Meta-analysis of Reward Processing in Major Depressive Disorder Reveals Distinct Abnormalities within the Reward Circuit

Supplementary Information

Supplementary Table 1

Comparison of Findings on Reward Responses (i.e., Reward > Punishment/Neutral) in Previous Meta-analyses

Brain Region	MNI Coordinates		
	x	y	z
Groenewold et al. [19]			
MDD > HC			
Lingual Gyrus	26	-92	-14
Olfactorius Cortex	4	22	-14
Middle Orbitofrontal	2	26	-14
Rectus	2	30	-24
Middle Orbitofrontal	0	26	-12
Rectus	0	24	-24
HC > MDD			
Cerebellum	-16	-74	-28
Lingual Gyrus	-18	-62	-6
Fusiform Gyrus	-22	-74	-14
Inferior Occipital Gyrus	-30	-80	-12
Rolandic Operculum	-40	-24	20
Insula	-36	-24	22
Superior Temporal Gyrus	-40	-36	12
Heschl Gyrus	-46	-16	12
Postcentral Gyrus	-50	-18	18
Supramarginal Gyrus	-50	-22	18
Anterior Cingulate Cortex	-2	28	16
Anterior Cingulate Cortex	4	32	14
Lingual Gyrus	-18	-62	-6
Cerebellum	-6	-58	-4
Calcarine Sulcus	-20	-54	4
Fusiform Gyrus	-26	-58	-12
Precuneus	-20	-52	2
Pallidum	18	0	-4
Putamen	28	-4	8
Thalamus	14	-8	0
Insula	38	10	-12
Amygdala	30	-2	-12
Caudate	16	26	6

Fusiform	44	-62	-20
Crus Cerebellum	44	-64	-20
Brain Region	TAL Coordinates		
	x	y	z
Zhang et al. [20]			
MDD > HC			
Cuneus	4	-86	18
Cuneus	-6	-86	22
Frontal Lobe	20	30	-6
Middle Frontal Gyrus	40	28	38
Superior Frontal Gyrus	-4	48	32
Fusiform Gyrus	-48	-74	-12
Middle Frontal Gyrus	-48	14	30
Lingual Gyrus	12	-52	4
Lingual Gyrus	14	-54	0
HC > MDD			
Caudate	-6	18	4
Caudate	-8	-8	10
Thalamus	-10	-12	8
Thalamus	-14	-14	16
Caudate	-12	-4	20
Cerebellum	4	-36	-4
Cerebellum	-4	-42	4
Putamen	14	8	2
Caudate	14	14	10
Anterior Cingulate	-8	30	10
Insula	34	-4	16
Cerebellum	-6	-60	-20
Brain Region	Coordinates		
	x	y	z
Keren et al. [21]			
HC > MDD			
Caudate Body	12	14	14
Caudate Head	6	2	-2
Caudate Body	-8	-2	-18

Abbreviations: MNI, Montreal Neurological Institute space; MDD, major depressive disorder; HC, healthy controls; TAL, Talairach space. Ventral striatum is the only area implicated in reward processing in MDD relative to HCs across the two previous meta-analyses and the current meta-analysis (see Table 1 for peak coordinates of group differences in neural responses to reward found in the current meta-analysis).

Supplementary Table 2

Characteristics of the Study Samples Included in the Meta-Analysis.

		MDD Patients						Healthy Controls		
Study	Diagnostic Criteria	*n*	Age	% Female	% Medicated	Mood States	Comorbidity	*n*	Age	% Female
Arrondo *et al.* [22]	DSM-IV	24	33.1	29.2%	54.2%	D	Exclusion of alcohol or drug dependence.	21	34.3	23.5%
Bremner *et al.* [23]	DSM-IV	18	40	66.7%	0.0%	D	Exclusion of organic mental disorders or comorbid psychotic disorders, post-traumatic stress disorder, childhood trauma, alcohol or substance abuse or dependence, or dyslexia. No current or past history of comorbid psychiatric disorders.	9	35	77.8%
Burger *et al.* [24]	DSM-IV	36	40.7	61.1%	100.0%	D	Exclusion of substance dependence. Inclusion of PD, agoraphobia, generalized anxiety disorder, social phobia, obsessive compulsive disorder, post-traumatic stress disorder, somatoform disorder, eating disorder, dysthymia, alcohol abuse, and substance abuse.	36	41.3	52.8%
Chantiluke *et al.* [25]	DSM-IV	20	16.2	50.0%	0.0%	D	Exclusion of major psychiatric disorders.	21	16.3	52.4%

Chase *et al.* [26]	DSM-IV	40	31	77.5%	77.5%	D	No exclusion of psychiatric comorbidities. Inclusion of lifetime comorbid anxiety disorders and substance use disorders.	37	33.1	67.6%
Demenescu *et al.* [1]	DSM-IV	59	36.2	66.1%	23.7%	D	Exclusion of axis I disorders, such as psychotic disorder or dementia, current alcohol or substance abuse.	56	39.8	60.7%
Dichter *et al.* [27]	DSM-IV	19	23.6	78.9%	0.0%	R	Exclusion of current axis I psychopathology.	19	27.9	63.2%
Elliott *et al.* [28]	DSM-IV	10	42.2	70.0%	100.0%	D	Exclusion of current comorbid anxiety disorders, substance abuse or dependence, bipolar disorder, or other psychiatric diagnoses. Inclusion of past history of PD and bulimia.	11	37.6	72.7%
Engelmann *et al.* [29]	DSM-IV	19	37.6	52.6%	0.0%	D	Exclusion of lifetime bipolar disorder, psychotic disorder, obsessive-compulsive disorder, tic disorder, eating disorder, cognitive disorder, substance abuse or dependence in the previous 6 months or positive urine drug screen, or clinically significant suicidal ideation.	23	33.7	60.9%

Fournier *et al.* [30]	DSM-IV	26	30.6	69.0%	69.2%	D	Exclusion of bipolar disorder, borderline personality disorder, and alcohol/substance use disorder within 2 months before the scan. Inclusion of history of anxiety disorder and substance abuse.	28	32.6	57.0%
Fu *et al.* [31] and [32]	DSM-IV	19	43.2	68.4%	100.0%	D	Exclusion of current axis I disorder and history of substance abuse within 2 months of study participation.	19	42.8	57.9%
Fu *et al.* [33]	DSM-IV	16	40	81.3%	0.0%	D	Exclusion of other axis I disorder, including anxiety disorder or history of substance within 2 months of study participation.	16	39.2	81.3%
Gotlib *et al.* [34]	DSM-IV	18	35.2	72.2%	50.0%	D	Exclusion of psychotic ideation, social phobia, PD, mania, or substance abuse in the past 6 months or behavioral indications of possible impaired mental status.	18	30.8	72.2%
Gradin *et al.* [35]	DSM-IV	25	25.5	68.0%	0.0%	D	Unspecified	25	25.4	68.0%
Hall *et al.* [36]	DSM-IV	29	37.4	55.2%	51.7%	D	Exclusion of history of alcohol or substance abuse.	25	37.7	55.2%
Johnston *et al.* [37]	DSM-IV/ ICD-10	19	50.8	78.9%	85.0%	D	Exclusion of other primary psychiatric disorder and substance misuse.	21	46.1	71.4%

Keedwell *et al.* [38]	ICD-10	12	43	66.7%	66.7%	D	Exclusion of other axis I disorder.	12	36	66.7%
Knutson *et al.* [39]	DSM-III-R	14	30.7	64.3%	0.0%	D	Exclusion of other current axis I disorder.	12	28.7	66.7%
Kumari *et al.* [40]	DSM-IV	6	47	100.0%	Unspecified	D	Unspecified	6	44	100.0%
Laurent *et al.* [41]	DSM-IV	11	24.1 (whole sample)	100.0%	23.1%	D	No exclusion of psychiatric comorbidities. Inclusion of past substance abuse/dependence, anxiety disorders, and eating disorder.	11	24.1 (whole sample)	100.0%
Liu *et al.* [42]	DSM-IV	21	30.7	57.1%	0.0%	D	Exclusion of axis I disorders (other than anxiety) and psychotic features and lifetime substance abuse or dependence.	17	28.3	58.8%
Murrough *et al.* [43]	DSM-IV	20	38.1	44.4%	0.0%	D	Exclusion of lifetime history of psychotic illness or bipolar disorder and current alcohol or substance abuse.	20	35	45.0%
Pizzagalli *et al.* [44]	DSM-IV	30	43.2	50.0%	0.0%	D	Exclusion of other axis I disorder except for anxiety disorders.	31	38.8	41.9%
Remijnse *et al.* [45]	DSM-IV	20	35	40.0%	0.0%	D	Exclusion of current alcohol or substance abuse at the time of study participation. Inclusion of social anxiety disorder, generalized anxiety disorder, PD without agoraphobia, PD,	27	32	70.4%

							and cannabis abuse in early and sustained full remission.			
Rizvi *et al.* [46]	DSM-IV	21	38.9	66.7%	0.0%	D	Exclusion of other primary axis I disorder, lifetime history of hypomania/mania, psychosis, obsessive compulsive disorder, or eating disorder, and substance abuse or dependence (except nicotine or caffeine) within the last 3 months.	18	36.2	66.7%
Rosenblau *et al.* [47]	DSM-IV	12	43.5	41.7%	0.0%	D	Exclusion of other axis I or II disorders.	12	45.8	41.7%
Scheuerecker *et al.* [48]	DSM-IV	13	37.9	23.1%	0.0%	D	Exclusion of past alcohol or substance abuse, other mental illnesses, and personality disorders.	15	35.5	33.3%
Schiller *et al.* [49]	DSM-IV	19	23.6	78.9%	0.0%	R	Exclusion of current axis I psychopathology.	19	27.9	63.2%
Segarra *et al.* [50]	DSM-IV	24	33.1	29.2%	54.0%	D	Exclusion of dependence on alcohol or recreational drugs.	21	34.3	19.0%
Sharp *et al.* [51]	DSM-IV	14	13.4	100.0%	Unspecified	D	Exclusion of current use of nicotine, illicit drugs, psychotic disorders, bipolar I disorder, learning disabilities, and mental retardation.	19	13.7	100.0%
Smoski *et al.* [52]	DSM-IV	14	34.8	50.0%	0.0%	D	Exclusion of current mood disorder, anxiety disorder,	15	30.8	60.0%

							psychotic disorder, substance abuse, or active suicidal ideation and history of psychosis or mania.			
Smoski *et al.* [53]	DSM-IV	9	34.4	Unspecified	44.4%	D	Inclusion of generalized anxiety disorder and binge eating disorder.	13	26.2	Unspecified
Surguladze *et al.* [54]	DSM-IV	16	42.3	37.5%	100.0%	D	Exclusion of illicit substance abuse.	14	35.1	42.9%
Surguladze *et al.* [55]	DSM-IV	9	42.8	44.4%	100.0%	D	Exclusion of illicit substance abuse and other axis I disorders.	9	39.7	44.4%
Townsend *et al.* [56]	DSM-IV	15	45.6	40.0%	0.0%	D	Exclusion of comorbid axis I disorder.	15	44.8	40.0%
Wagner *et al.* [2]	DSM-IV	19	39.9	55.0%	100.0%	D	Exclusion of current comorbid axis I disorder and a history of manic episodes.	20	34.1	60.0%
Wang *et al.* [57]	DSM-IV	12	69.1	58.3%	91.7%	D	Exclusion of another major psychiatric disorder and alcohol/drug abuse/dependence. Inclusion of generalized anxiety disorder.	20	73.1	60.0%
Young *et al.* [58]	DSM-IV-TR	16	37.1	87.5%	0.0%	D	Exclusion of serious suicidal ideation, psychosis, drug/alcohol abuse in the past year and dependence (except for nicotine) in their lifetime.	16	37.8	87.5%

Zhang *et al.* [59]	ICD-10	21	43.8	38.1%	100.0%	D	Exclusion of illicit substance use or substance use disorders.	25	39.3	36.0%
Zhong *et al.* [60]	DSM-IV	29	20.5	55.2%	0.0%	D	Exclusion of lifetime substance dependence and substance abuse in the last 6 months.	31	20.8	51.6%

Abbreviations: MDD, major depressive disorder; D, depressed; R, remitted; PD, panic disorder.

Supplementary Table 3

Characteristics of the Studies Included in the Meta-analysis

Study	fMRI or PET	Design	Space	Paradigm	Correction	Stimuli	Contrast
Arrondo *et al.* [22]	fMRI	Event-related	MNI	Modified monetary incentive delay task	Uncorrected	Money	HC > MDD, Anticipation: Reward > Non-Reward
Bremner *et al.* [23]	PET	Block	MNI	Verbal declarative memory tasks with neutral paragraph encoding compared to a control condition and sad word pair retrieval compared to a control condition.	Uncorrected at $p < .005$	Words and paragraphs	MDD > HC, Outcome: Negative > Neutral HC > MDD, Outcome: Negative > Neutral
Burger *et al.* [24]	fMRI	Event-related	MNI	Face matching paradigm	Corrected at $p < .05$ (TFCE)	Faces	HC > MDD, Outcome: Negative > Neutral HC > MDD, Outcome: Positive > Neutral
Chantiluke *et al.* [25]	fMRI	Event-related	TAL	Reward continuous performance task	Uncorrected at $p < .005$	Money	MDD > HC, Outcome: Reward > Non-Reward HC > MDD, Outcome: Reward > Non-Reward
Chase *et al.* [26]	fMRI	Event-related	MNI	Card guessing paradigm	Voxel-wise corrected at $p < .05$ and cluster-wise corrected at $p < .01$	Money	MDD > HC, Anticipation: Reward > Non-Reward HC > MDD, Anticipation: Reward > Non-Reward MDD > HC, Anticipation: Reward Expectancy HC > MDD, Anticipation: Reward Expectancy

							MDD > HC, Outcome: Prediction Error
Demenescu *et al.* [1]	fMRI	Event-related	MNI	Viewing faces with angry, fearful, sad, happy, and neutral expressions and scrambled faces; rating gender or pressing buttons in conformity with the instruction presented on the screen	Cluster-wise corrected at $p < .05$	Faces	MDD > HC, Outcome: Positive > Scrambled Face
Dichter *et al.* [27]	fMRI	Event-related	MNI	Modified monetary incentive delay task	Uncorrected at $p < .005$, $k \geq 10$	Money	MDD > HC, Anticipation: Reward > Non-Reward MDD > HC, Outcome: Reward > Non-Reward HC > MDD, Outcome: Reward > Non-Reward
Elliott *et al.* [28]	fMRI	Block	MNI	Affective go/no go task	Uncorrected at $p < .001$	Words	MDD > HC, Outcome: Negative > Positive HC > MDD, Outcome: Positive > Negative
Engelmann et al. [29]	fMRI	Event-related	MNI	Economic decision-making task	Cluster-wise corrected at $p < .05$	Money	MDD > HC, Outcome: Negative > Positive
Fournier *et al.* [30]	fMRI	Block	MNI	Labeling a color flash superimposed upon neutral faces that gradually morphed into angry, fearful, sad, or happy faces	Uncorrected at $p < .001$, $k > 20$	Faces	MDD > HC, Outcome: Negative > Neutral MDD > HC, Outcome: Positive > Neutral

Fu *et al.* [31] and [32]	fMRI	Event-related	TAL	Indicating the sex of faces morphed to represent low, medium, and high intensities of sadness	Cluster-wise corrected at $p < .005$	Faces	MDD > HC, Outcome: Negative (low, medium, and high intensity) HC > MDD, Outcome: Positive (low, medium, and high intensity)
Fu *et al.* [33]	fMRI	Event-related	TAL	Indicating the sex of faces morphed to represent low, medium, and high intensities of sadness	Unspecified	Faces	MDD > HC, Outcome: Negative (low, medium, and high intensity) HC > MDD, Outcome: Negative (low, medium, and high intensity)
Gotlib *et al.* [34]	fMRI	Block	MNI	Indicating the sex of faces that were fearful, angry, sad, happy, neutral, or scrambled	Uncorrected at $p < .001$, $k > 5$	Faces	MDD > HC, Outcome: Negative > Neutral HC > MDD, Outcome: Negative > Neutral MDD > HC, Outcome: Positive > Neutral HC > MDD, Outcome: Positive > Neutral
Gradin *et al.* [35]	fMRI	Event-related	MNI	Ultimatum game	Cluster-wise corrected at $p < .05$	Money	HC > MDD, Outcome: Increasing fairness (decreasing inequality) MDD > HC, Outcome: Increasing inequality (decreasing fairness)
Hall *et al.* [36]	fMRI	Event-related	TAL	Contingency reversal reward paradigm	Voxel-wise corrected at $p < .05$	Money	HC > MDD, Outcome: Magnitude of Loss: Large Loss > Small Loss HC > MDD, Outcome: Magnitude of Reward: Large Reward > Small Reward

							MDD > HC, Outcome: Reward Acquisition > Punishment Reversal HC > MDD, Outcome: Reward Acquisition > Punishment Reversal
Johnston *et al.* [37]	fMRI	Event-related	MNI	Modified Pessiglione task	Cluster-wise corrected at p < .01	Voucher	MDD > HC, Outcome: Loss > Non-Loss HC > MDD, Outcome: Loss > Non-Loss MDD > HC, Outcome: Reward > Non-Reward HC > MDD, Outcome: Reward > Non-Reward
Keedwell *et al.* [38]	fMRI	Block	TAL	Being exposed to happy, sad, or neutral autobiographical memory prompts and facial expressions	Cluster-wise corrected at p < .01	Autobiographical memory and faces	MDD > HC, Outcome: Negative > Neutral HC > MDD, Outcome: Negative > Neutral MDD > HC, Outcome: Positive > Neutral HC > MDD, Outcome: Positive > Neutral
Knutson *et al.* [39]	fMRI	Event-related	TAL	Monetary incentive delay task	Uncorrected at p < .05	Money	MDD > HC, Anticipation: Reward > Non-Reward HC > MDD, Anticipation: Reward > Non-Reward HC > MDD, Outcome: Non-Loss > Loss HC > MDD, Outcome: Reward > Non-Reward

Kumari *et al.* [40]	fMRI	Block	TAL	Viewing positive or negative pictures with a caption	Cluster-wise corrected at p < .005	Pictures and captions	HC > MDD, Outcome: Negative > Neutral MDD > HC, Outcome: Negative > Neutral HC > MDD, Outcome: Positive > Neutral MDD > HC, Outcome: Positive > Neutral HC > MDD, Outcome: Positive > Negative MDD > HC, Outcome: Positive > Negative
Laurent *et al.* [41]	fMRI	Event-related	MNI	Seeing own infant vs. other infant distress faces	Cluster-wise corrected at p < .05	Faces	HC > MDD, Outcome: Very negative > Negative
Liu et al. [42]	fMRI	Event-related	MNI	Instrumental probabilistic reward- and punishment-based associative learning task	Cluster-wise corrected at p < .05	Money	MDD > HC, Outcome: Negative > Neutral MDD > HC, Outcome: Punishment Prediction Errors
Murrough *et al.* [43]	fMRI	Event-related	MNI	Rating emotional valence of happy, sad, or neutral faces	Cluster-wise corrected at p < .05	Faces	HC > MDD, Outcome: 100% Positive > Neutral
Pizzagalli *et al.* [44]	fMRI	Event-related	MNI	Monetary incentive delay task	Uncorrected at p < .005	Money	MDD > HC, Anticipation: Loss > Non-Loss HC > MDD, Anticipation: Loss > Non-Loss MDD > HC, Anticipation: Reward > Non-Reward HC > MDD, Anticipation: Reward > Non-Reward

							MDD > HC, Outcome: Loss > Non-Loss HC > MDD, Outcome: Loss > Non-Loss MDD > HC, Outcome: Reward > Non-Reward HC > MDD, Outcome: Reward > Non-Reward
Remijnse *et al.* [45]	fMRI	Event-related	MNI	Reversal learning task	Uncorrected p < .001	Points	MDD > HC, Outcome: Loss > Baseline HC > MDD, Outcome: Loss > Baseline MDD > HC, Outcome: Reward > Baseline
Rizvi *et al.* [46]	fMRI	Blocked	MNI	Viewing IAPS pictures that elicit positive, negative or neutral affective states	Cluster-wise corrected at p < .05	Pictures	MDD > HC, Outcome: Positive > Neutral MDD > HC, Outcome: Negative > Neutral
Rosenblau *et al.* [47]	fMRI	Event-related	MNI	Viewing IAPS pictures that elicit positive, negative or neutral affective states with and without cues indicating their emotional valence	Uncorrected at p < .05 or p < .005	Pictures	MDD > HC, Anticipation: Negative > Neutral MDD > HC, Outcome: Negative > Neutral
Scheuerecker *et al.* [48]	fMRI	Block	MNI	Face matching paradigm	Uncorrected at p < .001	Faces	MDD > HC, Outcome: Negative > Neutral
Schiller *et al.* [49]	fMRI	Event-related	MNI	Monetary incentive delay task	Cluster-wise corrected at p < .05	Money	HC > MDD, Anticipation: Loss > Non-Loss HC > MDD, Outcome: Loss > Non-Loss

Segarra *et al.* [50]	fMRI	Event-related	MNI	Simulated slot-machine game	Cluster-wise corrected at $p < .05$	Money	HC > MDD, Outcome: Unexpected Reward > Full Miss
Sharp *et al.* [51]	fMRI	Event-related	TAL	Card guessing paradigm	Uncorrected at $p < .005$	Money	HC > MDD, Outcome: Reward > Non-Reward
Smoski *et al.* [53]	fMRI	Event-related	MNI	Modified monetary incentive delay task	Cluster-wise corrected	Money	MDD > HC, Anticipation: Money > Control HC > MDD, Anticipation: Money > Control MDD > HC, Outcome: Non-Win > Control HC > MDD, Outcome: Non-Win > Control MDD > HC, Outcome: Winning > Control HC > MDD, Outcome: Winning > Control MDD > HC, Selection: Money > Control HC > MDD, Selection: Money > Control
Smoski *et al.* [52]	fMRI	Event-related	MNI	Wheel of fortune task	Uncorrected at $p < .005$, $k \geq 10$	Money	HC > MDD, Anticipation: Reward > Non-Reward HC > MDD, Outcome: Reward > Non-Reward
Surguladze *et al.* [55]	fMRI	Event-related	TAL	Indicating the sex of neutral faces and faces morphed to represent mild and high intensities of fear and disgust	Cluster-wise corrected at $p < .001$	Faces	HC > MDD, Outcome: Increasing intensities of happy faces MDD > HC, Outcome: Increasing intensities of sad faces

Surguladze *et al.* [54]	fMRI	Event-related	TAL	Indicating the sex of neutral faces and faces morphed to represent mild and high intensities of sadness and happiness	Cluster-wise corrected at $p < .001$	Faces	MDD > HC, Outcome: Differential response to 100% disgust HC > MDD, Outcome: Differential response to 50% fear
Townsend *et al.* [56]	fMRI	Block	MNI	Face matching paradigm	Cluster-wise corrected at $p < .05$	Faces	HC > MDD, Outcome: Negative > Neutral
Wagner *et al.* [2]	fMRI	Event-related	MNI	Self-referential processing task	Cluster-wise corrected at $p < .05$	Statements	MDD > HC, Outcome: Neutral > Negative MDD > HC, Outcome: Neutral > Positive
Wang *et al.* [57]	fMRI	Event-related	MNI	Emotional oddball task	Uncorrected at $p < .001$, $k = 5$	Pictures	MDD > HC, Outcome: Negative > Neutral
Young *et al.* [58]	fMRI	Event-related	TAL	Autobiographical memory task	Cluster-wise corrected at $p < .05$, $k > 30$	Words and autobiographical memories	HC > MDD, Outcome: Very Positive > Positive HC > MDD, Outcome: Very Negative > Negative MDD > HC, Outcome: Very Negative > Negative
Zhang *et al.* [59]	fMRI	Event-related	MNI	Viewing IAPS positive, neutral, and negative pictures with or without valence cues	Cluster-wise corrected at $p < .05$, $k > 157$	Pictures	MDD > HC, Outcome: Reward > Non-Reward
Zhong *et al.* [60]	fMRI	Block	MNI	Face matching paradigm	Uncorrected at $p < .005$, $k = 8$	Faces	MDD > HC, Outcome: Negative > Neutral HC > MDD, Outcome: Negative > Neutral

Abbreviations: fMRI, functional magnetic resonance imaging; PET, positron emission tomography; MNI, Montreal Neurological Institute space; SVC, small volume correction; MDD, major depressive disorder; HC, healthy controls; TFCE, threshold-free cluster enhancement; TAL,

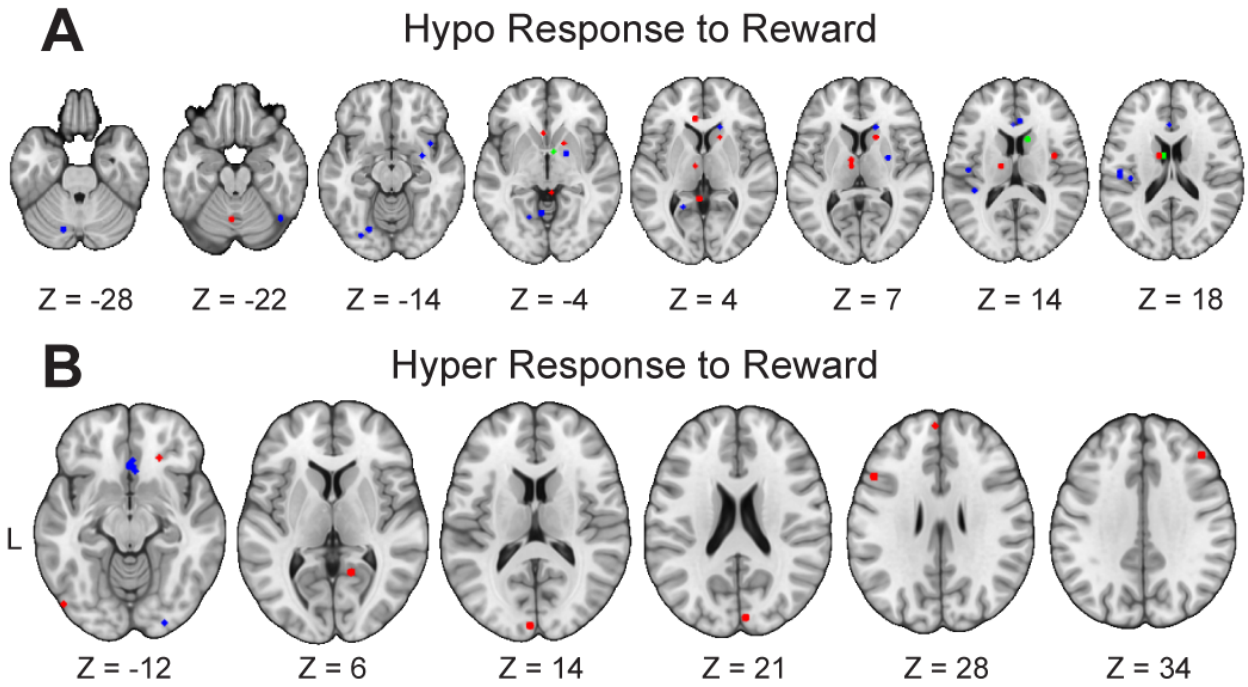
Talairach space; VS, ventral striatum; dACC, dorsal anterior cingulate cortex; rACC, rostral anterior cingulate cortex; ACC, anterior cingulate cortex; mPFC, medial prefrontal cortex; mOFC, medial orbitofrontal cortex; IAPS, International Affective Picture System.

Supplementary Table 4

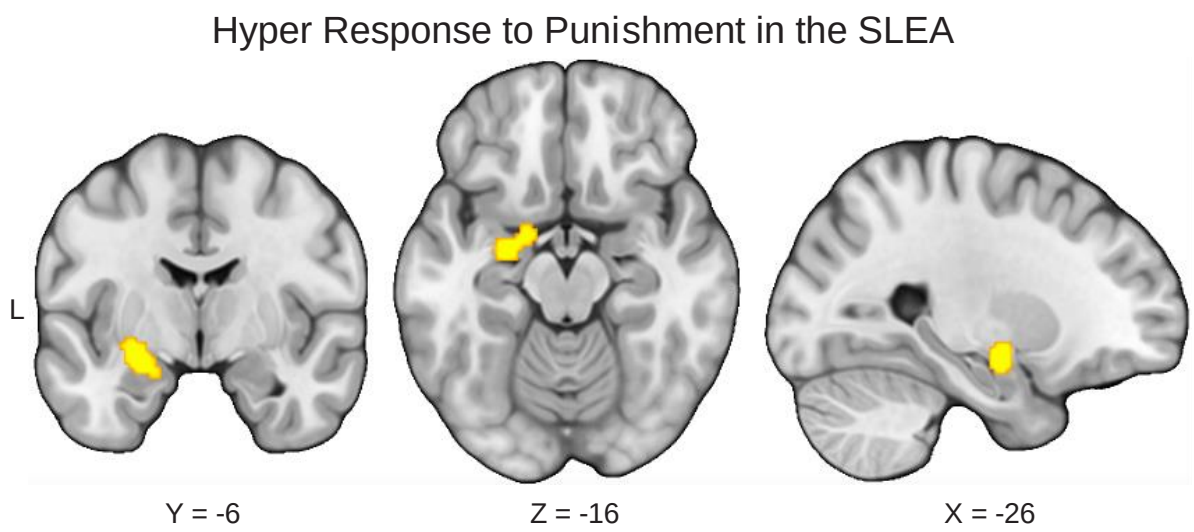
Peak Coordinates of Group Differences in Neural Responses to Reward (Excluding Neutral Stimuli > Punishment)

Contrast	Cluster Size (mm^3)	Probabilistic Anatomical Label	x	y	z
MDD > HC	968	Frontal Orbital Cortex (26%), Frontal Pole (13%)	20	32	-12
HC > MDD	1784	Subcallosal Cortex (14%)	-2	8	-4
		Caudate (32.1%), Accumbens (11.1%)	8	6	-2

Abbreviations: MDD, major depressive disorder; HC, healthy controls. Coordinates are x,y,z values of the locations of the maximum activation likelihood estimation (ALE) values in MNI space. Probabilistic labels reflect the probability that a coordinate belongs to a given region derived from the Harvard-Oxford probabilistic atlas. For clarity, we only report labels whose likelihood exceeds 5%.



Supplementary Figure 1. Illustration of Findings of Previous Meta-analyses on Reward Processing in Unipolar Depression. There is a striking degree of anatomical disagreement across these meta-analyses, with non-overlapping findings all throughout the brain. Blue represents Groenewold et al.[19] Green represents Keren et al.[21] Red represents Zhang et al.[20] **(A)** Previous meta-analyses examining convergence among studies reporting hypo-responses to reward include Groenewold et al.,[19] Keren et al.,[21] and Zhang et al.[20] **(B)** Previous meta-analyses examining convergence among studies reporting hyper-responses to reward include Groenewold et al.[19] and Zhang et al.[20]



Supplementary Figure 2. Hyper-responses to punishment in the sublenticular extended amygdala (SLEA) in major depressive disorder (MDD). To conduct exploratory analyses to examine which brain regions consistently show elevated response to punishment in MDD relative to healthy controls (HCs), we meta-analyzed 24 studies reporting greater activity in response to punishment in people with MDD than HCs. Our results indicated that these studies reliably report greater activation in the left SLEA in MDD.

Supplementary References

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