;order-Specific & Transdiagnostic Functional Neuroimaging Abnormalities in Major Depressive Disorder: A Meta-Analysis

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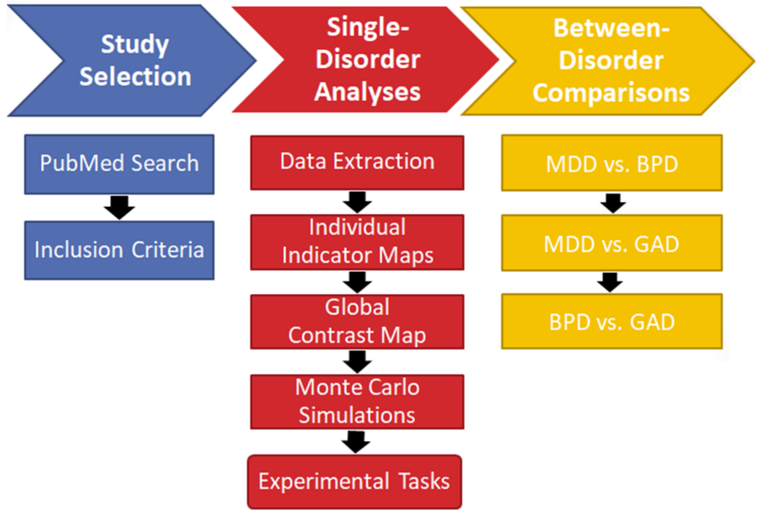
Abstract

Despite a large body of research that has documented numerous differences in neural activity between individuals diagnosed with major depressive disorder (MDD) and healthy controls, it is not clear whether these abnormalities are specific to depression or are shared across multiple psychiatric disorders. This study uses *multilevel kernel density analysis* – a voxel-wise, whole-brain, meta-analytic approach – to identify the neural abnormalities reported in functional neuroimaging studies of depression and related disorders (MDD: N=66 studies, 2463 subjects; bipolar mania: N=15 studies, 562 subjects; generalized anxiety disorder: N=15 studies, 510 subjects). We obtained results that identified several brain regions with abnormal patterns of activation in participants with MDD compared to HCs that were related reliably to depression but not to mania or anxiety, including hyperactivity in the orbitofrontal cortex ($p<0.0001$) and hypoactivity in the dorsolateral prefrontal cortex ($p<0.0001$), anterior cingulate cortex ($p<0.05$), and anterior insula ($p<0.001$). Other neural abnormalities were shared across groups of individuals with depression, mania, and anxiety, including hyperactive clusters in the inferior frontal gyrus ($p<0.005$) and inferior parietal lobe ($p<0.025$). These results demonstrate that patterns of abnormal activity in functional neuroimaging studies can be used as specific biomarkers for MDD and that depressed adults show neural abnormalities that are specific to depression as well as shared with other mood (i.e., bipolar disorder) or anxiety disorders (i.e., generalized anxiety disorder).

Methods



Criteria for Disorder Specificity

Comparison of Interest	Disorder-Specific (MDD) Finding	Category-Specific (Mood Disorders[1]) Finding	Category-Specific (Distress Disorders[2]) Finding	Transdiagnostic[3] Finding
MDD vs. HC participants	Significant difference	Significant difference	Significant difference	Significant difference
BPD vs. HC participants	Non-significant difference	Significant difference	Non-significant difference	Significant difference
GAD vs. HC participants	Non-significant difference	Non-significant difference	Significant difference	Significant difference
MDD vs. BPD participants	Significant difference	Non-significant difference	Significant difference	Non-significant difference
MDD vs. GAD participants	Significant difference	Significant difference	Non-significant difference	Non-significant difference
BPD vs. GAD participants	n/a	Significant difference	Significant difference	Non-significant difference

Abbreviations: MDD: major depressive disorder; HC: healthy control; BPD: bipolar disorder (active mania); GAD: generalized anxiety disorder
[1] The mood disorders label includes MDD and BPD
[2] The distress disorders label includes MDD and GAD
[3] The transdiagnostic label includes MDD, BPD, and GAD

Results

Brain Structure[a]	Hemisphere	Direction of Effect	Experimental Condition[b]	Talairach Coordinates[c]			Cluster Size (mm^3)	Statistical Threshold[d]
				x	y	z		
Dorsolateral Prefrontal Cortex Middle Frontal Gyrus	Right	HC > MDD	Aggregate, Affective Processing, Negative Valence	-29	-10	45	474	0.0001
Precuneus	Right	HC > MDD	Aggregate, Affective Processing	-5	55	39	531	0.0005
Anterior Insula	Right	HC > MDD	Aggregate, Executive Functioning	-32	-9	-7	946	0.001
Superior Temporal Gyrus *Anterior Insula*	Left	MDD > HC	Affective Processing, Negative Valence	42	3	-7	546	0.0005
Dorsolateral Prefrontal Cortex Middle Frontal Gyrus	Left	HC > MDD	Affective Processing, Negative Valence	29	-15	46	5170	0.025
Orbitofrontal Cortex Inferior Frontal Gyrus	Right	MDD > HC	Positive Valence, Negative Valence	-51	-32	1	291	0.0001
Nucleus Accumbens *Caudate Nucleus* *Anterior Cingulate Cortex*	Left	HC > MDD	Executive Functioning, Positive Valence	5	-3	-4	4780	0.01
Caudate Nucleus	Right	HC > MDD	Aggregate	-10	-22	8	1481	0.005