

The Multifaceted Role of Ventromedial Prefrontal Cortex in Emotion, Decision-making, Social Cognition, and Psychopathology

Supplementary Information

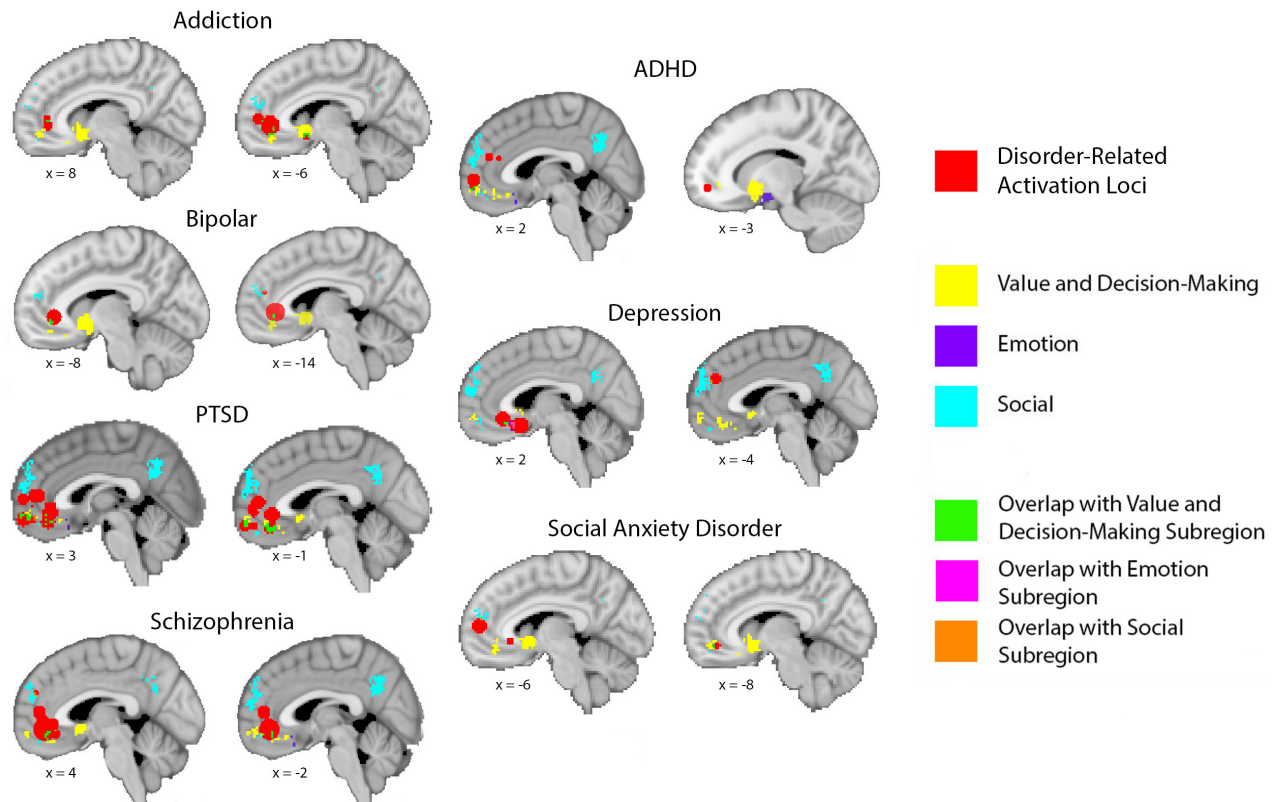
Supplementary Figure S1

Supplementary Methods

Supplementary Table S1

Supplementary References

SUPPLEMENTARY FIGURE



Supplementary Figure S1. Association between vmPFC subregions and psychiatric disorders. To define activation loci associated with each disorder, we used the results of previously published meta-analyses of fMRI findings related to each disorder to construct spheres representing the approximate volume of reported clusters at their respective peak coordinates (for details see **Supplementary Methods** and **Supplementary Table S1**). We plotted these disorder-related activation loci (in red) along with the domain-related loci (in separate colors; corresponding to the bottom row of **Figure 1**). Overlap between the disorder-related loci and domain-related loci is shown in green (for value and decision-making), pink (for emotion), and orange (for social). Using this approach, we found relatively large regions of overlap in some cases (*e.g.*, >30 voxels for the value and decision-making subregion and activation loci for addiction, depression, and schizophrenia, respectively), but fairly small regions of overlap in other cases (*e.g.*, <5 voxels for the social subregion and activation loci for bipolar, depression, and social anxiety disorder, respectively).

SUPPLEMENTARY METHODS

Meta-analyses of fMRI data for **Figure 2** and **Supplementary Figure S1** were obtained by searching the PubMed database. The search terms included the combination of terms for each disorder (e.g., “depression”, “PTSD”, “addiction”, “social anxiety disorder”, etc.), “fMRI”, and “meta-analysis”. The search was restricted to meta-analyses of event-related fMRI studies of adults that were listed in the database on or after January 1st, 2006. For **Supplementary Figure S1**, spheres were created representing the approximate volume of reported significant clusters at their respective peak coordinates. This figure only includes loci in PFC ventral to $z=30$, anterior to $y=8$, and medial to $-18 < x < 18$. These loci were obtained from 22 separate meta-analyses (**Supplementary Table S1**).

Our search included the following disorders: addiction, PTSD, major depressive disorder, bipolar disorder, schizophrenia, social anxiety disorder, ADHD, OCD, specific phobia, generalized anxiety disorder, panic disorder, and eating disorders. Our search returned five meta-analyses on addiction. We excluded one that focused specifically on visual cortex and one that focused specifically on internet gambling disorder. The remaining three articles all included vmPFC clusters. Our search returned eight meta-analyses on PTSD. We excluded one for which we were not able to obtain the full text. Of the remaining seven articles, six included vmPFC clusters. Our search returned eight meta-analyses on depression. We excluded two that did not report coordinates and one that focused solely on reward processing. Of the remaining five articles, four included vmPFC clusters. Our search returned six meta-analyses on bipolar disorder, two of which included vmPFC clusters. Our search returned ten meta-analyses on schizophrenia. We excluded one for which we were not able to obtain the full text, one that focused specifically on ventral striatum, and one that focused specifically on corpus callosum. Of the remaining seven articles, five included vmPFC clusters. Our search returned four meta-analyses on social anxiety disorder, three of which included vmPFC clusters. Our search returned six meta-analyses on ADHD. We excluded one that did not report

coordinates. Of the remaining five articles, two included vmPFC clusters. Our search returned two meta-analyses on specific phobia, neither of which included a vmPFC cluster. Our search returned one meta-analysis on OCD, which included a vmPFC cluster. Our search returned one meta-analysis on anorexia, which did not include a vmPFC cluster. Our search returned zero meta-analyses for generalized anxiety disorder or panic disorder. Hence, the majority of eligible meta-analyses of psychiatric disorders included vmPFC clusters (3/3 for addiction, 6/7 for PTSD, 4/5 for depression, 2/6 for bipolar, 5/7 for schizophrenia, 3/4 for social anxiety disorder, 2/5 for ADHD, 1/1 for OCD, and 0/1 for anorexia; total of 26/39 or 67% across disorders).

SUPPLEMENTARY TABLE

Supplementary Table S1. Meta-analyses yielding disorder-related fMRI activation loci for Figure 2 and Supplementary Figure S1.

Authors	Year	Title	Disorder	Coords			Size
				x	y	z	
Engelmann et al. (1)	2012	Neural substrates of smoking cue reactivity: A meta-analysis of fMRI Studies	Addiction	-1	41	0	6016 mm ³
Engelmann et al.			Addiction	-15	52	29	1096 mm ³
Schacht et al. (2)	2013	Functional neuroimaging studies of alcohol cue reactivity: A quantitative meta-analysis and systematic review	Addiction	-2	8	-10	2176 mm ³
Schacht et al.			Addiction	-2	52	6	872 mm ³
Luijten et al. (3)	2017	Disruption of Reward Processing in Addiction: An Image-Based Meta-analysis of Functional Magnetic Resonance Imaging Studies	Addiction	12	42	6	NA
Dickstein et al. (4)	2006	The neural correlates of attention deficit hyperactivity disorder: an ALE meta-analysis	ADHD	0	59	-7	17 voxels
Dickstein et al.	2006		ADHD	-14	51	-7	16 voxels
Dickstein et al.	2006		ADHD	6	35	19	25 voxels
McCarthy et al. (5)	2014	Identifying a consistent pattern of neural function in attention deficit hyperactivity disorder: a meta-analysis	ADHD	4	44	20	25 voxels
McCarthy et al.	2014		ADHD	2	58	0	88 voxels
Wegbreit et al. (6)	2014	Developmental Meta-Analysis of the Functional Neural Correlates of Bipolar Disorder	Bipolar	-2	36	0	1208 mm ³
Chen et al. (7)	2011	A quantitative meta-analysis of fMRI studies in bipolar disorder	Bipolar	-2	46	18	208 mm ³
Chen et al.	2011		Bipolar	-18	40	-6	272 mm ³
Groenwold et al. (8)	2013	Emotional valence modulates brain functional abnormalities in depression: Evidence from a meta-analysis of fMRI studies	Depression	4	22	-14	4 voxels

Authors	Year	Title	Disorder	Coords			Size
				x	y	z	
Palmer et al. (9)	2014	A meta-analysis of changes in brain activity in clinical depression	Depression	6	14	-14	1928 mm ³
Palmer et al.			Depression	14	8	-14	1928 mm ³
Graham et al. (10)	2013	Meta-analytic evidence for neuroimaging models of depression: State or trait?	Depression	-4	44	28	224 mm ³
Graham et al.			Depression	8	30	-8	1920 mm ³
Graham et al.			Depression	10	46	-6	464 mm ³
Sacher et al. (11)	2012	Mapping the depressed brain: a meta-analysis of structural and functional alterations in major depressive disorder.	Depression	8	35	-4	80 mm ³
Sacher et al.			Depression	12	20	-4	80 mm ³
Boccia et al. (12)	2016	Different neural modifications underpin PTSD after different traumatic events: an fMRI meta-analytic study	PTSD	-2	36	-2	704 mm ³
Boccia et al.			PTSD	6	38	-6	704 mm ³
Boccia et al.			PTSD	-6	54	6	1360 mm ³
Boccia et al.			PTSD	4	60	6	1360 mm ³
Hayes et al. (13)	2012	Quantitative meta-analysis of neural activity in posttraumatic stress disorder	PTSD	3	36	-6	1168 mm ³
Hayes et al.			PTSD	16	21	-12	440 mm ³
Hayes et al.			PTSD	3	36	-7	864 mm ³
Etkin and Wager (14)	2007	Functional Neuroimaging of Anxiety: A Meta-Analysis of Emotional Processing in PTSD, Social Anxiety Disorder, and	PTSD	2	38	-14	991 voxels
Etkin and Wager			PTSD	-14	20	-12	33 voxels
Etkin and Wager			PTSD	-12	50	20	245 voxels

Authors	Year	Title	Disorder	Coords			Size
				x	y	z	
Etkin and Wager			PTSD	18	52	22	43 voxels
Etkin and Wager			PTSD	12	46	22	23 voxels
Sartory et al. (15)	2013	In Search of the Trauma Memory: A Meta-Analysis of Functional Neuroimaging Studies of Symptom Provocation in Posttraumatic Stress Disorder (PTSD)	PTSD	-6	54	22	282 voxels
Sartory et al.			PTSD	-12	48	-4	133 voxels
Simmons and Matthews (16)	2012	Neural circuitry of PTSD with or without mild traumatic brain injury: A meta-analysis	PTSD	1	48	9	1424 mm ³
Stark et al. (17)	2015	Post-traumatic stress influences the brain even in the absence of symptoms: A systematic, quantitative meta-analysis of neuroimaging studies	PTSD	-2	52	0	3488 mm ³
Stark et al.			PTSD	2	60	-12	1112 mm ³
Stark et al.			PTSD	0	52	-12	1112 mm ³
Stark et al.			PTSD	-2	52	0	3248 mm ³
Bruhl et al. (18)	2014	Neuroimaging in Social Anxiety Disorder – a meta-analytic review resulting in a new neurofunctional model	SAD	-6	54	10	1288 mm ³
Bruhl et al.			SAD	-16	60	15	232 mm ³
Gentili et al. (19)	2016	Beyond emotions: A meta-analysis of neural response within face processing system in social anxiety	SAD	7	43	-8	96 mm ³
Gentili et al.			SAD	-2	18	-14	200 mm ³
Kirby and Robinson (20)	2015	Affective mapping: An activation likelihood estimation (ALE) meta-analysis	SAD	-2	26	-4	NA
Kirby and Robinson			SAD	2	48	2	NA
Sugraneys et al. (21)	2011	Autism Spectrum Disorders and Schizophrenia: Meta-analysis of the Neural Correlates of Social Cognition	Schiz	-6	50	26	64 mm ³

Authors	Year	Title	Disorder	Coords			Size
				x	y	z	
Alustiza et al. (22)	2017	Meta-analysis of functional magnetic resonance imaging studies of timing and cognitive control in schizophrenia and bipolar disorder: Evidence of a primary time deficit	Schiz	-4	30	30	2004 voxels
Thoma et al. (23)	2016	Functional MRI Evaluation of Multiple Neural Networks Underlying Auditory Verbal Hallucinations in Schizophrenia Spectrum Disorders	Schiz	-3	35	-2	NA
Thoma et al.	2016		Schiz	3	47	9	NA
Thoma et al.	2016		Schiz	-3	47	9	NA
Yan et al. (24)	2015	Rostral medial prefrontal dysfunctions and consummatory pleasure in schizophrenia: A meta-analysis of functional imaging studies	Schiz	-2	44	2	432 mm ³
Yan et al.	2015		Schiz	-6	32	-10	272 mm ³
Yan et al.	2015		Schiz	-2	32	-10	272 mm ³
Kronbichler et al. (25)	2017	Abnormal Brain Activation During Theory of Mind Tasks in Schizophrenia: A Meta-Analysis	Schiz	-2	42	-6	1573 voxels

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