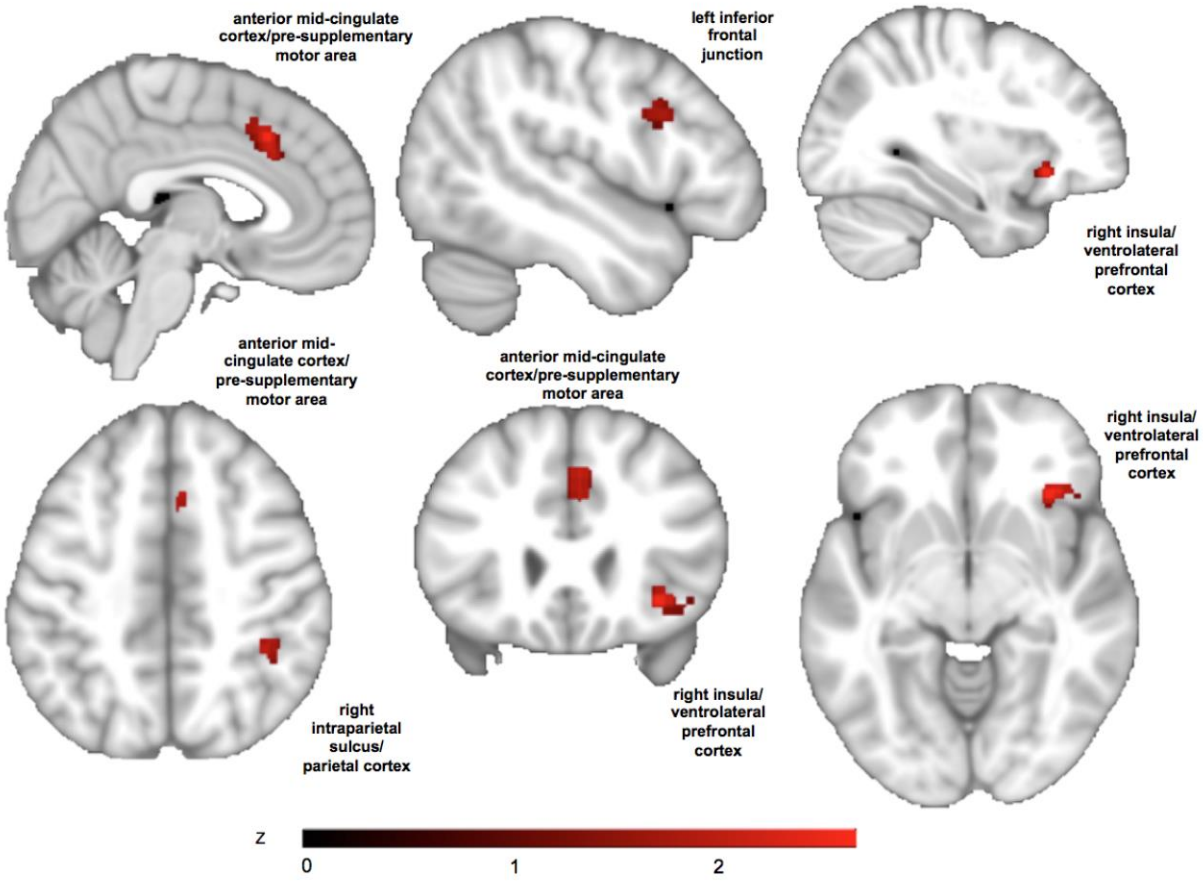

FIGURE S1. A conjunction with the multiple-demand network observed by Müller et al. (25), highlighting the overlap with multiple nodes in the distributed network of regions showing transdiagnostic aberrant activation (i.e., pooled across patient hyper- and hypo-activation (red)) during cognitive processing.

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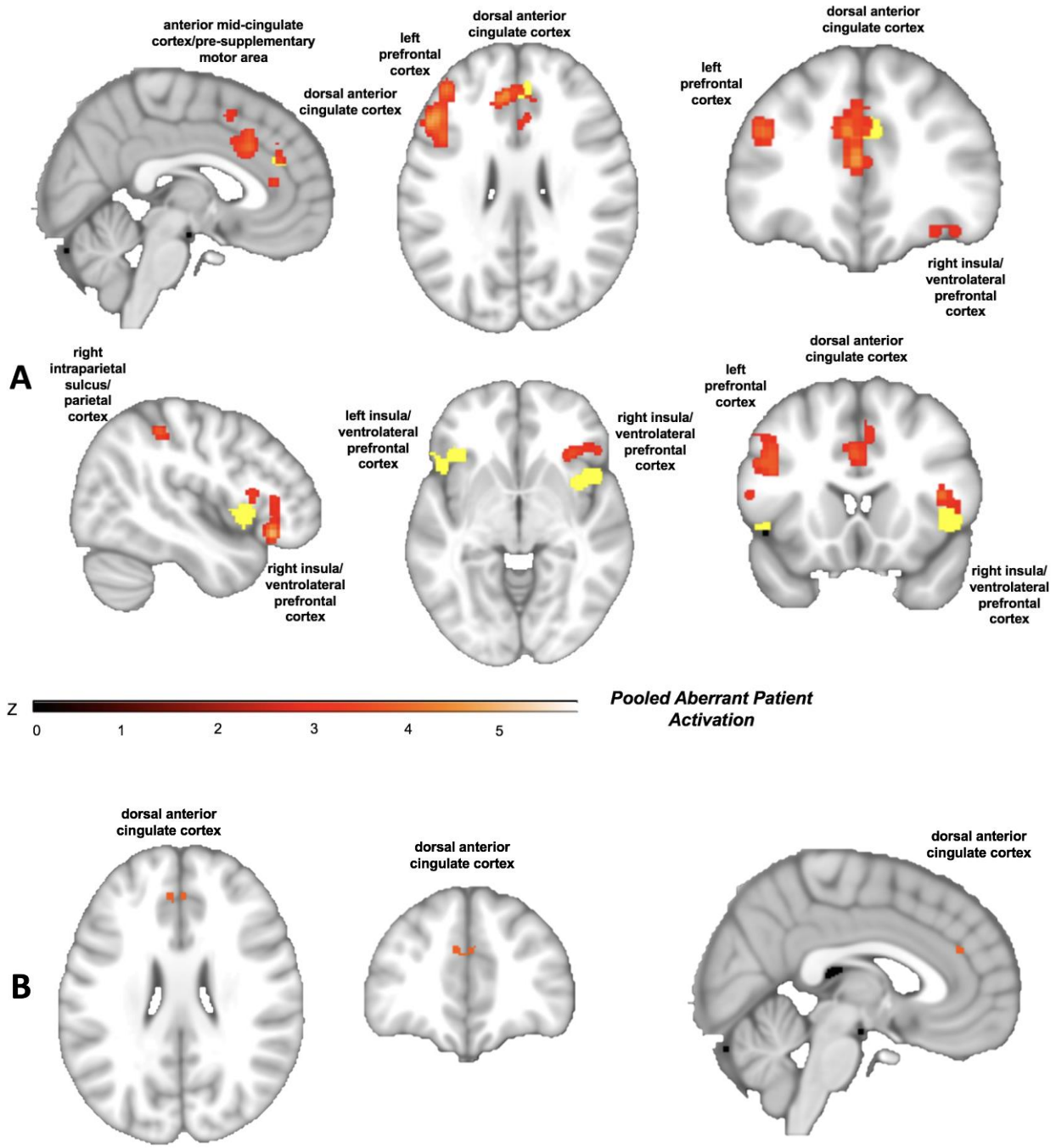

FIGURE S2. A) Regions of transdiagnostic aberrant activation (i.e., pooled across patient hyper- and hypo-activation (red), showing nodes very near and partially overlapping with the dorsal anterior cingulate and anterior insula regions of gray matter

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loss (yellow) observed by Goodkind and colleagues (9). B) A conjunction highlights anatomical and functional correspondence in dorsal anterior cingulate (orange).

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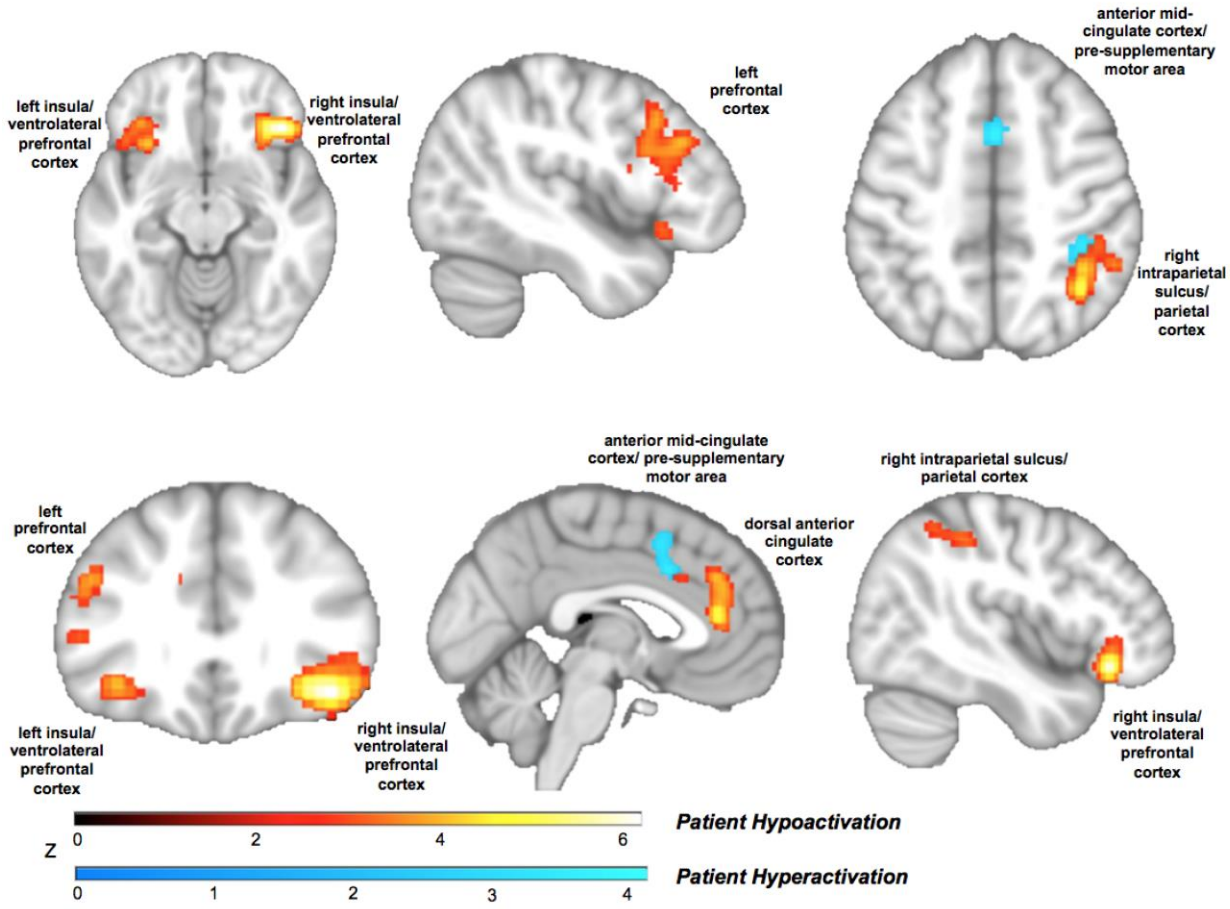

FIGURE S3. ALE analyses with the single SPECT and single ASL studies excluded did not affect the pattern of significant activations. For example, patient hyper- (blue) and hypoactivation (orange) across disorders are displayed for the remaining studies (n=260 functional magnetic resonance imaging; n=21 positron emission tomography).

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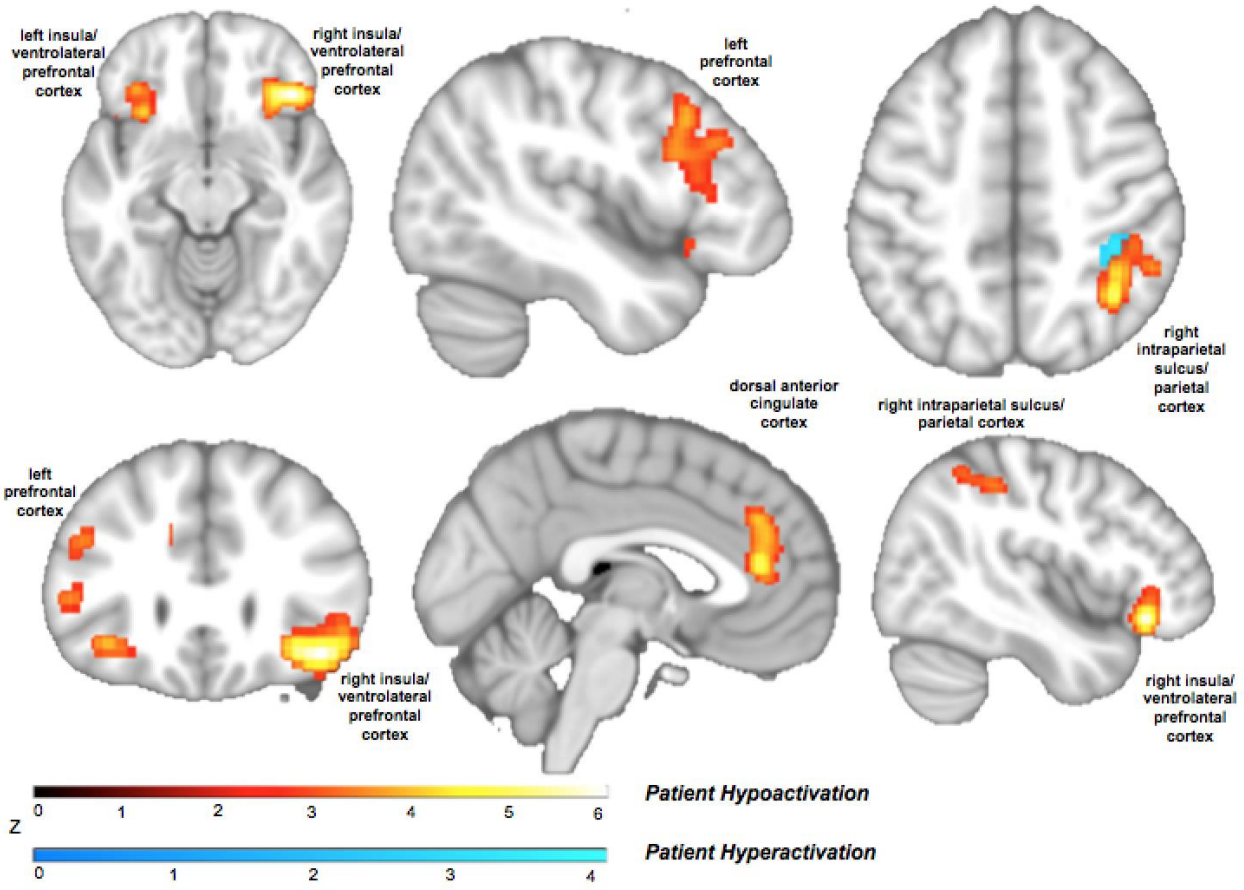

FIGURE S4. ALE analyses excluding the 18 diverse studies that did not cohere into any specific domain resulted in little change to the overall patterns, with the exception of no significant anterior mid-cingulate cortex/pre-supplementary motor area activation. For example, patient hypo- (orange) and hyperactivation (blue) across disorders are displayed for the remaining 265 studies.

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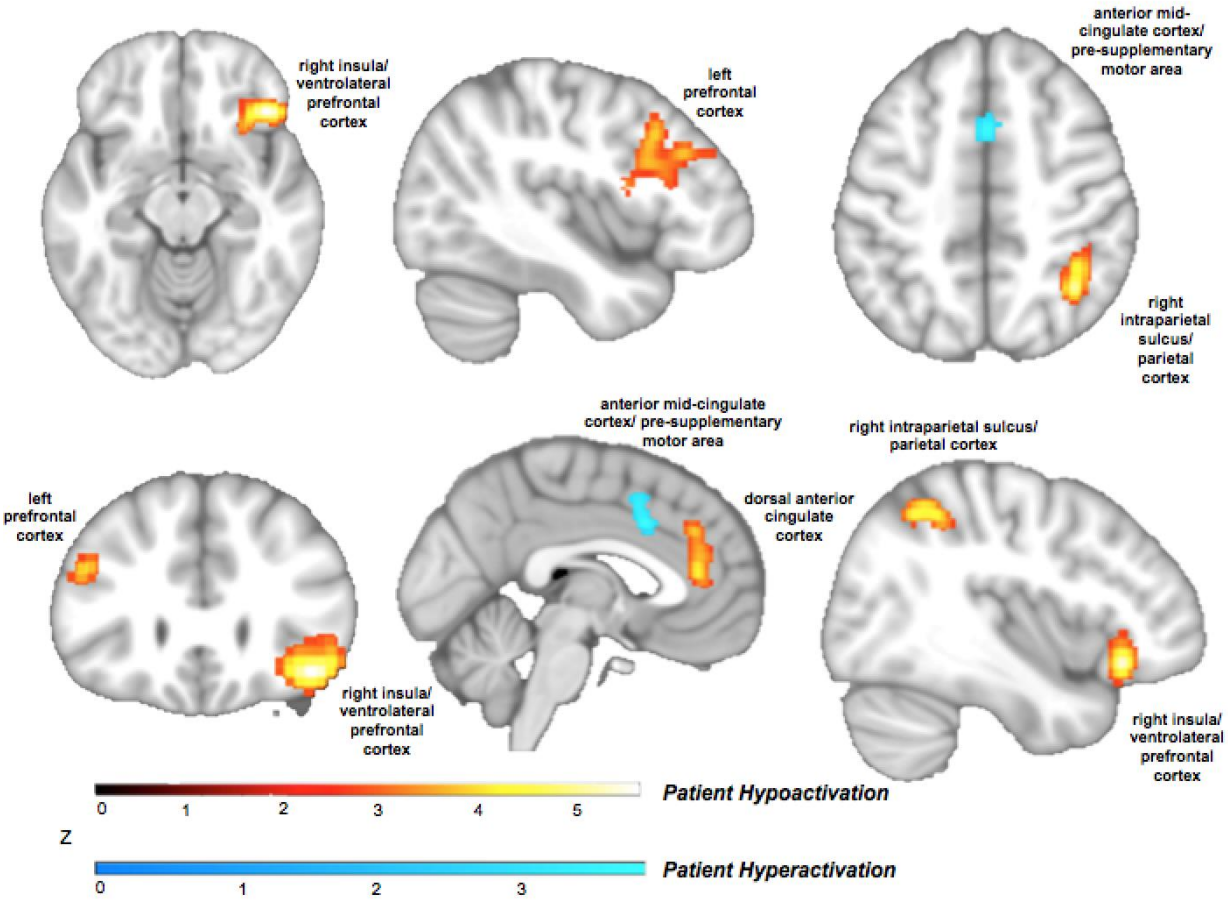

FIGURE S5. Results from separate ALE analyses for studies of children, adults and older adults showed that the overall pattern was primarily determined by the adult sample, the largest proportion of studies (n=248; 18-50 years). The child (n=27; <18 years) and older adult (n=8; >50 years) samples did not show any significant whole-brain activations. Displayed are the patient hypo- (orange) and hyperactivation (blue) across disorders for the subset of adult studies.

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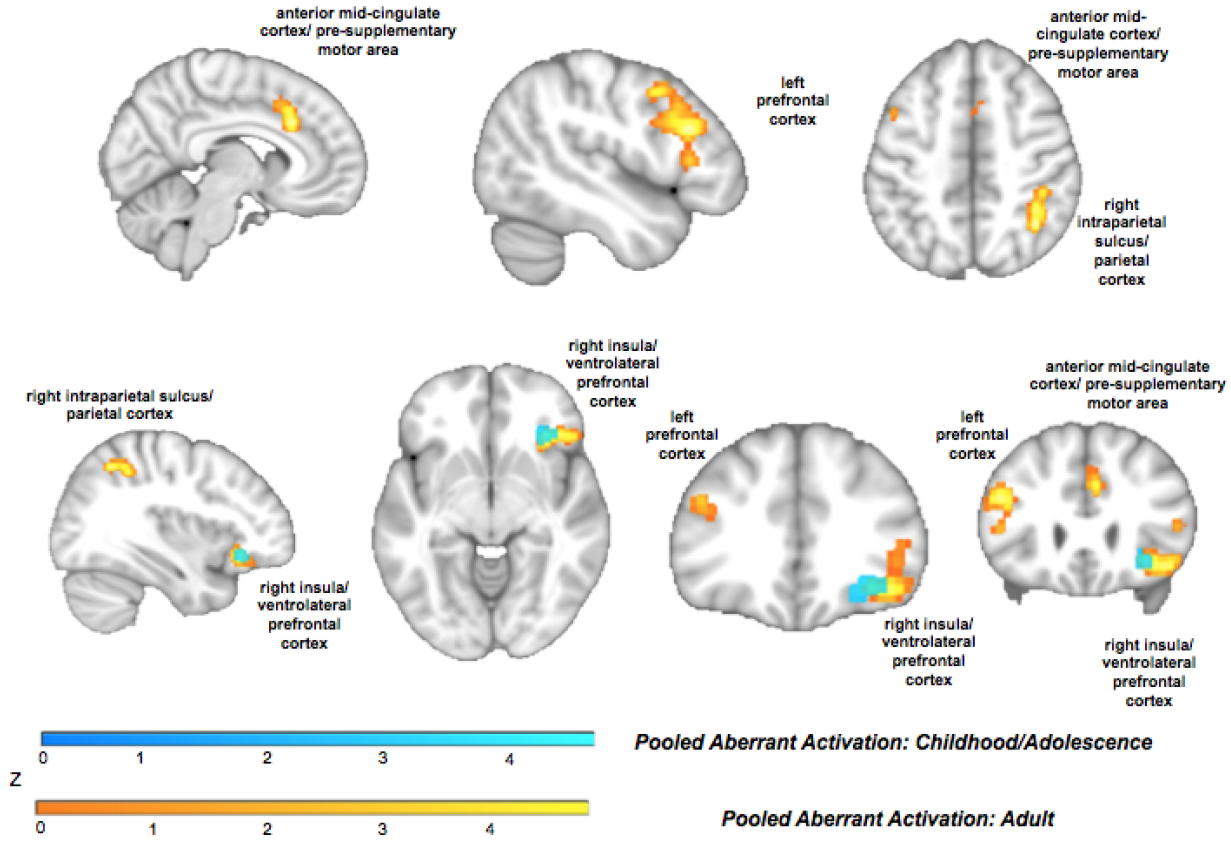

FIGURE S6. Patterns of “aberrant activation” (orange) when pooling across patient hyper- and hypoactivation foci across the whole brain separately for childhood/adolescence (<18 years; blue) and adulthood (18-50 years; orange) experiments. The older adult (>50 years) experiments did not show any significant whole-brain activations. Given the strong right anterior insula/ventrolateral prefrontal cortex aberrant activation overlapping in the childhood/adolescence and the adulthood samples, this node may have a prominent role in cognitive dyscontrol from childhood through adulthood.

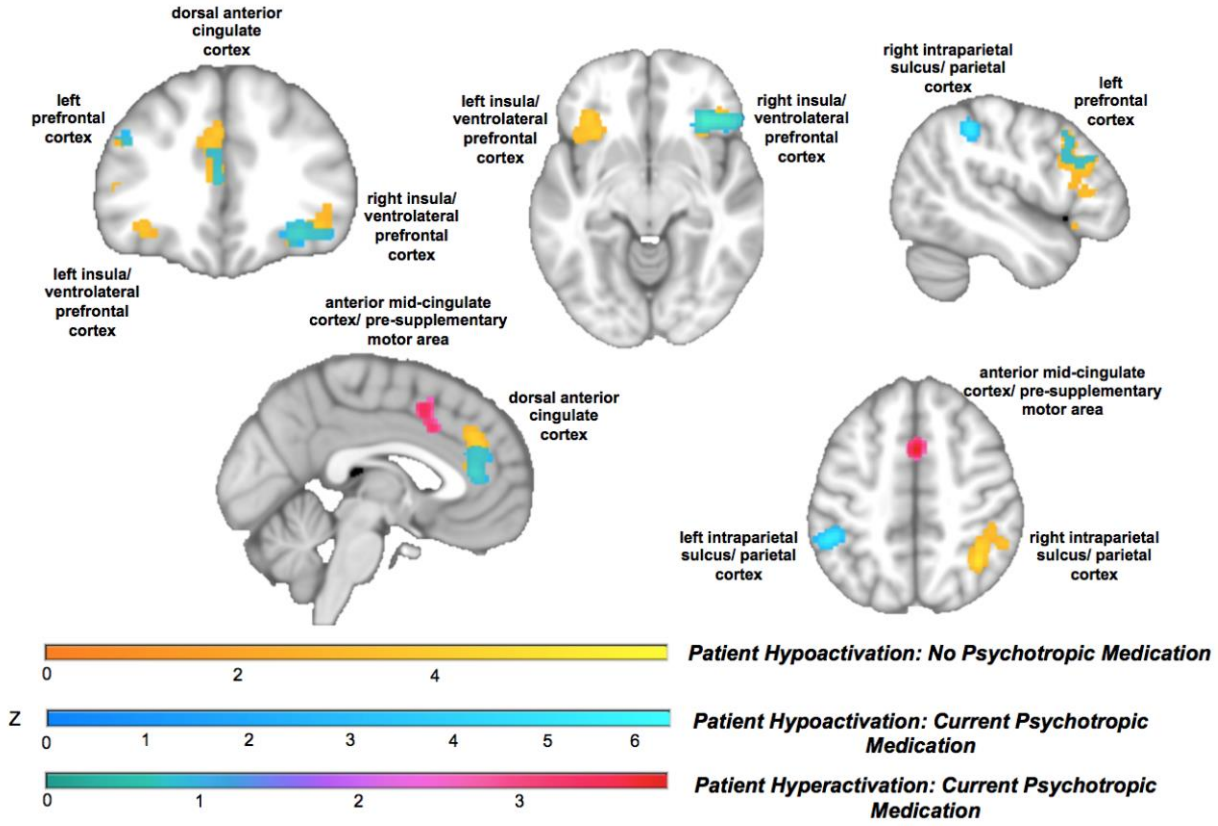

FIGURE S7. Results from separate ALE analyses of patient hypo- and hyper-activation for studies of medicated and unmedicated patients. Unmedicated (blue) and medicated (yellow) patients showed similar patterns of hypoactivation. Medicated patients showed hyperactivation (magenta) specific to the anterior mid-cingulate cortex/pre-supplementary motor cortex. Unmedicated patient experiments as a whole did not show any significant whole-brain hyperactivations.

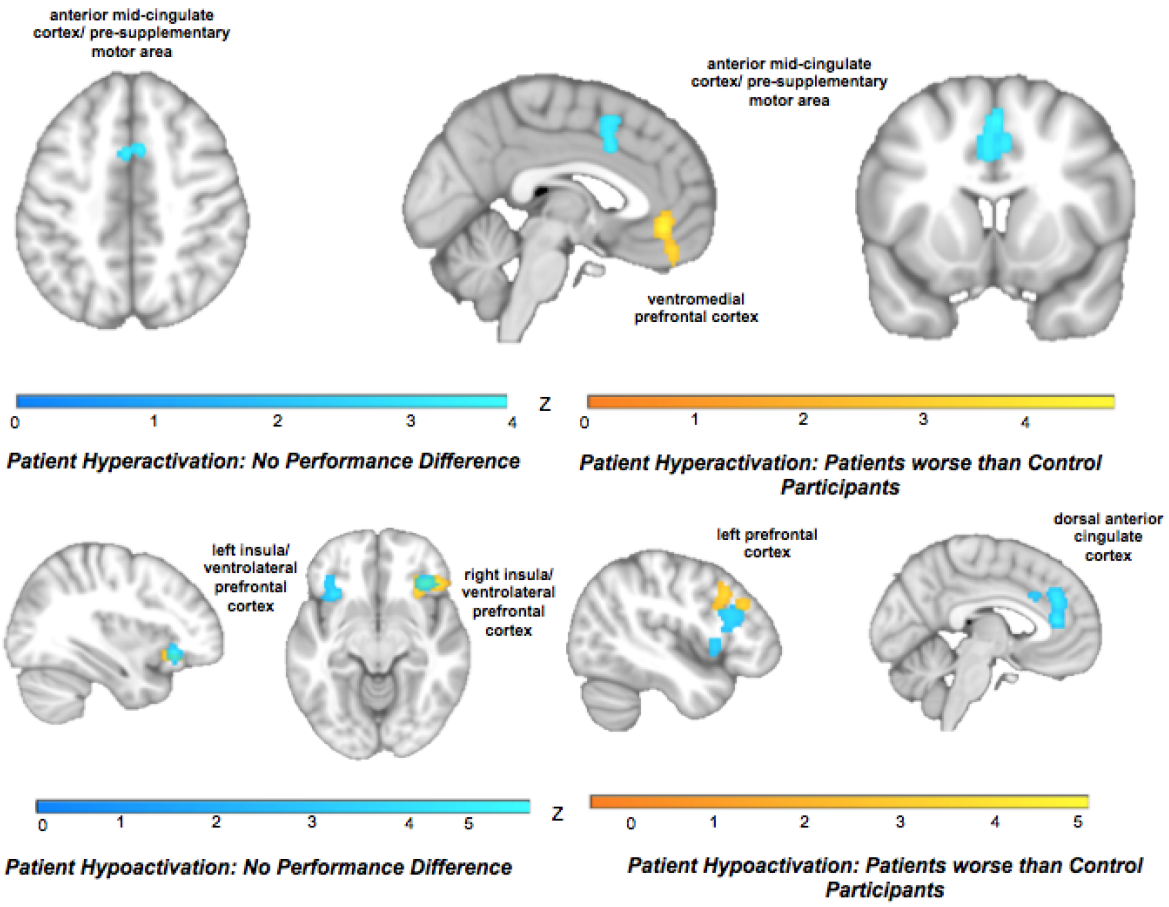

FIGURE S8. Accounting for behavioral performance on the scanner task demonstrated that patient hyperactivation in the anterior mid-cingulate/ pre-supplementary motor cortex cluster was primarily driven by patient groups that performed on par with as opposed to worse than control participants. This was confirmed in a test of the extracted per voxel probabilities for this region of interest (Mann-Whitney U Test, U=9,270, p<.05). By contrast, patient hypoactivation in multiple-demand network nodes were largely similar regardless of whether behavioral performance was impaired.

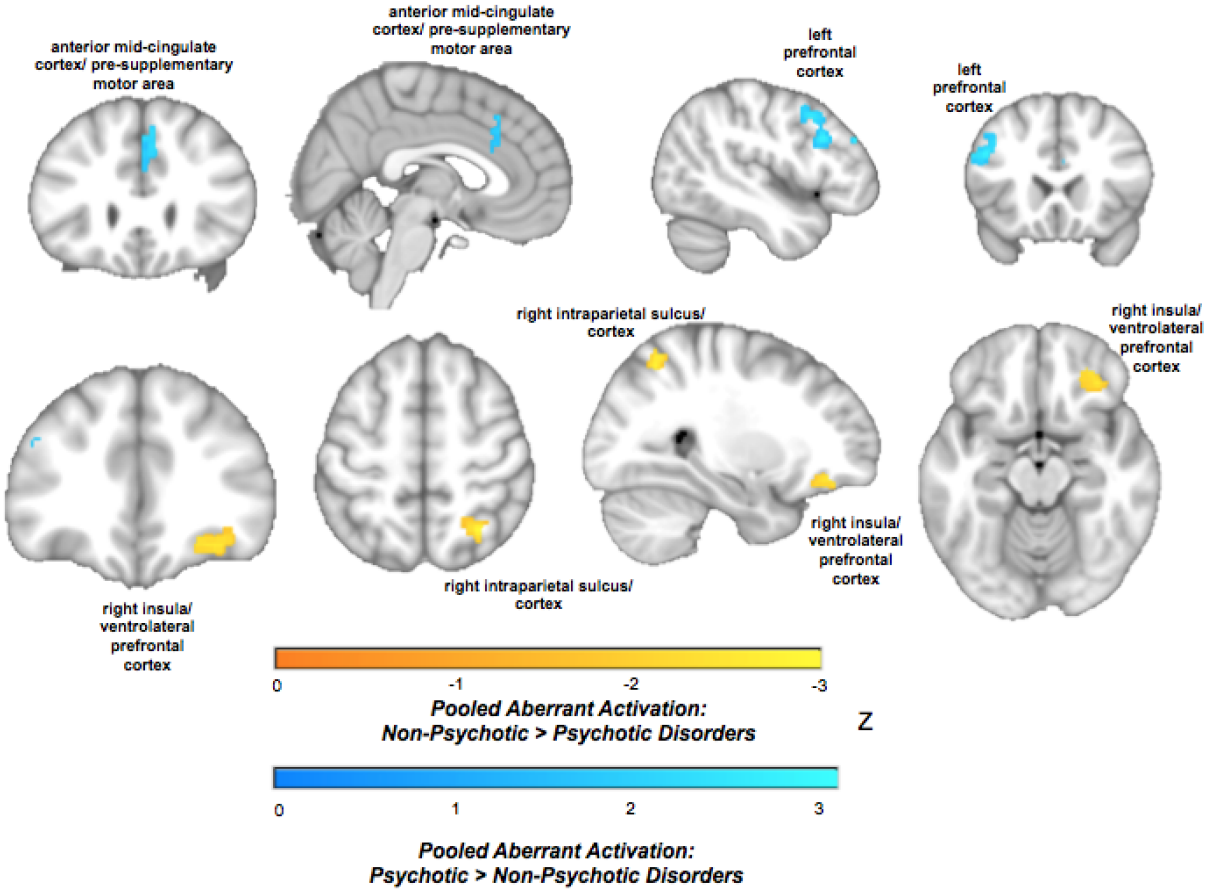

FIGURE S9. A contrast between pooled aberrant activation in psychotic and non-psychotic disorders revealed greater aberrant activation in psychotic versus non-psychotic disorders in a more posterior portion of the left prefrontal cluster and a portion of the mid-cingulate/pre-supplementary motor area. Additionally non-psychotic disorders showed reliably more aberrant activation in right intraparietal sulcus and a more anterior portion of the right anterior insula/ ventrolateral prefrontal cortex cluster.

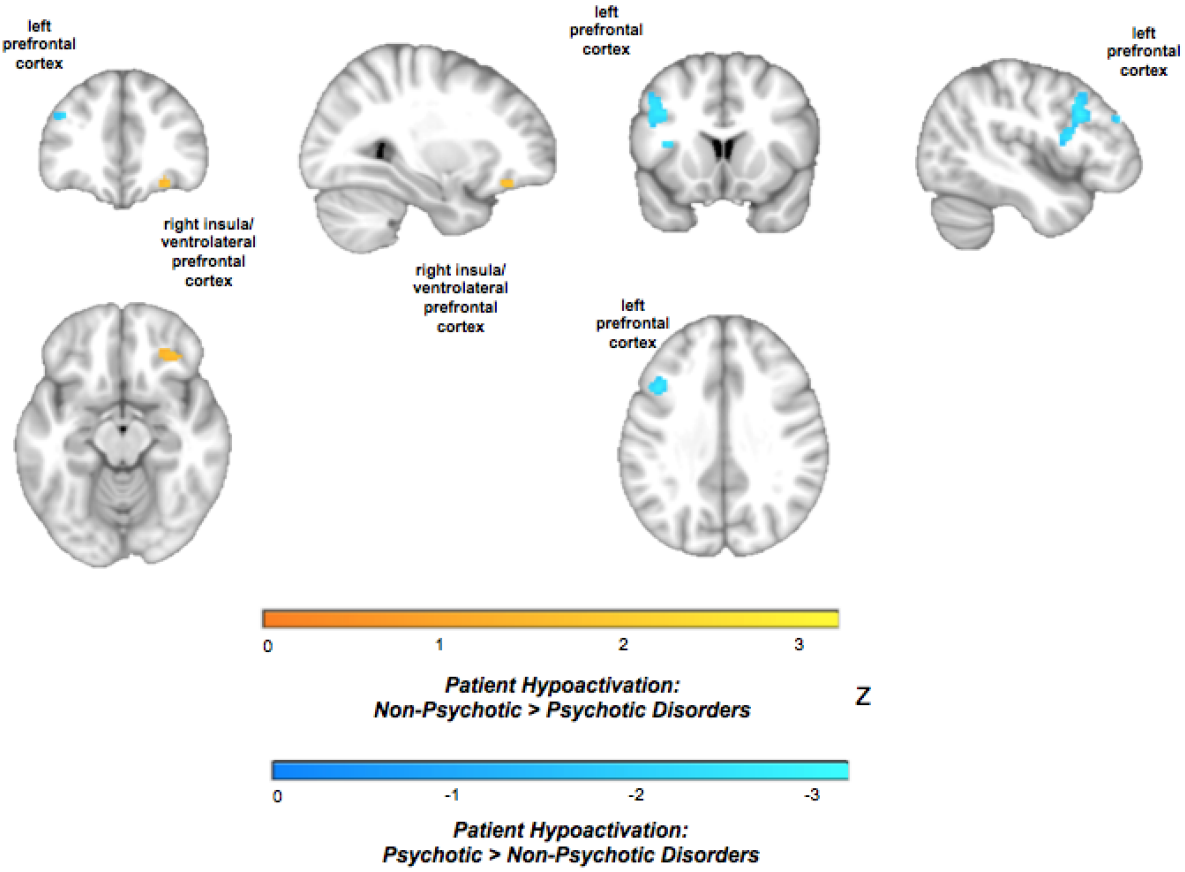

FIGURE S10. A contrast between hypoactivation in psychotic and non-psychotic disorders showed that the right anterior insula/ ventrolateral prefrontal cortex extended more anteriorly in non-psychotic disorders, whereas psychotic disorders showed stronger hypoactivation in the posterior portion of the left prefrontal cluster.

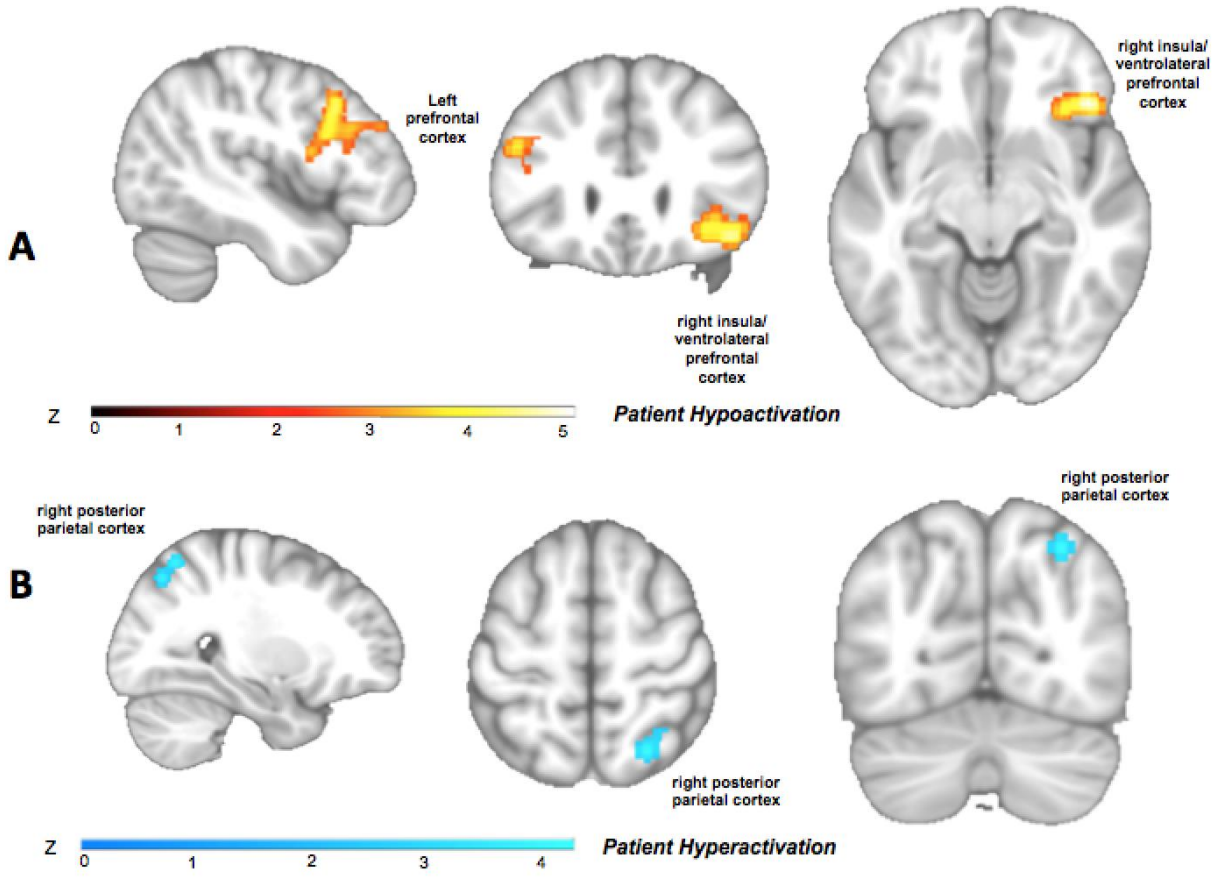

FIGURE S11. Refining to diagnostic classes revealed few activations that survived whole-brain correction. A) Schizophrenia spectrum disorders showed a reliable hypoactivation of left prefrontal cortex and right anterior insula/ventrolateral prefrontal cortex consistent with the overall pattern (orange). B) Substance use disorders showed patient hyperactivation in right posterior parietal cortex (more posterior than the overall pattern; blue). Contrasts specific to anxiety as well as bipolar and unipolar depressive disorders did not show any significant whole-brain activations.

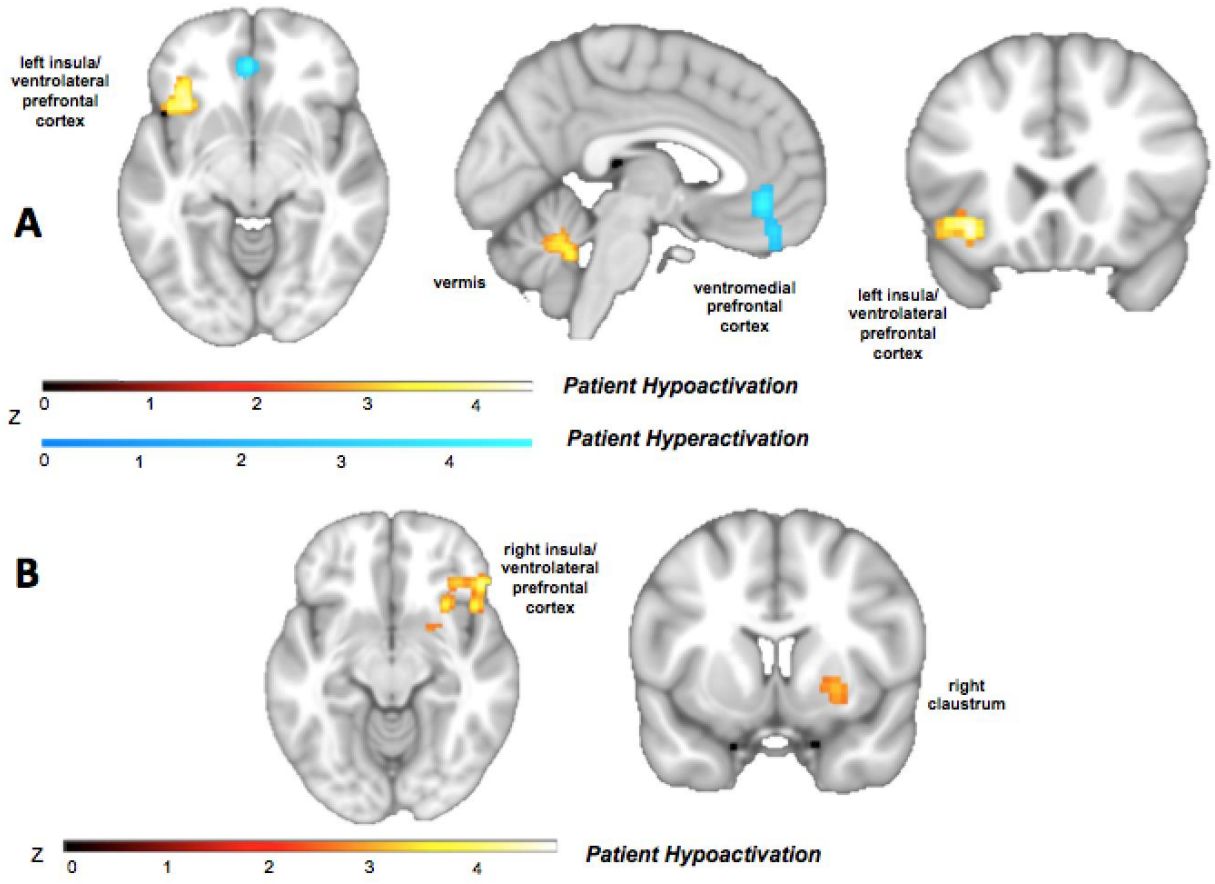

FIGURE S12. Domain-specific analyses were performed on domains with contrasts from more than 20 experiments and thus adequate power to detect convergence (i.e., working memory (n=100), response inhibition (n=42), recognition memory (n=37), conflict monitoring (n=31). A) During working memory tasks patient hyperactivation (blue) was observed in in ventromedial prefrontal cortex and hypoactivation (orange) in left anterior insula/ventrolateral prefrontal cortex. B) During response inhibition hyperactivation was evident in the right anterior insula/ ventrolateral prefrontal cortex and right claustrum (B). Recognition memory and conflict monitoring contrasts showed no significant whole-brain activations.

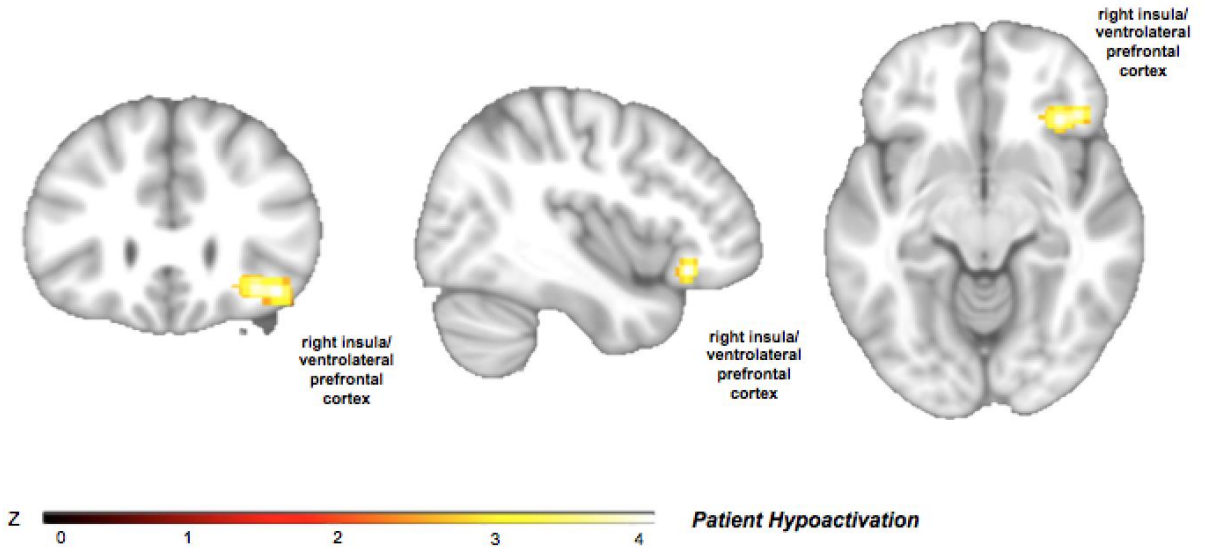

FIGURE S13. ALE by Disorder and Domain. Schizophrenia spectrum disorders showed patient hypoactivation in right insula/ ventrolateral prefrontal cortex during working memory (yellow). Other contrasts by disorder and domain showed no significant whole-brain activations. though this included too few studies for valid for ALE inference (31).

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TABLE S1. Experiments included in meta-analysis by diagnostic grouping, modality, domain and task

Ref #	Experiment #	PUBMEDID	Diagnostic Group	Imaging Modality	Domain	Task
1	1	17768265	Schizophrenia	MRI	Recognition Memory	Recognition
2	2	15541070	Bipolar	MRI	Working Memory	N-back
3	3	20146832	Bipolar	MRI	Verbal Fluency	Verbal Fluency
4	4	8790444	Schizophrenia	PET	Other	Recall
5	5	21914644	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
6	6	16199012	Schizophrenia	MRI	Other	Recall
7	7	16640486	Anxiety	MRI	Working Memory	Virtual Morris Water task
8	8	24022592	Bipolar	MRI	Recognition Memory	Transitive Inference
9	9	21782395	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
10	10	24381810	Schizophrenia	MRI	Response Selection	Delay Discounting
11	11	22805228	Substance Use	MRI	Working Memory	Spatial Working Memory
12	12	24557502	Unipolar	MRI	Verbal Fluency	Verbal Fluency
13	13	24296894	Substance Use	MRI	Other	Semantic Decision Making
14	14	17499456	Substance Use	MRI	Conflict Monitoring	Stroop
15	15	12150424	Schizophrenia	MRI	Working Memory	N-back
16	16	12614990	Unipolar	MRI	Working Memory	N-back
17	17	16952445	Schizophrenia	MRI	Working Memory	N-back
18	18	24675869	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
19	19	12796223	Bipolar	MRI	Conflict Monitoring	Stroop

20	20	21997605	Unipolar	MRI	Response Inhibition	Stop Signal Task
21	21	12880834	Substance Use	PET	Response Selection	Modified Iowa Gambling Task
22	22	21067898	Schizophrenia	MRI	Working Memory	N-back
23	23	25752642	Bipolar	MRI	Working Memory	N-back
24	24	19118321	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
24	25	19118321	Schizophrenia	MRI	Working Memory	N-back
25	26	22272986	Bipolar	MRI	Working Memory	N-back
26	27	11053229	Schizophrenia	MRI	Working Memory	N-back
27	28	14638592	Schizophrenia	MRI	Working Memory	N-back
28	29	9396944	Schizophrenia	PET	Conflict Monitoring	Stroop
29	30	22640382	Bipolar	MRI	Response Inhibition	Continuous Performanc e Task
30	31	21376542	Bipolar	MRI	Verbal Fluency	Hayling Sentence Completion Test
31	32	15289277	Bipolar	MRI	Working Memory	N-back
32	33	19538748	Anxiety	MRI	Recognition Memory	Recognition
33	34	20046409	Schizophrenia	MRI	Conflict Monitoring	Stroop
34	35	10080553	Schizophrenia	PET	Other	Recall
34	36	10080553	Schizophrenia	PET	Other	Recall
35	37	11241873	Schizophrenia	PET	Recognition Memory	Recognition
36	38	22539776	Schizophrenia	MRI	Other	Recall
37	39	9699694	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
38	40	10227106	Schizophrenia	MRI	Other	Semantic Decision Making
39	41	11578663	Bipolar	MRI	Verbal Fluency	Verbal Fluency

39	42	11578663	Bipolar	MRI	Verbal Fluency	Semantic Decision Making
40	43	17547582	Bipolar	MRI	Verbal Fluency	Verbal Fluency
41	44	23949205	Substance Use	MRI	Recognition Memory	Recognition
42	45	14561934	Substance Use	MRI	Working Memory	N-back
43	46	14597698	Schizophrenia	MRI	Conflict Monitoring	Stroop
44	47	12948707	Substance Use	MRI	Working Memory	Sternberg Working Memory Task
45	48	24639328	Unipolar	MRI	Recognition Memory	Recognition
46	49	23607410	Bipolar	MRI	Response Inhibition	Go/No-Go
47	50	18571627	Bipolar	MRI	Working Memory	N-back
48	51	25458072	Unipolar	MRI	Working Memory	N-back
49	52	24239131	Schizophrenia	MRI	Working Memory	Recognition
50	53	15528091	Substance Use	PET	Conflict Monitoring	Stroop
51	54	17018171	Anxiety	MRI	Working Memory	N-back
52	55	21331519	Schizophrenia	MRI	Working Memory	N-back
53	56	18787658	Anxiety	MRI	Response Inhibition	Go/No-Go
53	57	18787658	Anxiety	MRI	Response Inhibition	Go/No-Go
54	58	24615691	Schizophrenia	MRI	Conflict Monitoring	Stroop
55	59	22854099	Bipolar	MRI	Working Memory	N-back
56	60	15691530	Anxiety	MRI	Conflict Monitoring	Flanker
57	61	17525987	Unipolar	MRI	Response Selection	Tower of London
57	62	17525987	Unipolar	MRI	Working Memory	N-back
58	63	21546091	Bipolar	MRI	Response Inhibition	Go/No-Go
59	64	25749917	Schizophrenia	MRI	Recognition Memory	Recognition

60	65	22363273	Bipolar	MRI	Conflict Monitoring	Stroop
61	66	18485592	Substance Use	MRI	Response Inhibition	Go/No-Go
62	67	8988793	Schizophrenia	PET	Other	Recall
63	68	25037555	Schizophrenia	MRI	Other	Finger Tapping
63	69	25037555	Unipolar	MRI	Other	Finger Tapping
64	70	20063304	Bipolar	MRI	Recognition Memory	Recognition
65	71	18065438	Anxiety	MRI	Set Shifting	Set Shifting
66	72	21733286	Schizophrenia	MRI	Working Memory	N-back
67	73	19175815	Unipolar	MRI	Response Inhibition	Simon Task
67	74	19175815	Unipolar	MRI	Response Inhibition	Stop Signal Task
67	75	19175815	Unipolar	MRI	Set Shifting	Switch Task
68	76	19732478	Schizophrenia	MRI	Recognition Memory	Recognition
69	77	19449330	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
69	78	19449330	Bipolar	MRI	Working Memory	Delayed Match-to-sample
70	79	24672002	Substance Use	MRI	Response Inhibition	Stop Signal Task
71	80	17307337	Schizophrenia	MRI	Working Memory	Multi-Source Interference Task
72	81	17803757	Schizophrenia	MRI	Working Memory	Multi-Source Interference Task
73	82	15955496	Unipolar	MRI	Working Memory	N-back
74	83	25610794	Schizophrenia	MRI	Recognition Memory	Source Memory
75	84	10195166	Schizophrenia	PET	Other	Recall
76	85	16497485	Schizophrenia	MRI	Other	Recall
77	86	18592040	Anxiety	MRI	Working Memory	Delayed Match-to-sample
77	87	18592040	Anxiety	MRI	Working Memory	Delayed Match-to-sample

77	88	18592040	Anxiety	MRI	Working Memory	Delayed Match-to-sample
78	89	19686473	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
78	90	19686473	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
79	91	15590917	Substance Use	MRI	Response Inhibition	Go/No-Go
80	92	12727695	Schizophrenia	MRI	Recognition Memory	Recognition
81	93	14514494	Schizophrenia	MRI	Recognition Memory	Recognition
82	94	12946085	Schizophrenia	MRI	Working Memory	N-back
83	95	14754778	Unipolar	MRI	Working Memory	Mental Arithmetic
83	96	14754778	Schizophrenia	MRI	Working Memory	Mental Arithmetic
84	97	20036266	Schizophrenia	MRI	Set Shifting	Wisconsin Card Sorting Task
85	98	22985694	Schizophrenia	MRI	Recognition Memory	Recognition
85	99	22985694	Bipolar	MRI	Recognition Memory	Recognition
86	100	16054343	Schizophrenia	MRI	Conflict Monitoring	Stroop
87	101	21812622	Bipolar	MRI	Response Selection	Modified Iowa Gambling Task
87	102	21812622	Bipolar	MRI	Working Memory	N-back
88	103	21357880	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
89	104	16503328	Schizophrenia	MRI	Recognition Memory	Recognition
90	105	15601603	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
91	106	17291724	Schizophrenia	MRI	Response Inhibition	Go/No-Go
91	107	17291724	Schizophrenia	MRI	Response Inhibition	Go/No-Go
92	108	17855057	Schizophrenia	MRI	Response Inhibition	Go/No-Go

93	109	19624392	Bipolar	MRI	Response Inhibition	Go/No-Go
94	110	19442494	Bipolar	MRI	Response Inhibition	Go/No-Go
95	111	15205869	Substance Use	MRI	Working Memory	Delayed Match-to-sample
96	112	21703287	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
97	113	23146681	Anxiety	MRI	Response Inhibition	Go/No-Go
98	114	19426993	Schizophrenia	MRI	Working Memory	N-back
99	115	16199829	Schizophrenia	MRI	Conflict Monitoring	Stroop
100	116	22024484	Bipolar	MRI	Response Inhibition	Go/No-Go
101	117	11839367	Unipolar	PET	Performance Monitoring	Continuous Performanc e Task
102	118	11378312	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
103	119	18356025	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
104	120	24705568	Substance Use	MRI	Conflict Monitoring	Stroop
105	121	18359576	Schizophrenia	MRI	Working Memory	Sternberg Working Memory Task
106	122	22349440	Anxiety	MRI	Working Memory	N-back
107	123	16411978	Bipolar	MRI	Conflict Monitoring	Stroop
108	124	24325976	Schizophrenia	MRI	Response Selection	Beads in the Bottle Task
109	125	22917204	Schizophrenia	MRI	Working Memory	N-back
110	126	14683698	Schizophrenia	MRI	Recognition Memory	Recognition
111	127	18504037	Schizophrenia	MRI	Conflict Monitoring	Semantic Decision Making
112	128	17476364	Bipolar	MRI	Working Memory	Sternberg Working Memory Task

113	129	25331916	Schizophrenia	MRI	Working Memory	N-back
114	130	17585888	Unipolar	MRI	Response Inhibition	Go/No-Go
115	131	12566282	Schizophrenia	MRI	Response Inhibition	Go/No-Go
116	132	20488673	Schizophrenia	MRI	Recognition Memory	Recognition
117	133	24179809	Schizophrenia	MRI	Performance Monitoring	Continuous Performance Task
118	134	25588194	Schizophrenia	MRI	Performance Monitoring	Continuous Performance Task
119	135	14511805	Schizophrenia	MRI	Recognition Memory	Recognition
120	136	17895916	Substance Use	MRI	Response Inhibition	Stop Signal Task
121	137	19170662	Substance Use	MRI	Response Inhibition	Stop Signal Task
122	138	25497221	Schizophrenia	ASL	Response Selection	Tower of London
123	139	19693783	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
124	140	22583916	Schizophrenia	MRI	Working Memory	N-back
125	141	25242360	Schizophrenia	MRI	Working Memory	N-back
126	142	15627591	Anxiety	MRI	Response Inhibition	Go/No-Go
127	143	23489416	Anxiety	MRI	Conflict Monitoring	Simon Task
128	144	16983390	Unipolar	MRI	Working Memory	N-back
129	145	24262681	Schizophrenia	MRI	Working Memory	Sternberg Working Memory Task
130	146	19239982	Unipolar	MRI	Response Inhibition	Stop Signal Task
131	147	18586275	Bipolar	MRI	Response Inhibition	Go/No-Go
132	148	11839364	Schizophrenia	MRI	Response Inhibition	Antisaccade
133	149	18198268	Bipolar	MRI	Verbal Fluency	Hayling Sentence Completion Test

133	150	18198268	Schizophrenia	MRI	Verbal Fluency	Hayling Sentence Completion Test
134	151	24119150	Bipolar	MRI	Working Memory	Delayed Match-to-sample
135	152	17151834	Schizophrenia	MRI	Working Memory	N-back
136	153	15841676	Schizophrenia	MRI	Working Memory	N-back
137	154	11691686	Schizophrenia	PET	Working Memory	N-back
138	155	15221201	Substance Use	MRI	Working Memory	Delayed Match-to-sample
139	156	20153142	Substance Use	MRI	Working Memory	Delayed Match-to-sample
140	157	24258223	Substance Use	MRI	Conflict Monitoring	Stroop
141	158	15541071	Bipolar	MRI	Working Memory	N-back
142	159	23609131	Substance Use	MRI	Response Inhibition	Stop Signal Task
143	160	18667293	Anxiety	MRI	Conflict Monitoring	Stroop
144	161	20219248	Unipolar	MRI	Other	Serial Reaction Time Task
145	162	15970434	Anxiety	MRI	Conflict Monitoring	Stroop
146	163	19081580	Anxiety	MRI	Working Memory	N-back
147	164	19105218	Anxiety	MRI	Conflict Monitoring	Stroop
148	165	18076530	Bipolar	MRI	Set Shifting	Switch Task
149	166	22047731	Substance Use	MRI	Conflict Monitoring	Stroop
150	167	24120302	Schizophrenia	MRI	Response Inhibition	Continuous Performanc e Task
151	168	23764381	Bipolar	MRI	Recognition Memory	Recognition
152	169	25164120	Bipolar	MRI	Recognition Memory	Recognition
153	170	24841112	Schizophrenia	MRI	Working Memory	N-back

154	171	12353245	Schizophrenia	PET	Working Memory	Match Stimuli
155	172	16585464	Schizophrenia	MRI	Recognition Memory	Recognition
156	173	21727234	Schizophrenia	MRI	Working Memory	N-back
157	174	18072830	Substance Use	MRI	Working Memory	N-back
158	175	18788030	Schizophrenia	MRI	Working Memory	N-back
159	176	19906516	Anxiety	MRI	Conflict Monitoring	Stroop
159	177	19906516	Anxiety	MRI	Response Inhibition	Go/No-Go
159	178	19906516	Anxiety	MRI	Set Shifting	Switch Task
160	179	19926457	Bipolar	MRI	Response Inhibition	Go/No-Go
161	180	12062884	Schizophrenia	MRI	Response Selection	Two-choice prediction task
162	181	11751032	Substance Use	MRI	Response Selection	Two-choice prediction task
163	182	20816040	Bipolar	MRI	Response Inhibition	Stop Signal Task
164	183	22554566	Schizophrenia	MRI	Set Shifting	Wisconsin Card Sorting Task
164	184	22554566	Schizophrenia	MRI	Set Shifting	Wisconsin Card Sorting Task
164	185	22554566	Schizophrenia	MRI	Set Shifting	Wisconsin Card Sorting Task
165	186	25555505	Bipolar	MRI	Response Inhibition	Go/No-Go
166	187	11431233	Schizophrenia	MRI	Working Memory	N-back
167	188	11525339	Substance Use	MRI	Working Memory	N-back
168	189	25497222	Schizophrenia	MRI	Recognition Memory	Recognition
169	190	22585315	Substance Use	MRI	Recognition Memory	Recognition
170	191	18507885	Schizophrenia	MRI	Working Memory	N-back
171	192	21604958	Bipolar	MRI	Working Memory	N-back

172	193	25497296	Bipolar	MRI	Working Memory	N-back
172	194	25497296	Bipolar	MRI	Working Memory	N-back
172	195	25497296	Bipolar	MRI	Working Memory	N-back
173	196	11823264	Schizophrenia	PET	Performance Monitoring	Continuous Performance Task
173	197	11823264	Schizophrenia	PET	Performance Monitoring	Continuous Performance Task
174	198	24016726	Schizophrenia	MRI	Working Memory	N-back
175	199	9673996	Schizophrenia	PET	Set Shifting	Wisconsin Card Sorting Task
175	200	9673996	Schizophrenia	PET	Recognition Memory	Recognition
176	201	11431234	Schizophrenia	PET	Recognition Memory	Recognition
177	202	15169688	Schizophrenia	MRI	Recognition Memory	Recognition
178	203	16199830	Schizophrenia	MRI	Recognition Memory	Recognition
179	204	18155880	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
180	205	21907293	Schizophrenia	MRI	Recognition Memory	Recognition
181	206	19224116	Schizophrenia	MRI	Recognition Memory	Recognition
181	207	19224116	Schizophrenia	MRI	Recognition Memory	Recognition
182	208	24382711	Schizophrenia	MRI	Recognition Memory	Recognition
183	209	23637737	Anxiety	MRI	Set Shifting	Switch Task
183	210	23637737	Unipolar	MRI	Set Shifting	Switch Task
184	211	20417713	Substance Use	MRI	Response Inhibition	Go/No-Go
185	212	19500088	Bipolar	MRI	Working Memory	Delayed Match-to-sample
186	213	25066663	Unipolar	MRI	Working Memory	N-back
187	214	17511967	Anxiety	MRI	Response Inhibition	Go/No-Go
188	215	16837832	Bipolar	MRI	Conflict Monitoring	Stroop

189	216	20418447	Schizophrenia	MRI	Recognition Memory	Recognition
190	217	19643585	Schizophrenia	MRI	Response Inhibition	Hayling Sentence Completion Test
190	218	19643585	Schizophrenia	MRI	Working Memory	N-back
191	219	11595391	Schizophrenia	MRI	Response Inhibition	Go/No-Go
192	220	12732667	Schizophrenia	PET	Working Memory	N-back
193	221	15006650	Schizophrenia	MRI	Performance Monitoring	Continuous Performance Task
194	222	24332795	Schizophrenia	MRI	Working Memory	N-back
194	223	24332795	Schizophrenia	MRI	Working Memory	N-back
195	224	17097072	Anxiety	MRI	Other	Serial Reaction Time Task
196	225	17559877	Schizophrenia	MRI	Working Memory	N-back
197	226	17707869	Schizophrenia	MRI	Working Memory	Sternberg Working Memory Task
198	227	22137506	Substance Use	MRI	Conflict Monitoring	Stroop
199	228	16002029	Substance Use	MRI	Working Memory	Delayed Match-to-sample
200	229	10855761	Anxiety	PET	Performance Monitoring	Continuous Performance Task
201	230	23036083	Bipolar	MRI	Performance Monitoring	Continuous Performance Task
202	231	16224612	Schizophrenia	MRI	Verbal Fluency	Verbal Fluency
203	232	20166792	Bipolar	MRI	Response Inhibition	Go/No-Go
204	233	20401748	Substance Use	MRI	Working Memory	N-back
205	234	17136217	Schizophrenia	PET	Other	Reading
206	235	15173843	Bipolar	MRI	Performance Monitoring	Continuous Performance Task

207	236	16135630	Bipolar	MRI	Conflict Monitoring	Stroop
208	237	19190727	Bipolar	MRI	Response Inhibition	Go/No-Go
209	238	22475381	Schizophrenia	MRI	Working Memory	N-back
210	239	18004121	Schizophrenia	MRI	Working Memory	N-back
211	240	16199831	Schizophrenia	MRI	Working Memory	N-back
212	241	17074949	Schizophrenia	MRI	Working Memory	N-back
213	242	17274020	Substance Use	MRI	Response Selection	Modified Iowa Gambling Task
214	243	11236838	Substance Use	MRI	Working Memory	N-back
215	244	15597092	Substance Use	MRI	Working Memory	Recognition
216	245	17558500	Substance Use	MRI	Response Inhibition	Go/No-Go
217	246	18586109	Unipolar	MRI	Set Shifting	Probabilitistic Reversal Learning
218	247	15380297	Schizophrenia	MRI	Other	Semantic Decision Making
219	248	17765877	Substance Use	MRI	Working Memory	N-back
220	249	22631623	Bipolar	MRI	Response Inhibition	Go/No-Go
221	250	14754781	Schizophrenia	MRI	Performance Monitoring	Smooth Pursuit
222	251	19963356	Schizophrenia	MRI	Conflict Monitoring	Stroop
223	252	15753243	Anxiety	MRI	Response Selection	Tower of London
224	253	16045067	Anxiety	MRI	Conflict Monitoring	Stroop
225	254	24709020	Unipolar	MRI	Working Memory	Spatial Working Memory
225	255	24709020	Unipolar	MRI	Working Memory	Delayed Match-to-sample
226	256	18321870	Schizophrenia	MRI	Recognition Memory	Recognition

227	257	12729869	Schizophrenia	MRI	Working Memory	N-back
228	258	17197035	Unipolar	MRI	Working Memory	Delayed Match-to-sample
229	259	17363277	Schizophrenia	MRI	Working Memory	Delayed Match-to-sample
230	260	24948034	Unipolar	MRI	Other	Recall
231	261	12738340	Schizophrenia	MRI	Conflict Monitoring	Stroop
232	262	17188464	Schizophrenia	MRI	Conflict Monitoring	Stroop
233	263	24405183	Anxiety	SPECT	Set Shifting	Wisconsin Card Sorting Task
234	264	19346000	Unipolar	MRI	Recognition Memory	Recognition
235	265	21211946	Schizophrenia	MRI	Working Memory	Sternberg Working Memory Task
236	266	20731964	Schizophrenia	MRI	Set Shifting	Wisconsin Card Sorting Task
237	267	9665622	Schizophrenia	PET	Recognition Memory	Recognition
238	268	24478729	Schizophrenia	MRI	Working Memory	N-back
239	269	22355285	Schizophrenia	MRI	Recognition Memory	Recognition
240	270	19179050	Schizophrenia	MRI	Response Selection	Choice Reaction Time Task
241	271	18174505	Anxiety	MRI	Conflict Monitoring	Stroop
241	272	18174505	Anxiety	MRI	Set Shifting	Switch Task
241	273	18174505	Anxiety	MRI	Response Inhibition	Go/No-Go
242	274	12151286	Schizophrenia	MRI	Working Memory	N-back
243	275	24491458	Substance Use	MRI	Response Selection	Modified Iowa Gambling Task
244	276	19218875	Unipolar	MRI	Response Inhibition	Stop Signal Task
245	277	15804721	Schizophrenia	MRI	Working Memory	N-back

246	278	18519527	Schizophrenia	MRI	Performance Monitoring	Continuous Performance Task
247	279	24895735	Bipolar	MRI	Verbal Fluency	Verbal Fluency
248	280	17679639	Anxiety	MRI	Conflict Monitoring	Multi-Source Interference Task
249	281	17245325	Substance Use	MRI	Conflict Monitoring	Multi-Source Interference Task
250	282	16945506	Schizophrenia	MRI	Other	Serial Reaction Time Task
251	283	20702070	Schizophrenia	MRI	Recognition Memory	Recognition

Ref=Reference number; Schizophrenia=schizophrenia, schizoaffective, schizophreniform, and delusional disorders; Bipolar=bipolar disorders; Unipolar= major depression, dysthymia; Anxiety=obsessive compulsive disorder, posttraumatic stress disorder, social anxiety disorder, Substance Use=mixed substance abuse and/or dependence).

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TABLE S2. Proportion of studies within each diagnostic group corresponding to each task domain

Diagnostic Group (# of Studies by Diagnosis)	*Total # of Studies (N=283)*	*Schizophrenia Spectrum Disorders (N=139)*	*Bipolar Disorders (N=50)*	*Unipolar Depressive Disorders (N=27)*	*Anxiety Disorders (N=32)*	*Substance Use Disorders (N=35)*
Domain						
Performance Monitoring	11	0.05	0.04	0.04	0.03	0
Response Selection	12	0.04	0.02	0.04	0.03	0.11
Set Shifting	15	0.04	0.02	0.11	0.16	0
Verbal Fluency	17	0.06	0.14	0.04	0	0
Other	18	0.09	0	0	0.03	0.03
Conflict Monitoring	31	0.07	0.10	0	0.28	0.20
Recognition Memory	37	0.19	0.10	0.07	0.03	0.06
Response Inhibition	42	0.06	0.26	0.22	0.22	0.23
Working Memory	100	0.39	0.32	0.37	0.22	0.37

The Other domain consisted of a diverse set of low frequency studies that did not cohere into a particular cognitive control domain (i.e., recall memory n=9; implicit learning n=5; decision making n=3; reading n=1).

TABLE S3. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic pooled patient hyper- and hypoactivation (i.e., aberrant activation) during functional neuroimaging of cognitive control tasks.

Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
dorsal anterior cingulate	354	4.39	-2	36	14
anterior mid-cingulate cortex/pre-supplementary motor area	355	4.30	4	22	32
right insula (extending to ventrolateral prefrontal cortex)	679	5.42	34	28	-10
right intraparietal sulcus	531	4.67	38	-44	46
left prefrontal cortex extending from mid-dorsolateral prefrontal to premotor cortex	1049	4.48	-48	22	26

TABLE S4. Percent contribution to clusters of convergence for whole-brain pooled aberrant activation meta-analytic contrasts by experiment sample and design characteristics.

Experiment sample/ design characteristics	Cluster of convergence				
	Right anterior insula/ ventrolateral prefrontal cortex	Left frontal cortex	Dorsal anterior cingulate	Anterior mid-cingulate/ pre-SMA	Right Intra-parietal sulcus/ parietal cortex
Contrast Direction					
Control > Patient	79.47	61.54	76.98	56.08	60.35
Patient > Control	20.53	38.46	23.02	43.92	39.65
Disorder Class					
Non-psychotic	52.07	37.18	48.69	34.52	59.61
Psychotic	47.93	62.82	51.31	65.48	40.39
Diagnosis					
Schizophrenia	47.93	62.82	51.31	65.48	40.39
Substance Use	16.88	9.54	14.84	8.76	22.06
Anxiety	16.06	10.38	16.53	10.02	7.33
Bipolar Disorder	15.06	6.26	2.82	10.87	17.86
Major Depression	4.07	11.0	14.5	4.87	12.36
Domain					
Working Memory	34.69	45.08	26.98	27.64	36.77
Recognition	16.09	13.99	13.85	18.92	11.24
Response Inhibition	15.84	6.98	17.69	2.75	18.69
Set Shifting	9.74	4.65	14.15	7.51	7.62
Conflict Monitoring	7.22	7.82	15.88	12.01	11.56
Response Selection	4.97	5.75	3.33	4.5	10.44
Performance Monitoring	3.65	0	0.22	5.03	3.6
Verbal Fluency	3.35	7.76	7.9	15.08	0.03
Other	4.46	7.96	0	6.57	0.06
Age Group					
Child/adolescent	12.99	6.72	18.48	1.2	10.36
Adult	86.09	92.89	77.0	98.79	85.05
Older adult	0.91	0.39	4.51	0.01	4.59
Current Psychotropic Medication					
Yes	69.82	66.18	57.72	73.45	57.81
No	14.63	25.78	35.54	12.09	28.98
Not reported	15.55	8.04	6.74	14.47	13.21
Behavioral Performance					
Worse than Control Group	47.52	42.65	28.97	32.08	44.63
Equivalent to Control Group	52.37	57.35	71.03	67.67	55.91
Not reported	0.11	0	0	0.25	0.05
Imaging Modality					
Functional MRI	95.77	84.69	92.15	93.55	9142
PET	4.23	14.86	7.85	6.22	8.57

ASL	0	0.46	0	0.22	0.01
SPECT	0	0	0	0	0
Tasks					
Antisaccade	0	0	0	0	0
Beads in the bottle	0.11	0	0	0.15	2.36
Choice reaction time	0	3.23	0	4.04	0
Continuous performance	3.65	0.07	0.22	5.03	3.6
Delay discounting	0	2.07	0	0.02	1.95
Delayed match-to-sample	7.15	13.66	5.21	0.09	9.55
Finger tapping	0	0.57	0	0	0
Flanker	0	0	0	1.52	0
Go/no-go	14.2	4.55	8.7	2.75	14.73
Hayling sentence completion	0.06	0	0	0	0
Match stimuli	0	0	0	0	0
Mental arithmetic	0	0	0	4.15	1.11
Modified Iowa gambling task	4.66	0	3.21	0.05	6.05
Multi-source interference	0.31	0.92	8.68	0.1	5.38
N-back	23.5	21.04	9.23	23.29	19.82
Probabilitistic reversal learning	0	0.08	0	0	0
Reading	0	0.05	0	1.31	0
Recall	0.12	2.47	0	5.12	0.06
Recognition	16.13	12.32	13.85	14.77	11.24
Semantic decision making	1.69	2.92	0.05	0.78	0.03
Serial reaction time	2.65	1.95	0	0.07	0
Set shifting	2.65	0	2.4	0.02	0.01
Simon task	0	0	0	0	0
Smooth pursuit	0	0	0	0	0
Source memory	0.02	1.67	0	0	0
Spatial working memory	0	4.95	6.33	0	0
Sternberg working memory	3.98	5.44	1.2	0.01	6
Stop signal task	1.64	2.36	8.98	0	3.96
Stroop	6.91	6.9	12.16	9.78	6.45
Switch task	6.06	0.04	0	3.62	3.95
Tower of London	0.19	0.46	0.13	0.23	0.08
Transitive inference	0	0	0	4.14	0
Two-choice prediction task	0	0	0	0	0
Verbal fluency	3.28	7.76	7.9	15.08	0.03
Virtual Morris water task	0	0	0	0	0
Wisconsin card sorting	1.02	4.53	11.75	3.86	3.66

TABLE S5. Coordinates of clusters derived from a conjunction of the transdiagnostic pooled patient hyper- and hypoactivation (i.e., aberrant activation) and the multiple-demand network identified from meta-analyses of healthy participants (25).

Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
left inferior frontal gyrus/junction	76	2.02	-44	12	28
pre- supplementary motor area	170	2.16	4	22	40
right anterior insula/ventrolateral prefrontal cortex	79	2.16	36	26	-8
right intraparietal sulcus	48	2.05	40	-42	46

TABLE S6. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Patient					
dorsal anterior cingulate	380	4.98	-2	38	14
right insula (extending to ventrolateral prefrontal cortex)	586	6.09	42	28	-12
left insula (extending to ventrolateral prefrontal cortex)	307	4.37	-32	20	-10
right intraparietal sulcus	336	4.98	38	-56	48
left prefrontal cortex extending from mid-dorsolateral prefrontal to premotor cortex	608	4.17	-48	24	26
Patient > Control					
anterior mid-cingulate cortex/pre-supplementary motor area	216	3.91	0	10	50

TABLE S7. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks excluding the experiments of arterial spin labeling and single-photon emission computerized tomography

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Patient					
dorsal anterior cingulate	565	5.0	-2	38	14
right insula (extending to ventrolateral prefrontal cortex)	592	6.10	42	28	-12
left insula (extending to ventrolateral prefrontal cortex)	310	4.38	-32	20	-10
right intraparietal sulcus	343	5.0	38	-56	48
left prefrontal cortex extending from mid-dorsolateral prefrontal to premotor cortex	622	4.17	-48	24	26
Patient > Control					
anterior mid-cingulate cortex/pre-supplementary motor area	219	3.92	0	10	50
right intraparietal sulcus	216	4.12	24	-60	56

TABLE S8. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks excluding tasks that did not cohere in a domain

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Patient					
dorsal anterior cingulate	444	5.08	-2	38	14
right insula (extending to ventrolateral prefrontal cortex)	597	6.05	42	28	-12
left insula (extending to ventrolateral prefrontal cortex)	263	4.46	-32	20	-10
right intraparietal sulcus	367	5.08	38	-56	48
left prefrontal cortex extending from mid-dorsolateral prefrontal to premotor cortex	573	3.93	-44	18	38
Patient > Control					
right intraparietal sulcus	236	4.17	24	-60	56

TABLE S9. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks excluding studies of children and older adults

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Patient					
dorsal anterior cingulate	302	4.32	-4	38	14
right insula (extending to ventrolateral prefrontal cortex)	554	5.56	44	28	-12
right intraparietal sulcus	255	5.11	38	-56	48
left prefrontal cortex	585	4.22	-48	24	26
Patient > Control					
anterior mid-cingulate cortex/pre-supplementary motor area	211	3.67	-2	12	36

TABLE S10. Percent contribution to clusters of convergence for whole-brain patient hypo- and hyper-activation contrasts by experiment sample and design characteristics.

Experiment sample/ design characteristics	Cluster of convergence: Right anterior insula/ ventrolateral prefrontal cortex	Left anterior insula/ ventro-lateral prefrontal cortex	Left frontal cortex	Dorsal anterior cingulate	Right intraparietal sulcus/parietal cortex	Anterior mid-cingulate/ pre-SMA
Contrast Direction						
Control > Patient	100	100	100	100	100	0
Patient > Control	0	0	0	0	0	100
Disorder Class						
Non-psychotic	49.34	51.25	29.31	47.06	47.87	55.02
Psychotic	50.66	48.75	70.69	52.94	52.13	44.98
Diagnosis						
Schizophrenia	50.66	48.75	70.69	52.94	52.13	44.98
Substance Use	5.74	7.86	13.05	12.26	8.95	8.32
Anxiety	20.41	4.77	3.56	16.81	9.5	13.41
Bipolar Disorder	18	20.87	5.68	4.54	20.62	10.63
Major Depression	5.19	17.75	7.01	13.45	8.8	22.65
Domain						
Working Memory	30.45	56.4	36.84	26.14	26.59	33
Recognition	15.54	14.45	17.73	18.7	19.39	13.69
Response Inhibition	24.74	10.47	8.18	15.68	15.6	8.33
Set Shifting	11.28	0.3	4.62	9.28	12.89	1.21
Conflict Monitoring	8.04	5.14	11.94	16.9	11.94	12.31
Response Selection	0	4.3	3.44	0.13	9.26	0.46
Performance Monitoring	1.64	0	0	0.53	4.2	0
Verbal Fluency	4.04	2.07	10.06	12.64	0	28.8
Other	4.28	6.86	7.19	0	0.13	2.21
Age Group						
Child/adolescent	12.9	19.65	7.49	15.64	4.26	8.32

Adult	87.1	80.32	92.1	84.36	92.4	91.68
Older adult	0	0.03	0.41	0	3.35	0
Current Psychotropic Medication						
Yes	84.36	52.26	52.2	61.57	70	82.87
No	5.19	29.23	36.61	31.61	21.05	9.52
Not reported	10.44	18.51	11.19	6.82	8.95	7.61
Behavioral Performance						
Worse than Control Group	50.49	39.81	41.08	16.37	47.89	21.19
Equivalent to Control Group	49.51	60.19	58.92	83.63	51.98	77.97
Not reported	0	0	0	0	0.13	0.84
Imaging Modality						
Functional MRI	94.86	93.15	83.76	88.22	86.79	99.89
PET	5.14	6.85	15.82	11.78	13.2	0.11
ASL	0	0	0.42	0	0	0
SPECT	0	0	0	0	0	0
Tasks						
Antisaccade	0	0	0	0	0	0
Beads in the bottle	0	0	0	0	6.38	0
Choice reaction time	0	0	0	0	0	0.46
Continuous performance	1.64	0	0	0.53	4.2	0
Delay discounting	0	0	3.02	0	2.83	0
Delayed match-to-sample	5.77	24.05	8.26	0.27	0.53	0
Finger tapping	0	0	0	0	0	0
Flanker	0	0	0	0	0	12.31
Go/no-go	21.96	10.47	4.84	10.07	7.84	8.33
Hayling sentence completion	0	0	0	0	0	0
Match stimuli	0	0	0	0	0	0
Mental arithmetic	0	0	0	0	0	0.2
Modified Iowa gambling task	0	0	0	0.07	0.05	0
Multi-source interference	0	0	0	11.96	0	0.21
N-back	19.86	14.6	17.06	7.69	26.05	32.59
Probabilitistic reversal learning	0	0	0.03	0	0	0

Reading	0	0	0.07	0	0	0
Recall	0.01	6.79	3.78	0	0.13	0.84
Recognition	15.54	8.77	14.82	18.7	19.39	13.69
Semantic decision making	0	0	0	0.04	0	1.37
Serial reaction time	4.27	0.08	3.34	0	0	0
Set shifting	2.98	0.3	0	2.53	0	0
Simon task	0	0	0	0	0	0
Smooth pursuit	0	0	0	0	0	0
Source memory	0	5.68	2.91	0	0	0
Spatial working memory	0	17.75	6.99	8.99	0	0
Sternberg working memory	4.81	0	4.53	2.44	0	0
Stop signal task	2.78	0	3.33	5.62	7.76	0
Stroop	8.04	5.14	11.94	11.64	11.94	0
Switch task	8.3	0	0.2	0	6.22	1.1
Tower of London	0	4.3	0.42	0.06	0	0
Transitive inference	0	0	0	0	0	0
Two-choice prediction task	0	0	0	0	0	0
Verbal fluency	4.04	2.07	10.06	12.64	0	28.8
Virtual Morris water task	0	0	0	0	0	0
Wisconsin card sorting	0	0	4.39	6.76	6.67	0.11

TABLE S11. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic pooled patient hyper- and hypoactivation (i.e., aberrant activation) during functional neuroimaging of cognitive control tasks separately for studies of children and adults.

Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Adult Studies					
anterior mid-cingulate /pre-supplementary motor area	403	4.46	4	22	32
right insula (extending to ventrolateral prefrontal cortex)	599	4.85	44	28	-12
right intraparietal sulcus	272	4.42	38	-56	48
left prefrontal cortex extending from mid-dorsolateral prefrontal to premotor cortex	1028	4.63	-48	22	26
Child Studies					
right ventrolateral prefrontal cortex	180	4.49	32	30	-10

TABLE S12. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks separately for medicated and unmedicated patients.

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Patient No Medication					
dorsal anterior cingulate	380	4.98	-2	38	14
right insula (extending to ventrolateral prefrontal cortex)	586	6.08	42	28	-12
left insula (extending to ventrolateral prefrontal cortex)	307	4.37	-32	20	-10
right intraparietal sulcus	336	4.98	38	-56	48
left prefrontal cortex	608	4.17	-48	24	26
Control > Patient Medication					
dorsal anterior cingulate	213	4.14	-4	38	12
right insula (extending to ventrolateral prefrontal cortex)	593	6.0	42	28	-12
left prefrontal cortex	232	3.57	-44	18	36
left intraparietal sulcus	212	5.6	-48	-42	46
Patient > Control Medication					
anterior mid-cingulate cortex/pre-supplementary motor area	286	3.94	0	10	48

Unmedicated patient experiments did not show any convergent whole-brain significant hyperactivations.

TABLE S13. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of transdiagnostic patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks separately for patients samples who performed no differently or worse than control groups.

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Patient					
No performance difference					
dorsal anterior cingulate	653	4.96	-4	38	12
right insula (extending to ventrolateral prefrontal cortex)	231	5.30	36	28	-10
left prefrontal cortex	661	4.62	-48	24	24
Control > Patient					
Worse Performance					
anterior mid-cingulate cortex/pre-supplementary motor area	228	3.83	6	30	50
right insula (extending to ventrolateral prefrontal cortex)	342	5.39	44	28	-12
left prefrontal cortex	261	4.10	-42	30	30
Patient > Control					
No performance difference					
ventromedial prefrontal cortex	224	4.74	-2	40	-8
Patient > Control Medication					
Worse Performance					
anterior mid-cingulate cortex/pre-supplementary motor area	247	3.78	0	10	52

TABLE S14. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of pooled activation during functional neuroimaging of cognitive control tasks separately for psychotic and non-psychotic samples.

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Psychotic Pooled Activation					
left prefrontal cortex	836	4.90	-48	22	26
anterior mid-cingulate cortex/pre-supplementary motor area	364	4.32	4	24	32
Non-Psychotic Pooled Activation					
right insula (extending to ventrolateral prefrontal cortex)	355	4.75	34	32	-12
right intraparietal sulcus	415	4.90	26	-58	54
Psychotic Pooled Activation > Non-Psychotic Pooled Activation					
left insula	29	2.79	-36	12	12
left anterior middle frontal gyrus	123	2.92	-40	46	24
left posterior middle frontal gyrus	312	3.18	-50	8	46
anterior mid-cingulate cortex	75	2.55	4	28	32
mid-cingulate cortex/pre-supplementary motor area	20	2.25	-8	12	40
Non-Psychotic Pooled Activation > Psychotic Pooled Activation					
right insula (extending to ventrolateral prefrontal cortex)	136	2.69	32	36	-14
right intraparietal sulcus	114	3.11	30	-58	58

TABLE S15. Percent contribution to clusters of convergence for whole-brain non-psychotic and psychotic pooled aberrant activation contrasts by experiment sample and design characteristics.

	Cluster of convergence			
Experiment sample/ design characteristics	Right anterior insula/ ventrolateral prefrontal cortex	Right intraparietal sulcus/ parietal cortex	Left frontal cortex	Anterior mid-cingulate/ pre-SMA
Contrast Direction				
Control > Patient	69.72	49.17	68.16	58.49
Patient > Control	30.28	50.83	31.84	41.51
Disorder Class				
Non-psychotic	100	100	0	0
Psychotic	0	0	100	100
Diagnosis				
Schizophrenia	0	0	100	100
Substance Use	30.6	43.46	0	0
Anxiety	34.27	10	0	0
Bipolar Disorder	26.68	24.36	0	0
Major Depression	8.45	22.18	0	0
Domain				
Working Memory	15.27	35.83	39	40.28
Recognition	8.91	3.33	21.02	9.03
Response Inhibition	23.25	21.35	0	0.32
Set Shifting	23.54	5.27	6.99	6.11
Conflict Monitoring	10.8	17.57	6.34	11.85
Response Selection	10.17	12.31	9.51	8.98
Performance Monitoring	7.74	4.33	0	6.33
Verbal Fluency	0.31	0	7.98	9.53
Other	0	0	9.16	7.56
Age Group				
Child/adolescent	29.93	17.64	0.66	0.57
Adult	70.07	72.47	99.34	99.43
Older adult	0	9.9	0	0
Current Psychotropic Medication				
Yes	54.58	36.46	81.96	84.46
No	22.18	42.92	15.77	9.04
Not reported	23.23	20.62	2.27	6.5
Behavioral Performance				
Worse than Control Group	27.35	21.18	59.44	38.92
Equivalent to Control Group	72.65	78.82	40.56	61.05
Not reported	0	0	0	0.02
Imaging Modality				
Functional MRI	94.51	95.74	74.61	91.07

PET	5.39	4.26	24.85	7.59
ASL	0	0	0.54	1.35
SPECT	0.1	0	0	0
Tasks				
Antisaccade	0	0	0	0
Beads in the bottle	0	0	0	2.4
Choice reaction time	0	0	5.93	5.23
Continuous performance	7.74	4.33	0	6.33
Delay discounting	0	0	3.04	0
Delayed match-to-sample	4.88	14.19	8.92	0.72
Finger tapping	0	0	0.88	0
Flanker	0	0	0	0
Go/no-go	20.46	14.74	0	0.32
Hayling sentence completion	0.31	0	0	0
Match stimuli	0	0	0	0
Mental arithmetic	0	0	0	6.27
Modified Iowa gambling task	9.97	12.25	0	0
Multi-source interference	2.71	9.12	0	0.65
N-back	9.82	13.89	20.9	32.64
Probabilitistic reversal learning	0	0	0	0
Reading	0	0	0.86	2.63
Recall	0	0	3.75	4.8
Recognition	8.91	3.33	18.75	9.03
Semantic decision making	0	0	3.68	0.41
Serial reaction time	0	0	0	0.13
Set shifting	8.75	0	0	0
Simon task	0	0	0	0
Smooth pursuit	0	0	0	0
Source memory	0	0	2.27	0
Spatial working memory	0	0	0	0
Sternberg working memory	0.57	7.75	9.18	0
Stop signal task	2.79	6.62	0	0
Stroop	8.09	8.45	6.34	11.44
Switch task	14.68	5.27	0	0
Tower of London	0.2	0.06	0.54	1.35
Transitive inference	0	0	0	0
Two-choice prediction task	0	0	0	0
Verbal fluency	0	0	7.98	9.53
Virtual Morris water task	0	0	0	0
Wisconsin card sorting	0.1	0	6.99	6.11

TABLE S16. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of patient hypoactivation during functional neuroimaging of cognitive control tasks separately for psychotic and non-psychotic samples.

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Psychotic Control > Patient					
right insula (extending to ventrolateral prefrontal cortex)	309	5.20	44	28	-12
left prefrontal cortex	686	4.42	-48	24	26
Non-psychotic Patient > Control					
right insula (extending to ventrolateral prefrontal cortex)	363	4.87	38	30	-12
Conjunction Non-psychotic Control > Patient & Psychotic Control > Patient					
right insula (extending to ventrolateral prefrontal cortex)	56	4.23	40	28	-12
Psychotic Control > Patient > Non-Psychotic Control > Patient					
anterior middle frontal gyrus	57	3.0	-40	42	26
posterior middle frontal gyrus	353	3.22	-38	10	14
Non-psychotic Control > Patient > Psychotic Control > Patient					
right ventrolateral prefrontal cortex	56	2.46	34	34	-16

Patient hyperactivation experiments did not show any convergent whole-brain significant hyperactivations separately for psychotic and non-psychotic disorder samples.

TABLE S17. Percent contribution to clusters of convergence for whole-brain non-psychotic and psychotic patient hypo- and hyper-activation activation contrasts by experiment sample and design characteristics.

	Cluster of convergence		
Experiment sample/ design characteristics	Right anterior insula/ ventrolateral prefrontal cortex	Right anterior insula/ ventrolateral prefrontal cortex	Left frontal cortex
Contrast Direction			
Control > Patient	100	100	100
Patient > Control	0	0	0
Disorder Class			
Non-psychotic	100	0	0
Psychotic	0	100	100
Diagnosis			
Schizophrenia	0	100	100
Substance Use	11.61	0	0
Anxiety	43.74	0	0
Bipolar Disorder	32.76	0	0
Major Depression	11.89	0	0
Domain			
Working Memory	10.49	49.34	40.12
Recognition	9.84	23.66	20.38
Response Inhibition	39.95	6.03	0
Set Shifting	25.33	0	7.79
Conflict Monitoring	12.19	0.41	8.85
Response Selection	0	0	5.46
Performance Monitoring	2.19	1.3	0
Verbal Fluency	0	8.31	10.93
Other	0	10.95	6.48
Age Group			
Child/adolescent	28.42	0	0.3
Adult	71.58	100	99.7
Older adult	0	0	0
Current Psychotropic Medication			
Yes	76.3	97.92	73.87
No	9.9	0.16	21.7
Not reported	13.8	1.92	4.43
Behavioral Performance			
Worse than Control Group	35.11	59.78	53.71
Equivalent to Control Group	64.89	40.22	46.29
Not reported	0	0	0
Imaging Modality			

Functional MRI	97.81	90.63	74.38
PET	2.19	9.37	24.36
ASL	0	0	1.26
SPECT	0	0	0
Tasks			
Antisaccade	0	0	0
Beads in the bottle	0	0	0
Choice reaction time	0	0	0
Continuous performance	2.19	1.3	0
Delay discounting	0	0	4.19
Delayed match-to-sample	3.42	11.05	11.7
Finger tapping	0	0	0
Flanker	0	0	0
Go/no-go	36.99	6.03	0
Hayling sentence completion	0	0	0
Match stimuli	0	0	0
Mental arithmetic	0	0	0
Modified Iowa gambling task	0	0	0
Multi-source interference	0	0	0
N-back	1.68	38.3	21.59
Probabilitistic reversal learning	0	0	0
Reading	0	0	2.37
Recall	0	0.01	4.11
Recognition	9.85	23.66	16
Semantic decision making	0	0	0
Serial reaction time	0	10.94	0
Set shifting	7.99	0	0
Simon task	0	0	0
Smooth pursuit	0	0	0
Source memory	0	0	4.38
Spatial working memory	0	0	0
Sternberg working memory	5.38	0	6.82
Stop signal task	2.96	0	0
Stroop	12.19	0.41	8.85
Switch task	17.34	0	0
Tower of London	0	0	1.26
Transitive inference	0	0	0
Two-choice prediction task	0	0	0
Verbal fluency	0	8.31	10.93
Virtual Morris water task	0	0	0
Wisconsin card sorting	0	0	7.79

No significant clusters were observed in the contrasts of patient > control for either psychotic or non-psychotic disorder experiments.

TABLE S18. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks separately by disorder classes

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Schizophrenia Patient					
right insula (extending to ventrolateral prefrontal cortex)	309	5.20	44	28	-12
left prefrontal cortex	686	4.42	-48	24	26
Control > Substance Use Disorder Patient					
right insula (extending to ventrolateral prefrontal cortex)	177	4.26	30	-70	48

Patient hyperactivation experiments did not show any convergent whole-brain significant hyperactivations separately for disorder classes. Anxiety, unipolar and bipolar depressive disorder classes showed no convergent whole-brain significant hypoactivations.

TABLE S19. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks separately by domain

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Patient: Inhibition					
right insula (extending to ventrolateral prefrontal cortex)	500	4.9	52	30	-10
Control > Patient: Working Memory					
right cerebellum	250	4.0	4	-46	-20
right insula (extending to ventrolateral prefrontal cortex)	252	4.52	-34	20	-10
Patient > Control: Working Memory					
ventromedial prefrontal cortex	287	4.89	-2	40	-8

Patient hyperactivation experiments did not show any convergent whole-brain significant hyperactivations separately for disorder classes. Anxiety, unipolar and bipolar depressive disorder classes showed no convergent whole-brain significant hypoactivations.

TABLE S20. Peak coordinates of clusters derived from Activation Likelihood Estimation (ALE) meta-analysis of patient hyper- and hypoactivation during functional neuroimaging of cognitive control tasks separately by domain and disorder class

Contrast/ Region	Cluster Size (voxels)	Peak Intensity (Z)	MNI Coordinates X	Y	Z
Control > Schizophrenia Patient: Working Memory					
right insula (extending to ventrolateral prefrontal cortex)	217	4.15	34	26	-12