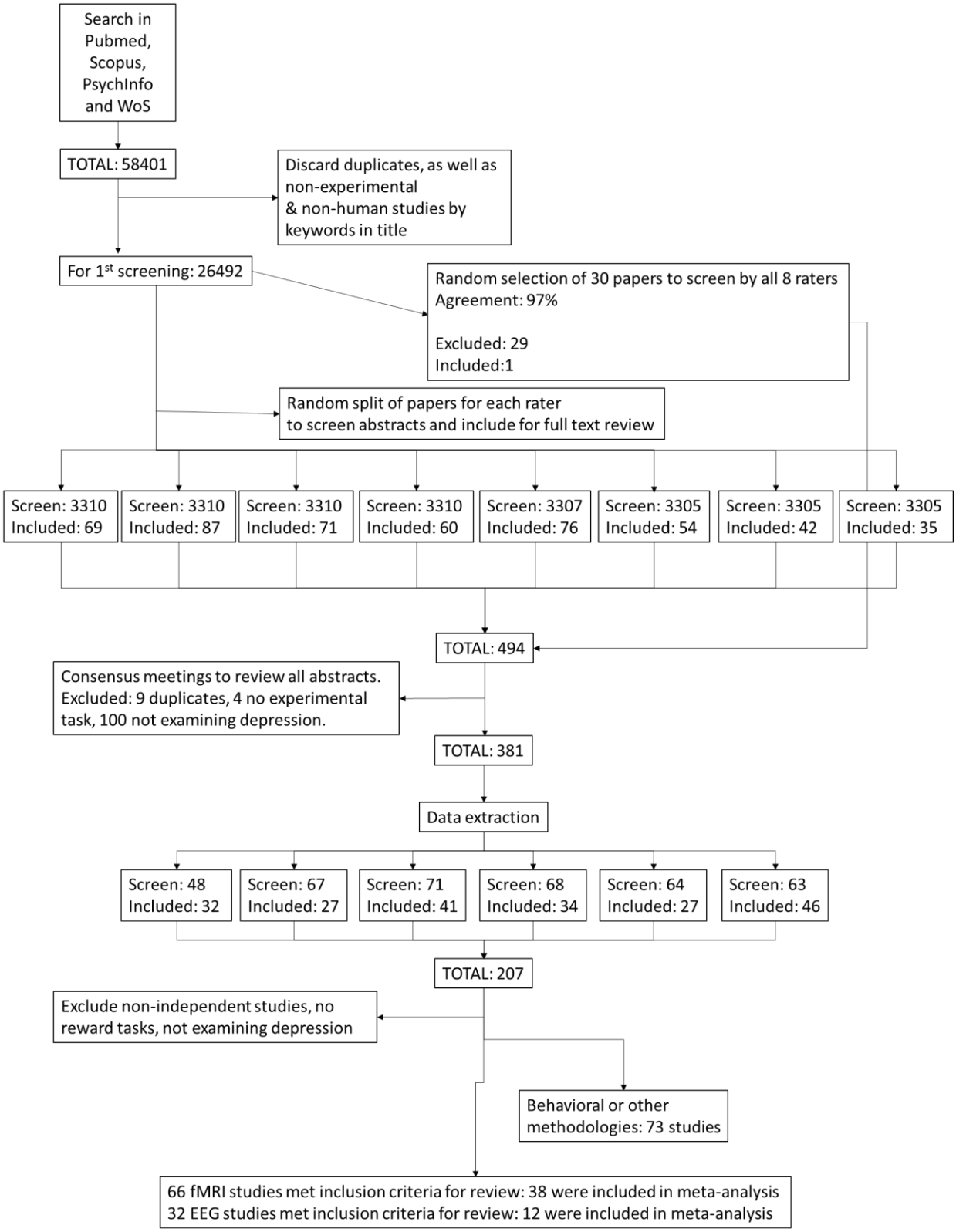
FIGURE S1. Search History



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1. Additional study selection details:

Exclusion criteria: Studies were excluded if they lacked a standard measure of depression. We excluded studies that measured depressive symptoms in patients with another disorder (e.g. bipolar or schizophrenia, etc.), but did not include in addition a depressed group. This was done because our primary question concerns the effects of depression on reward processing and in the absence of a depressed control group, drawing inferences about such effects would be impossible. We do, however, mention such studies in the Discussion section. We also excluded studies in which reward processing was only measured through non-experimental methods such as self-report measures or questionnaires. Furthermore, to guard against heterogeneity, we excluded studies in which physical punishment was delivered (e.g. heat, pain, electrical shock, etc.) as these are likely to engage different brain networks. Similarly, studies were excluded if they employed passive exposure to pleasant/unpleasant stimuli such as facial emotions or images. For included studies, relevant methodological details, where available, were recorded, as outlined below.

As shown in Figure S1, the initial search returned 58,401 studies; these were reduced to 26,492 after removing duplicates as well as non-human and non-experimental studies (based on keyword searches). Then, 30 articles were randomly selected and screened for inclusion/exclusion by 8 independent investigators (A. S., H. K., G. O'C., P. V-R., S. W., P. P., L. M., and A. K.). An inter-rater reliability analysis showed 97% of agreement across investigators, with one of the 30 articles meeting inclusion criteria. The remaining sample of studies (n=26,462) was randomly assigned to these 8 investigators who screened titles and abstracts in order to include articles for full text review. At this stage, 494 were included for review. However, after having consensus meetings to discuss doubtful articles with the principal investigator (A.S.) we identified 9 duplicates, 4 studies with no experimental tasks and 100 that did not examine depression. Therefore, 381 articles were selected.

These 381 were randomly assigned to six of the investigators (A. S., H. K., G. O'C., P. V-R., S. W., and P. P.), who excluded more articles based on a more in-depth reading, and extracted the data for the ones meeting full inclusion criteria. This yielded 207 articles from which data were extracted. The principal investigator (A. S.) examined the list of studies and excluded additional ones that did not examine depression, were not using reward tasks or were not independent from other studies due to sample overlap.

For the remaining 171 studies (which included 66 fMRI studies, 32 EEG studies and 73 studies employing mostly behavioural tasks or other methodologies), data extracted, if available, were a) type of study (observational or/and treatment study; cross-sectional or longitudinal), b) sample characteristics (healthy, at-risk of depression (defined as the presence of either MDD in a parent, high depression scale scores in the absence of MDD diagnosis, or remitted MDD), depressed, or participants with other disorder; total sample size; percentage and sample size of depressed group; percentage of females in depressed group; percentage of medicated; mean, SD, and age range of depressed and comparison groups), and c) methodology employed (behavioural, EEG, FC, or fMRI; reward task; depression measure; type of reward). Rewards were defined as monetary (i.e., the participant wins -or is led to believe they will win money based on performance), affective or primary. Additional data necessary for the meta-analyses were extracted from papers that contained fMRI and EEG measures, as described below and in the main text.

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fMRI meta-analysis:

There were n=66 fMRI studies of which 50 reported coordinates for reward-related neural activity. Upon inspection of the studies, there was only a sufficient number of studies for the following contrasts: Reward Anticipation (mostly vs. baseline or vs. a neutral outcome); Reward Feedback (mostly vs. baseline or vs. a neutral cue); Loss Feedback + Loss Anticipation (mostly vs. a neutral cue /outcome). As a result, 38 studies could be included (1-38), as presented in Table S2, while 16 studies were excluded because they did not report on any of these contrasts or related variations (e.g., risky vs. safe choices, inequality vs. fairness).

The distribution of studies in terms of group comparisons: A total of 24 studies used a case control design to compare people diagnosed with Major Depressive Disorder (MDD) and healthy volunteers (HV), 10 used non-depressed subjects at-risk of MDD (HR). A final group of 8 studies measured symptoms of depression continuously in subjects recruited from the community. Three of these studies belong to more than one definition. The studies included in the fMRI meta-analysis had the following information extracted: brain coordinates, name of activated regions, cluster size, direction of activity, and reported statistic.

EEG meta-analysis:

Of the relevant papers identified from the review of the literature, 32 contained EEG measures. These papers had the following information extracted: electrodes sampled from, type of signal extracted (FRN, RewP, etc.), sampling method (mean amplitude, peak, etc.), window defined for mean amplitude sampling, high and loss pass filter applied, reference electrode, the type of EEG net used, direction of effect, and reported statistic.

From these 32, an initial 9 papers were excluded as they analysed a signal unrelated to feedback, such as error-related negativity (ERN) or EEG asymmetry. Feedback signal had to be sampled from midline frontal electrodes - Fz, FCz, Cz - or some pooled combination of these. A further criterion was the method of feedback signal extraction; it was required that papers sampled the mean amplitude of the feedback response. Other extraction methods were excluded; for example, peak amplitude, base-to-peak or peak-to-peak. These alternative analysis approaches were excluded because it has been proposed that they may obscure measurement of the underlying signal of interest. Briefly, trial-averaged ERP waveforms reflect the summation of several underlying latent neural components, with any particular peak in the trial-averaged ERP waveform being an arbitrary inflection point that does not directly map onto a particular neural component (25). Moreover, peak amplitude is known to be heavily confounded by variability in the latency of these latent components across trials; this issue is mitigated by a mean amplitude approach (25). Analysis approaches that further subtract one peak from another have the strong possibility of confounding a given signal of interest (e.g. the FRN) with an unrelated signal (e.g. the P2). Furthermore, studies that identified the FRN through a principal components analysis (PCA) decomposition of the signal were excluded as these components were not consistent with the definition provided by the other studies. Although such alternative approaches may be useful within particular analysis contexts, studies that used these approaches were excluded here in order to more closely examine the underlying signals reflected in the FRN/RewP.

The longitudinal analyses reported in Bress, Meyer, and Proudfit (39) were not included in the meta-analysis. Instead, the timepoint one results from Bress et al. (40) and timepoint two from Bress, Meyer, and Proudfit (39) were entered as separate studies, as they contained independent EEG measurements

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and analyses of the relationship between depressive symptoms and the FRN. Foti and colleagues (41) was not included in the meta-analysis based on the same criterion; that is, the data from this study was not independent of Bress (42) and, therefore, only Bress (42) was included. See Table S5 for details of excluded studies. The initial 9 papers that did not examine feedback response are not included in this table.

The corresponding authors of 10 studies that met all but one inclusion criteria were contacted by G. O'C. to inquire whether a compatible analysis had been conducted, such as mean amplitude extraction, rather than a peak approach. Where such analyses had been conducted, the means were requested for inclusion in the meta-analysis, which resulted in five of these being included (46-50).

As a consequence of the criteria outlined above, only 12 papers were selected for the EEG meta-analysis (39, 40, 42-51). Within these studies, 7 included samples of depressed and/or HR compared to healthy matched controls, and 5 conducted correlational analyses between continuous measures of depression and the FRN/RewP in healthy, community based samples. The majority of participants included in these analyses were female (70.21%); indeed, 4 out of the 10 papers that reported a gender breakdown had all female samples. Further demographic and methodological details for these studies can be found in Tables S2 and S6, respectively.

2. Analytical Methods:

2.1 fMRI Activation Likelihood Estimation (ALE) analysis:

We used the program GingerALE to analyse the ALE across studies. This analysis uses the number of subjects (here, the depression group sample size) and the reported spatial coordinates sets (foci). The foci of each study are grouped by the different experiments (e.g., the effect directions "depressed > HV" and "depressed < HV" would be considered two experiments within a single study). For each ALE result we present the overall sum of these features, across the included studies (i.e., total number of experiments, foci and subjects). The algorithm creates a Gaussian distribution for each reported foci, centred at the reported coordinates, using a random effect model. The shape of this distribution is weighted by the sample size of the study (52). The overlap of these distributions across different experiments is then calculated by taking the maximum across each focus's Gaussian (53). Using the maximum, rather than the unity, across all distributions limits the biasing effect of an experiment with multiple foci very near one another, as described in (52).

GingerALE estimates p-values for the ALE scores, by computing the random spatial overlap across studies and generating a null distribution of the ALE statistic (in a permutation procedure) (54). The ALE maps computed from the activation coordinates are tested against the ALE scores from this null distribution, producing a statistical map of the p values of ALE scores. The non-parametric p values are then transformed into z scores (52, 53, 55).

The threshold value correcting for multiple comparisons at the whole brain level was received using a cluster-level inference. This threshold sets the cluster minimum volume such that only 5% of the simulated clusters of the data exceed this size. We used $p<0.001$ as a cluster-forming threshold. The resulting thresholded ALE maps were imported into AFNI and overlaid on an anatomical template for representation purposes (56).

2.2 EEG meta-analysis:

Firstly, all studies were converted to a consistent direction of effect. The first level contrast of interest was loss minus gain feedback response (i.e., FRN). As the response to gains was greater than response to losses, this resulted in a negative score, where more negative values indicated a greater differentiation between gain and loss signals. Consistent with this, two correlations based on the RewP (i.e., gain minus loss) were recorded by multiplying r by minus one. Therefore, a positive correlation between depressive symptoms and FRN would indicate less differentiation between gain and loss feedback response with increasing symptomology. For consistency, group means for FRN were subtracted in the direction of 'depressed' minus control, meaning that positive effect sizes would result if the depressed group had less differentiation between feedback signals than control.

Conversion and calculation of values to standardized effect sizes (ES) were conducted in Excel using equations from Borenstein and colleagues (57), reproduced in Table S1. Values were then transferred to Stata, where they were subjected to a random effects meta-analysis for pre-calculated ES using the 'metan' command (58). We tested for between-study heterogeneity using the I^2 statistic, which is the percentage of variation attributable to heterogeneity. The values of I^2 lie between 0% and 100%, with larger values showing increasing heterogeneity. Higgins et al (59) suggest that I^2 values between 25% and 50% are low, between 50% and 75% moderate, and for >75% high. As mentioned in the main text, a secondary meta-analysis to investigate the potential moderating effect of age on the relationship between the FRN and depression was then conducted. This meta-analysis produced separate pooled, weighted, ES and between study variances (tau-squared; τ^2), for studies that contained samples aged under 18 and over 18 years. These ESs were then formally compared according to recommendations made by Borenstein and colleagues (57), by computing a z-score based on the difference between the group ES and estimating between study variance within each age group separately (τ^2).

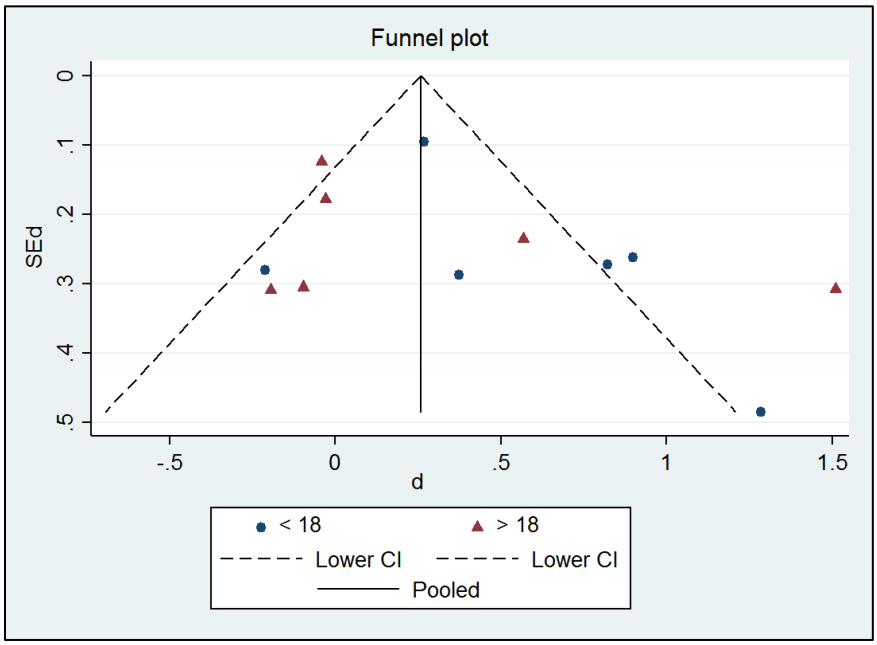
TABLE S1: Formulae used to convert all values to standardized ESs for later meta-analysis

	Variance (V_r)	**d**	**SE_d**
Pearson's r	$\frac{(1-r^2)^2}{n-1}$	$\frac{2r}{\sqrt{1-r^2}}$	$\sqrt{\frac{4V_r}{(1-r^2)^3}}$
Means and SDs	$\frac{(n_1-1).SD_1^2+(n_1-1).SD_2^2}{n_1+n_2-2}$	$\frac{M_1-M_2}{\sqrt{V_r}}$	$\sqrt{\frac{n_1+n_2}{n_1n_2}+\frac{d^2}{2(n_1+n_2)}}$

2.3 Assessing publication bias within the EEG papers:

Analysis of publication bias in the EEG studies was conducted using the 'metabias' command in Stata and illustrated with 'metafunnel' (58), see Figure S2. Egger's test for small-study effects found no bias, $t<1$.

FIGURE S2: Funnel plot demonstrating the distribution of study effect sizes (d), relative to standard error (SEd). Studies containing younger samples (<18 years) are denoted by blue circles and older adult samples (>18) by red triangles.



3. Additional results:

3.1 fMRI results:

TABLE S2: Demographic information for the studies included in the EEG and fMRI meta-analyses

Study	Sample Type	Age M(SD)	Total n	MDD/HR n	HV n	Female %	Medicated	Depression measure/s	Reward type	Task
fMRI meta-analysis (N=38):										
Admon et al. (2015)	MDD vs. HV	42.6(11.7) 37.7(14)	55	26	29	50	No	SCID, HAMD-21	Monetary	MID
Arrondo et al. (2015)	MDD vs. HV	33.08(9.15) 34. 33(10.11)	67	24	21	32	Yes	PANS, BPRS, SANS, BDI, SHAPS, TEPS	Monetary	MID
Casement et al. (2016)	Depression on continuum	16(-)	123	N/A	N/A	100	-	KSADS, NRS	Monetary	Reward guessing task
Chan et al. (2016)	HR (high anhedonia score^) vs. HV	18.8(1.8)	28	8	20	71	No	CPAS, CSAS, TEPS	Affective	AID
Chandrasekhar Pammi et al. (2015)	MDD vs. HV	31.9(7.5) 27.5(2.4)	20	10	10	20	-	HADS	Monetary	Decision making task
Chung & Barch (2015)	Depression on continuum (anhedonia^)	35.56(8.61)	27	N/A	N/A	44.4	-	SHAPS, BDI, Chapman Social and physical anhedonia	Monetary	Monetary reward paradigm
Dichter et al. (2012)	HR vs. HV	23.6(4) 27.9(6.3)	38	19	19	78	No	BDI	Monetary	MID
Dillon et al. (2014)	MDD vs. HV	34.3(12.1) 36.6(13.3)	42	21	21	50	No	BDI-II, SHAPS, MASQ	Monetary	Memory task
Felder et al. (2012)	Depression on continuum	23.3(4.3)	12	N/A	N/A	100	No	BDI-II	Monetary	Wheel of Fortune
Forbes et al. (2009)	MDD vs. HV	13.5(2.1) 13.1(2.6)	43	15	28	70	No	PANAS-C, MFQ, KSADS	Monetary	Card guessing
Forbes et al. (2010)	Depression on continuum	11.9(0.9)	77	N/A	N/A	50	No	PANAS-C, MFQ	Monetary	Event-related card guessing
Gorka et al. (2014)	MDD vs. HV	25.4(7.7) 29.5(13.1)	40	9	18	66.7	Yes	HAMD, IDAS	Monetary	Passive slot machine
Gotlib et al. (2010)	HR vs. HV	12.2(1.7) 12.6(1.4)	26	13	13	100	No	KSADS, CDS-I	Monetary	MID

Gradin et al. (2011)	MDD vs. HV	45.2(12.3) 40.6(11.8)	46	15	17	60	-	BDI, HAMD, anhedonia measured from a BDI derived subscale of items	Primary	Instrumental reward-learning task
Hagele et al. (2015)	MDD vs. HV + Depression on continuum	40.1(11.6) 37.7(11.1)	184	24	54	29.1	No	HRSD-21, BDI	Monetary	MID
Johnston et al. (2015)	MDD vs. HV + Depression on continuum	50.79(10.6) 46.14(13.97)	40	19	21	75	Yes	MINI PLUS, HAMD, HADS, MADRS, BDI, BHS	Accuracy	Modified Pessiglione reward task
Knutson et al. (2008)	MDD vs. HV	30.7(8.8) 28.6(4.2)	26	14	12	64.2	No	SCID	Monetary	MID
Luking et al. (2016)	HR vs. HV	9.2(1) 9(1.1)	48	16	32	50	No	CDIC, CBCL, CDIP	Monetary	Card guessing
Mori et al. (2016)	HR vs. HV	18.5(0.6) 19.1(0.7)	30	15	15	60	No	BDI-II	Monetary	MID
Olino et al. (2011)	HR vs. HV + Depression on continuum	13.3(2.4)	26	10	16	73.1	No	KSADS	Monetary	Card guessing
Olino et al. (2014)	MDD vs. HV	15.8(3) 15.5(2.5)	26	14	12	73.1	-	SCID	Monetary	Card guessing
Pizzagalli et al. (2009)	MDD vs. HV	43.1(12.9) 38.8(14.4)	61	30	31	42	No	SCID, HAMD	Monetary	MID
Redlich et al. (2015)	MDD vs. HV	38.4(12) 38.5(12.2)	67	33	34	51.5	Yes	SCID-IV, BDI, HAMD, SHAPS-D	Monetary	Card guessing
Remijnse et al. (2009)	MDD vs. HV	35(-) 32(-)	67	20	27	40	Yes	BDI, HAMD, MADRS	Monetary	Reversal learning task
Robinson et al. (2012)	MDD vs. HV	36(11) 31(6)	27	13	14	38	No	SCID	Affective	Pavlovian reward-punishment prediction
Rzepa et al. (2017)	HR vs. HV	16.6(1.2) 16.2(1.6)	33	16	17	75	No	MFQ	Primary	Taste
Satterthwaite et al. (2015)	Depression on continuum	38.8(12.8) 39.5(11.6)	77	22	32	44	Yes	BDI	Monetary	MID
Schiller et al. (2013)	HR vs. HV	23.6(4.1) 27.9(6.3)	38	19	19	78.9	No	BDI-II, RRS	Monetary	MID
Segarra et al. (2016)	MDD vs. HV	33.0(9.1) 34.3(10.1)	66	24	21	21.9	Yes	DSM-IV, SHAPS, BDI	Monetary	Simulated slot machine

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Sharp et al. (2014)	MDD + HR vs. HV	13.3(1.8) 13.7(1.8)	52	33	19	100	-	SCID, MFQ, BDI, DISC-IV	Monetary	Card guessing
Smoski et al. (2009)	MDD vs. HV	34.8(14.3) 30.8(9.7)	29	14	15	50	No	HAMD	Monetary	Wheel of fortune
Smoski et al. (2011)	MDD vs. HV	34.4(15.1) 26.2(6.3)	22	9	13	-	Yes	BDI	Monetary, Affective	MID
Steele et al. (2007)	MDD vs. HV	45.9(10.7) 43(13.3)	29	15	14	62	Yes	BDI, STAI, SHAPS, HAMD	Accuracy	Gambling task
Stoy et al. (2012)	MDD vs. HV	41.9(12.2) 39.5(11.9)	30	15	15	33.3	Yes	HRSD	Monetary	MID
Stringaris et al. (2015)	MDD vs. HV + HR vs. HV	14.4(0.3) 14.4(0.4)	1576	22	123	86	Yes	DAWBA	Monetary	MID
Ubl et al. (2015)	MDD vs. HV	46(11.8) 43.9(12.8)	58	30	28	16	No	SCID, BDI-II, SHAPS, HAMD	Monetary	Modified version of a paradigm by Kirsch
Ubl et al. (2015)	HR vs. HV	41.1(12) 42.7(12.1)	46	23	23	53.3	No	BDI II, HAMD, SHAPS, SCID	Monetary	Monetary reward paradigm
Yang et al. (2016)	MDD vs. HV	28.9(7) 28.3(7.8)	50	25	25	50	No	HAMD, BDI	Monetary	EEfRT
EEG meta-analysis (N=12):										
Liu et al. (2014)	MDD vs. HV	30.7(10.1); 34.1(10.2)	54	27	27	74.1	Yes	BDI-II, HRSD	Monetary	Doors Guessing Task
Foti et al. (2014)	MDD vs. HV	26(8.9); 23.8(2.9)	76	34	42	100	No	MASQ	Monetary	Doors Guessing Task
Weinberg & Shankman (2017)	HR (remitted non-melancholic MDD) vs. HV	23(3.3); 21.8(2.9)	156	56	71	6	Yes	IDAS-II	Monetary	Gambling task
Mueller et al. (2015)	MDD vs. HV	31.4(11.1); 29.4(11.1)	42	22	20	61.5	Yes	BDI-II	Monetary	Gambling task
Webb et al. (2017)	MDD vs. HV	15.9(1.7); 15(1.6)	51	26	25	100	Yes	BDI-II	Monetary	Guessing task
Padrao et al. (2013)	High vs. low anhedonia^	22(2.3)	43	21	22	83.7	No	PAS	Points	Gambling task
Bress et al. (2013)	With and without MDE+ by follow up	17.6(0.9); 17.8(0.9)	68	16	52	100	No	PHQ-9	Monetary	Reward guessing task

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Nelson et al. (2016)	Depression on continuum	14.4(0.6)	444	N/A	N/A	100	Yes	Dysphoria subscale of the IDAS-II	Monetary	Doors Guessing Task
Bress, Meyer, & Hajcak (2015)	Depression on continuum	12.1(0.8)	25	N/A	N/A	48	-	CDI:T	Monetary	Doors Guessing Task
Bress, Meyer, & Proudfit (2015)	Depression on continuum	12.8(1.5)	71	N/A	N/A	-	-	CDI:T	Monetary	Doors Guessing Task
Bress et al. (2012)	Depression on continuum	10.6(1.6)	64	N/A	N/A	40.6	-	CDI:T	Monetary	Doors Guessing Task
Ait Oumeziane & Foti (2016)	Depression on continuum	23.6(10.3)	260	N/A	N/A	62.2	-	DASS-21	Monetary	Doors Guessing Task

- information not provided; ^A continuous measure of anhedonia; +MDE = major depressive episode; where possible, ages are presented separately for the depression and the HV group (the latter below).

Abbreviation of measures: BDI = Beck's Depression Inventory; BHS = Beck Hopelessness Scale; BPRS = Brief Psychiatric Rating Scale; CDI:T = Child Depression Inventory, total of child and parent reports; CDIP = The Cervical Dystonia Impact Profile; CDS = Cardiac Depression Scale; DASS = Depression, Anxiety, and Stress Scale; DAWBA = development and well-being assessment; HADS = Hospital Anxiety and Depression Scale; HAMD = Hamilton Depression Rating Scale; HRSD = Hamilton Rating Scale for Depression; IDAS = Inventory of Depression and Anxiety Symptoms; KSADS = Kiddie Schedule for Affective Disorders and Schizophrenia; MADRS = Montgomery–Åsberg Depression Rating Scale; MASQ = Mood and Anxiety Symptom Questionnaire; MFQ = Mood and Feelings Questionnaire; MINI = Mini International Neuropsychiatric Interview; NRS = Nutritional Risk Screening; PANAS-C = Positive and Negative Affect Scale for Children; PAS = Physical Anhedonia Scale; PHQ = Patient Health Questionnaire; RRS = Ruminative Responses Scale; SANS = Scale for the Assessment of Negative Symptoms; SCID = Structured Clinical Interview for DSM-IV Axis I Disorders; SHAPS = Snaith-Hamilton Pleasure Scale; STAI = State-Trait Anxiety Inventory; TEPS = Temporal Experience of Pleasure Scale.

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TABLE S3: Summary of the analyses and results of the studies included in the fMRI meta-analysis

Study	Whole brain results	Task condition contrasts	Brain regions of activity difference	
			MDD <HV HR<HV Decrease with depression	**MDD >HV HR>HV Increase with depression**
Admon et al. (2015)	Yes	Feedback: reward + loss > neutral	L caudate; R caudate	-
Arrondo et al. (2015)	No	Anticipation: reward > neutral	R accumbens; L accumbens	-
Casement et al. (2016)	No	Anticipation: reward > baseline	-	dmPFC
Chan et al. (2015)	Yes	Anticipation: reward > neutral	L thalamus; R insula; L thalamus/pulvinar	-
Chandrasekhar et al. (2015)	Yes	Anticipation: reward > loss (parametric modulation, decision phase)	-	R middle temporal cortex (p<0.001)
		Loss: Neural Loss Aversion (parametric modulation with loss values of feedback phase)	R anterior insula; R dorsal striatum (putamen); R parahippocampal cortex	L cuneus; R lingual gyrus; R middle occipital cortex; L VTA/midbrain; L lingual gyrus; R posterior cerebellum; L middle occipital cortex; R inferior occipital cortex; R lingual gyrus; L posterior cerebellum; R posterior cingulate cortex; R precuneus
Chung & Barch (2015)	No	Anticipation: reward > baseline	Lateral globus pallidus	-
Dichter et al. (2012)	Yes	Anticipation: reward > neutral	-	L caudate; R anterior cerebellum; R cingulate gyrus (anterior); L cingulate gyrus (anterior); R frontal gyrus (middle); R frontal orbital cortex; L occipital fusiform gyrus; R occipital fusiform gyrus; R paracingulate gyrus (anterior); L parahippocampal gyrus (anterior); L parietal lobule (superior); R precuneous cortex, lingual gyrus; R Supplementary motor cortex; R supramarginal gyrus (posterior); L supramarginal gyrus (posterior)
		Feedback: reward > neutral	R angular gyrus; L central opercular cortex; R central opercular cortex; L cingulate gyrus (posterior); L frontal orbital cortex; R frontal orbital cortex; R frontal pole; L insular cortex; R intracalcarine cortex; L planum polare; L precentral gyrus; R Superior lateral occipital cortex; L supramarginal gyrus (anterior); R supramarginal gyrus (posterior); L temporal fusiform cortex (posterior); L temporal gyrus (posterior, superior); R temporal Pole; R thalamus; L thalamus; L precuneous cortex; L supramarginal gyrus (posterior)	-

Dillon et al. (2014)	Yes	Feedback: reward > neutral	R parahippocampal gyrus; VTA/SN	-
Felder et al. (2012)	Yes	Loss: feedback on non-win trials	L angular gyrus; R caudate; R cingulate gyrus (Posterior); R frontal gyrus (middle); L frontal gyrus (middle); R frontal gyrus (superior); L frontal gyrus (Superior); R inferior frontal gyrus, pars opercularis; L frontal pole; R occipital cortex (lateral, superior); L paracingulate gyrus; L postcentral gyrus; L precentral gyrus; precuneous cortex; L temporal gyrus (middle, posterior); R middle temporal gyrus	-
Forbes et al. (2009)	No	Anticipation: reward > baseline	L caudate head	R DLPFC; L DLPFC; L DLPFC
		Feedback: reward > baseline	L caudate head	L medial frontal gyrus (Brodmann's area 10); L DLPFC (Brodmann's area 9); R DLPFC (brodmann's area 9)
Forbes et al. (2010)	No	Anticipation: reward > baseline	-	medial frontal gyrus; anterior cingulate
		Feedback: reward > baseline	VS	-
Gorka et al. (2014)	Yes	Anticipation: reward > neutral	-	R dACC
Gotlib et al. (2010)	No	Anticipation: reward > neutral	L putamen; L insula	R insula
		Feedback: reward > neutral	R anterior cingulate gyrus; L posterior cingulate gyrus; L midcingulate gyrus; L putamen or lentiform nucleus; L anterior cingulate gyrus; R anterior thalamic nucleus; L anterior cingulate gyrus	-
		Loss: anticipation loss > neutral + feedback loss > neutral	L lentiform nucleus or globus pallidus; L midcingulate gyrus; R caudate; L putamen	L cingulate gyrus
Gradin et al. (2011)	Yes	Anticipation: parametric modulation of the cue value, decision phase	R hippocampus; R posterior parahippocampal gyrus	-
		Feedback: Parametric modulation of the Reward Prediction Error + parametric modulation of reward value	L putamen; L nacc; R nacc; L caudate; R caudate & thalamus; midbrain; R hippocampus	-
Hagele et al. (2015)	Yes	Anticipation: reward > neutral	R VS; L VS; R ventral striatal	-
Johnston et al. (2015)	Yes	Feedback: reward > neutral	ACC; nACC; posterior cingulate	insula
		Loss: feedback loss > neutral	nACC	DRN hippocampus; amygdala; insula

Knutson et al. (2008)	Yes	Anticipation: reward > neutral	L superior frontal gyrus	L anterior cingulate; L precental gyrus; R postcentral gyrus
		Feedback: reward > neutral	R MPFC; L insula; R putamen; L putamen; L superior frontal gyrus; L insula; L postcental gyrus; L inferior parietal lobe	-
		Loss: feedback loss > neutral	L parahippocampal gyrus	-
Luking et al. (2016)	Yes	Feedback: reward > neutral	caudate body; L ventral putamen; R ventral putamen; L medial globus pallidus; R medial globus pallidus; parahippocampal gyrus; anterior insula; anterior insula; anterior insula	-
		Loss: feedback loss > neutral	caudate body; L ventral putamen; R ventral putamen; L medial globus pallidus; R medial globus pallidus; parahippocampal gyrus; anterior insula; anterior insula; anterior insula	-
Mori et al. (2016)	Yes	Anticipation: reward > neutral	-	L angular gyrus; R angular gyrus; R middle frontal gyrus; R Inf parietal lobe
		Loss: anticipation loss > neutral	L angular gyrus; L inferior frontal gyrus	-
Olino et al. (2011)	No	Anticipation: reward > baseline	caudate body	-
Olino et al. (2014)	No	Anticipation: reward > baseline	striatum	-
		Feedback: reward > baseline	striatum	-
Pizzagalli et al. (2009)	Yes	Anticipation: reward > neutral	L putamen,report voxel peak p-value); R occipitofrontal fasciculus; R middle occipital gyrus	R uncus/parahippocampal gyrus; R inferior frontal gyrus; L inferior frontal gyrus; R middle frontal gyrus; R middle frontal gyrus; L middle frontal gyrus; R subgenual cingulate; R superior temporal gyrus; L occipitofrontal fasciculus/cingulum; L inferior parietal lobule; R lingual gyrus; R cerebellum
		Feedback: reward > neutral	R caudate; R caudate; L caudate; L caudate; R insula; R insula; R inferior frontal gyrus; R middle frontal gyrus; R middle frontal gyrus; R middle frontal gyrus; R medial frontal gyrus; L precentral gyrus; R rostral anterior cingulate; R dorsal anterior cingulate; L posterior cingulate; R middle temporal gyrus; L cerebellum; L cerebellum	L fusiform gyrus
		Loss: anticipation loss > neutral + feedback loss > neutral	R cerebellum; R caudate; L caudate; L thalamus; R inferior frontal gyrus; R middle frontal gyrus; L precentral gyrus; L posterior cingulate; R superior temporal gyrus; R middle temporal gyrus; L middle temporal gyrus; L inferior occipital gyrus	L insula; R medial frontal gyrus; L postcentral gyrus; dorsal anterior cingulate; R posterior cingulate; L middle temporal gyrus; L lingual gyrus; L precuneus; R cerebellum
Redlich et al. (2015)	No	Feedback: reward > neutral	nACC	-

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Remijnse et al. (2009)	Yes	Feedback: reward > neutral	-	gyrus temporalis superior; gyrus precentralis; occipital; putamen
Robinson et al. (2012)	Yes	Feedback: unexpected reward (after learning)	R putamen; L mid-cingulate cortex; L mid-occipital cortex	-
Rzepa et al. (2017)	No	Feedback: reward > neutral	pgACC; vmPFC	-
	Yes	Loss: anticipation aversive taste > neutral + feedback aversive taste > neutral	MFG; IFG; frontal pole; PCC; ACC	-
	No		pgACC; pgACC; pgACC; vmPFC	-
Satterthwaite et al. (2015)	No	Feedback: reward > loss	posterior cingulate; R anterior insula; L ventral striatum; R ventral striatum; anterior cingulate	-
Schiller et al. (2013)	Yes	Loss: anticipation loss > no loss + feedback loss > no loss	L SFG; L IFG (pars triangularis); L SFG	-
Segarra et al. (2016)	Yes	Feedback: reward > neutral	medial frontal cortex; R VS OFC thalamus and midbrain; L lingual gyrus, occipital lobe; L OFC; R inferior and middle temporal gyri; R angular and supramarginal gyri, parietal lobe; L angular and supramarginal gyri, parietal lobe	-
Sharp et al. (2014)	Yes	Feedback: reward > baseline	R middle temporal gyrus; inferior frontal gyrus; R ventral striatum; R inferior frontal gyrus; R inferior parietal lobe; supramarginal gyrus; medial frontal gyrus; L cingluate gyrus	-
	No		R VS	-
Smoski et al. (2009)	Yes	Anticipation: reward > neutral	caudate; cingulate gyrus; L cingulate gyrus; R cingulate gyrus; R frontal gyrus (inferior, pars triangularis); L frontal gyrus; R frontal gyrus; frontal pole; hippocampus; lingual gyrus; L occipital cortex; R occipital cortex; occipital cortex lateral superior; occipital fusiform gyrus; L post central gyrus; L precentral gyrus; R precentral gyrus; L precuneous cortex; R precuneous cortex; R subcallosal; R temporal gyrus; temporal gyrus; temporal pole; L thalamus; R thalamus	parietal operculum cortex
		Feedback: reward > neutral	R thalamus; frontal gyrus; frontal gyrus; lingual gyrus; occipital; occipital cortex lateral superior	anuglar gyrus; cuneal cortex; frontal gyrus; occipital fusiform gyrus; precuneous cortex; R temporal pole; thalamus left
		Loss: feedback no win > neutral	frontal gyrus; frontal orbital cortex; amygdala; caudate; central opercular cortex; cingulate gyrus; frontal operculum; frontal pole; heschl's gyrus; R hippocampus; insular cortex; lingual gyrus; occipital cortex (lateral inferior); R occipital cortex (lateral, superior); parietal lobe; planum temporale; postcentral gyrus; precuneous cortex; putamen; subcallosal cortex; temporal gyrus; temporal pole; thalamus	frontal gyrus

Smoski et al. (2011)	Yes	Anticipation: reward > neutral	R frontal orbital cortex; R frontal pole/OFC; L hippocampus; R occipital pole; R subcallosal cortex	-
		Feedback: reward > neutral	R occipital fusiform gyrus; R occipital pole	-
Steele et al. (2007)	No	Feedback: reward > loss	R VS; L VS	
		Loss: feedback loss > reward	Medial frontal cortex	-
Stoy et al. (2012)	No	Anticipation: reward > neutral	R VS	-
		Loss: anticipation loss > neutral	R VS; L VS	-
Stringaris et al. (2015)	No	Anticipation: reward > neutral	R caudate head; R caudate; L caudate; R medial frontal gyrus; R superior frontal gyrus; L superior frontal gyrus; L middle frontal gyrus; L caudate head; L putamen; Right caudate head; R caudate	-
Ubl et al. (2015)	No	Anticipation: high reward > neutral	R VS; R middle OFC; L rostral ACC	-
		Loss: anticipation high loss > neutral	L rAcc	-
Ubl et al. (2015) (2)	No	Anticipation: reward > neutral	-	right frontal superior gyrus; right amygdala; left hippocampus
Yang et al. (2016)	Yes	Anticipation: high reward > low reward + reward > baseline	L anterior lobe; L caudate; L frontal lobe middle frontal gyrus; L parietal lobe supramarginal gyrus	

TABLE S4: Results of the fMRI meta-analysis

Type of included studies	Group / task condition contrasts	Ages	No. of experiments/ foci/subjects	Brain region	Coordinates of peak Ale value			Volume (mm^3)	Cluster size (voxels)	Peak Ale value
					x	y	z			
Whole brain	Depression vs. HV / Reward anticipation*	All	16/84/274	R caudate head	10	12	-2	720	90	0.0168
	Depression vs. HV / Reward feedback	All	17/110/306	R caudate body	12	14	14	1936	246	0.0166
				R caudate head	6	2	-2			0.016
				L caudate body	-8	-2	18	632	79	0.016
Whole brain + ROI	Depression vs. HV / Reward anticipation	All	32/119/822	R caudate head	8	14	0	5344	668	0.035
				L caudate head	-8	12	4			0.03
				L putamen	-16	6	-2			0.017
		<18	11/25/429	L caudate head	-8	14	4	3000	375	0.021
				R caudate head	2	10	4			0.014
		>18	21/94/393	R caudate head	8	14	-2	1520	190	0.029
		<18 vs. >18*	32/119/822	L caudate body	-10	14	10	40	-	3.29^
	Depression vs. HV / Reward feedback	All	27/135/572	R putamen	16	12	4	4168	533	0.022
				R caudate head	8	2	0		265	0.02
				L putamen	-16	10	0	2024		0.017
				L globus pallidus	-14	0	-8			0.016
				L putamen	-24	0	4			0.01
		<18	9/34/194	R thalamus	10	0	8	1144	143	0.011
				L lentiform nucleus	-14	0	-8	616	77	0.015
		>18	18/101/378	R caudate head	14	12	0	2112	264	0.018
				R caudate body	12	14	14			0.016
				R caudate head	6	2	0			0.011
				L caudate body	-8	-2	18	632	79	0.016
				L putamen	-16	8	2	584	73	0.013
		<18 vs. >18*	27/135/572	-	-	-	-	-	-	-

* the largest cluster received for an uncorrected p<0.001. ^ the ALE contrast value is converted to a z score.
When not stated otherwise, all ALE results are corrected for FWE with a cluster level inference of an uncorrected p<0.001 threshold.

FIGURE S3: Alterations in brain activity during reward anticipation, in depression versus healthy subjects. Activation Likelihood Estimation (ALE) results across whole brain studies only (A) and for whole brain + ROI studies (B).

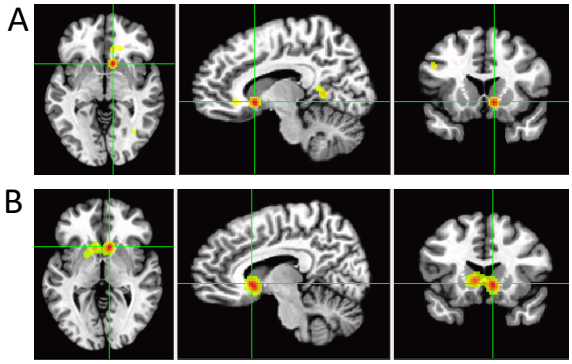


FIGURE S4: Reported alterations in brain activity during reward anticipation, in depressed versus healthy subjects. The studies included in the meta-analysis of "reward anticipation", broken down by age and type (whole-brain results are depicted black), along with the cluster size (x axis values) and direction of effect (increased vs decreased in depression).
It is notable, that all studies examining reward anticipation in under 18 year olds were ROI-based; moreover, the proportion of ROI studies in under 18 year olds was significantly higher than of adults ($z=3.23$, $p<0.005$).

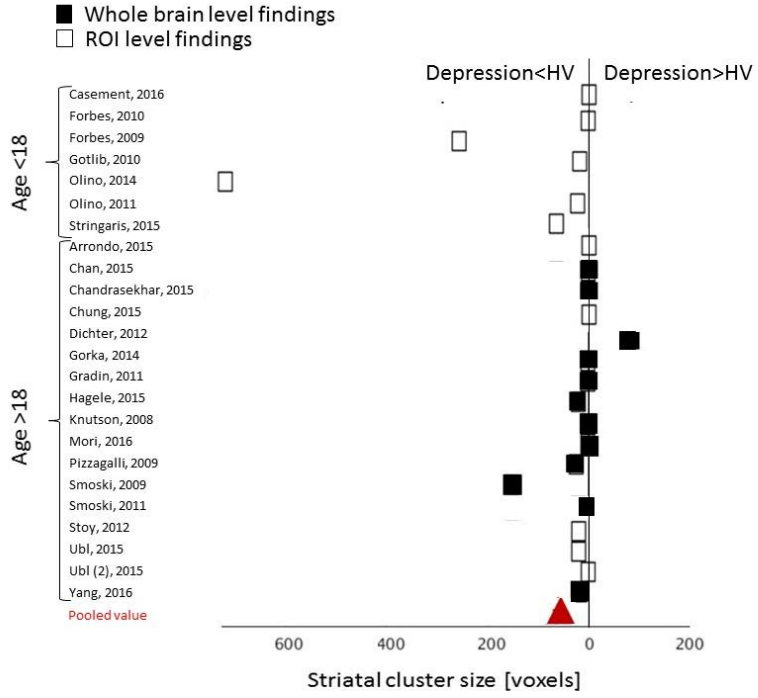


FIGURE S5: Alterations in brain activity during reward anticipation, in depressed versus healthy subjects. Activation Likelihood Estimation (ALE) results across whole brain + ROI studies, of ages younger than 18 years old (A) or older (B).

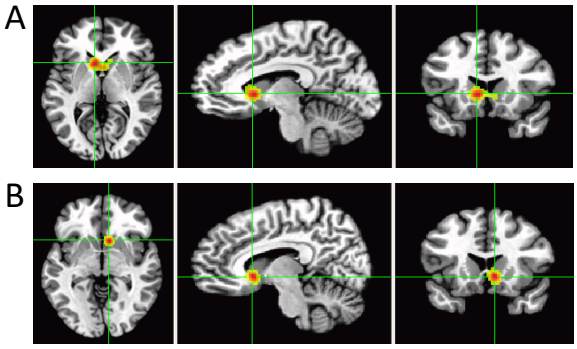
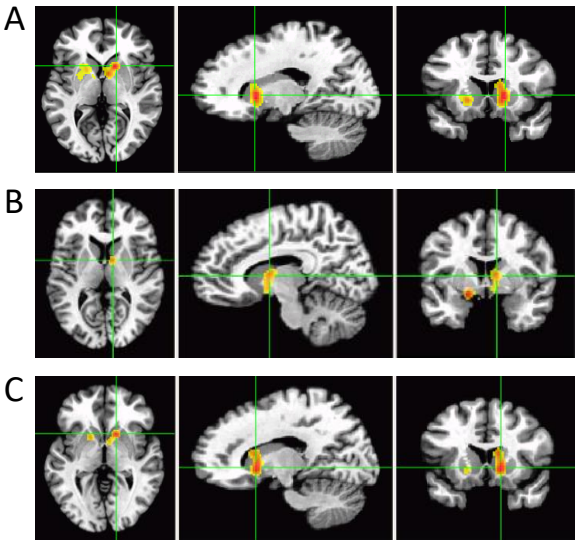


FIGURE S6: Alterations in brain activity during reward feedback, in depressed versus healthy subjects. Activation Likelihood Estimation (ALE) results across whole brain + ROI studies (A), also split by ages younger than 18 years old (B) and older (C).



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3.2 A summary of fMRI reports of loss activation differences, during anticipation and feedback:

The merged contrast of 'loss anticipation + feedback' showed no significant difference between depressed and healthy subjctes. This analysis included 21 experiments, with 109 foci and 379 depression subjects. Activation differences between healthy and depressed were reported for loss feedback phase by 11 studies (as detailed in Table S3). All of these studies reported decreased activation in depression, mostly in frontal cortical regions (3, 6, 10, 13, 14, 18, 22, 24, 34, 38, 60), and some (5 studies) also reported decreased activity in the caudate, putamen and insula (3, 10, 14, 38, 60). Increased activity in depression during feedback of a loss is rarely reported, but, when reported, was found in frontal regions (3, 10, 18, 60) while no clusters were found in the striatum.
For anticipation of a loss, 5 of the 6 studies reporting differences in depression, reported decreased activation in frontal regions (10, 15, 18, 22, 24, 30), and a single study also reported decreased activity in the striatum (28). A single study reported increased activation, but not in the striatum (18).

3.3 Sensitivity analysis of the fMRI data:

Controlling for influential fMRI studies: as the current approach weights studies by sample size, larger samples could drive ALE signal. Therefore, we conducted a sensitivity analysis where we excluded studies with an outlier sample size (larger than the average plus standard deviation, which is n=50): Forbes et al., 2010 (n=77), Casement et al., 2016 (n=123), as well as the coordinates for correlation with depression in Stringaris et al., 2015 (n=120). These studies were part of the reward anticipation contrast (whole brain and ROI studies analysis).
Results were not affected by these exclusions- there was a significant cluster focused in left and right caudate head, with and without these studies (see Table S5). It should be noted that no studies met the outlier criterion for sample size in the feedback results.
As for cluster size- in the feedback analyses, we wanted to ensure that outliers in cluster size did not impact on our results. In particular, the Segarra study (2016) reported several clusters (coordinates) in the same region, which are then summed up. This could have unduly inflated the results. However, even after excluding the Segarra study, there was a significant cluster in the striatum, albeit smaller in size. Moreover, as presented in the table below, two additional control analyses were conducted. One controlled for studies contrasting reward versus loss (rather than neutral or baseline conditions). A second analysis only included studies comparing an MDD group versus a healthy group; this analysis excluded studies with HR groups and those what used continuous depression scores. These additional analyses did not alter the reported results.

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TABLE S5: Sensitivity results of the fMRI meta-analysis

Type of included studies	Group / task condition contrasts	Ages	No. of experiments/ foci/subjects	Brain region	Coordinates of peak Ale value			Volume (mm^3)	Cluster size (voxels)	Peak Ale value
					x	y	z			
Whole brain	Depression vs. HV / Reward anticipation excluding Chandrasekhar 2015 (reward>loss)*	All	25/83/264	R caudate head	10	12	-2	720	90	0.0168
	Depression vs. HV / Reward feedback excluding Segarra 2016	All	15/103/281	R caudate body	12	14	14	1048	246	0.0166
Whole brain + ROI	Depression vs. HV / Reward anticipation excluding Casement 2016 (n=123)	All	31/118/699	R caudate head	8	14	0	5368	671	0.035
				L caudate head	-8	12	4			0.03
				L putamen	-16	6	-2			0.017
	Depression vs. HV / Reward anticipation excluding Stringaris 2015, Depression on continuum results (n=120)	All	31/115/721	R caudate head	8	14	0	4024	503	0.03
				L caudate head	-6	12	4			0.028
	Depression vs. HV / Reward anticipation excluding Forbes 2010 (n=77)	All	31/117/745	R caudate head	8	14	0	5384	673	0.035
				L caudate head	-8	12	4			0.03
				L putamen	-16	6	-2			0.017
	MDD group only vs. HV / Reward anticipation	All	19/79/339	R caudate head	8	14	0	4840	405	0.024
				L caudate head	-6	14	4			0.022
	Depression vs. HV / Reward feedback excluding Segarra 2016	All	24/126/532	R caudate body	16	12	6	3280	296	0.019
				R caudate body	12	14	14			0.0167
				R medial globus pallidus	8	2	-2			0.0166
				L medial globus pallidus	-14	0	-8	1608	201	0.015
				L putamen	-16	8	2			0.014
				L putamen	-24	0	4			0.011
	Depression vs. HV / Reward feedback excluding Steele 2007 and Satterthwaite 2015 (reward>loss)	All	25/128/503	R caudate head	8	2	0	3216	411	0.02
				R caudate body	12	14	14			0.0166
				R caudate head	12	12	-2			0.01
	MDD group only vs. HV / Reward feedback	All	19/88/349	R caudate body	12	14	14	2088	367	0.016
				R putamen	14	12	-2			0.015
				R caudate head	6	2	0			0.011

* the largest cluster received for an uncorrected p<0.001

When not stated otherwise, all ALE results are corrected for FWE with a cluster level inference of an uncorrected p<0.001 threshold.

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3.4 EEG results:

TABLE S6: Summary of the methods and results of the studies included in the EEG meta-analysis

Order	Electrode	Mean amplitude window	HP filter	LP filter	EEG net	Signal measured (feedback contrast):	Main finding reported for the relationship between depression and the FRN/RewP:
Liu et al. (2014)	FCz	250-350	0.1	30	-	FRN (loss – gain)	MDD: M= -0.66, SD= 4.67 HV: M= -7.89, SD= 4.91
Foti et al. (2014)	Fz, FCz	250-350	0.01	30	Custom cap and the ActiveTwo BioSemi system	FRN (loss – win)	MDD: M= -2.69, SD= 4.39 HV: M= -4.9, SD= 3.43
Weinberg & Shankman (2017)+	Cz, FCz	220-360	0.1	30	ActiveTwo BioSemi system	FRN (loss – gain)	At risk (remitted non-melancholic MDD): M= -4.43, SD= 6.23 HV: M= -4.27, SD= 5.04
Mueller et al. (2015)+	FCz, Cz	250-400	0.5	50	ActiveTwo BioSemi system	FRN (negative – positive)	MDD: M= -.09, SD= 1.98 HV: M= 0.38, SD= 2.78
Webb et al. (2017)+	FCz	250-350	0.1	30	HydroCel Geodesic Sensor Net	FRN (loss – win)	MDD: M= -4.71, SD= 6.83 HV: M= -3.31, SD= 6.44
Padrao et al. (2013)+	Fz	260-310	0.01	70	-	FRN (loss – gain)	High anhedonia: M= -6.31, SD= 3.75 Low anhedonia: M= -5.9, SD= 4.77
Bress et al. (2013)	Fz, FCz	250-350	-	104	Custom cap and the ActiveTwo BioSemi system	FRN (loss – gain)	With MDE at follow up: M= -2.32, SD= 8.97 Without MDE at follow up: M= -5.9, SD= 9.76
Nelson et al. (2016)+	FCz	250-350	0.1	30	ActiveTwo BioSemi system	RewP (gain – loss)	r = -0.133
Bress, Meyer, & Hajcak (2015)	Fz, FCz*	275-375	0.1	30	ActiveTwo BioSemi system	FRN (loss – gain)	r = 0.54
Bress, Meyer, & Proudfit (2015)	Fz	275-375	0.1	30	ActiveTwo BioSemi system	FRN (loss – gain)	r = 0.41
Bress et al. (2012)	Fz, FCz, Cz*	275-375	0.1	30	ActiveTwo BioSemi system	FRN (loss – gain)	r = 0.38
Ait Oumeziane & Foti (2016)	Fz, Cz, FC1, FC2*	260-310	0.01	30	ActiCAP and the actiCHamp system	RewP (gain – loss)	r = 0.02

- information not provided; * = electrodes were pooled, + = authors were contacted and provided data

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TABLE S7: FRN/RewP Studies excluded from EEG meta-analysis

Paper	Sample	N	Age	Task	Finding	Contacted	Reason for exclusion
Foti et al. (2011)	High familial risk for MDD vs. low (female only)	81	Adolescent	Doors Guessing Task	Post induction sadness rating was positively associated with the FN in high but not low risk participants	No	The longitudinal follow up from this study was included instead as it differentiated between participants who did/did not have a subsequent MDE and made group comparisons
Belden et al. (2016)	MDD vs. HV	78	Children	Doors Guessing Task	Depressed had a smaller response to rewards compared to control. No difference to losses	No	Sampled from the Pz electrode
Foti & Hajcak (2009)	Healthy	85	Young adults	Doors Guessing Task	Positive correlation between the FN (TF3/SF1 PCA component) and the DAS-21	No	PCA
Whitton et al. (2016)	rMDD vs. HV	60	Adults	Probabilistic reward task	Reward-related neural activity, derived from PCA, was reduced in remitted depressed participants, relative to controls	No	PCA
Weinberg et al. (2015)	Healthy, enriched for internalizing symptomology, plus a sibling pair	140	Adults	Doors Guessing Task	Neural response to rewards did not differ between siblings with and without a history of MDD	No	PCA
Foti et al. (2015)	Healthy	88	Young adults	Doors Guessing Task	Higher depressive symptoms were associated with blunted FN-Delta activity but not FN-Theta activity	No	PCA
Ruchsow et al. (2004)	MDD vs. HV	32	Adults	Eriksen Flanker with monetary gains and losses based on performance	Controls had a more negative response to errors following errors compared to correct following an error, whereas depressed didn't demonstrate this difference	Yes	Peak extraction and conducted a trial n-1 analysis
Santesso et al. (2012)	Healthy	29	Young adults	Monetary Incentive Delay task	Higher negative emotionality (combined BDI-II and PANAS NA scales) was associated with a more negative response to penalties	Yes	Peak extraction
Santesso et al. (2008)	rMDD vs. HV	27	Adults	Probabilistic punishment task	Found a larger negative deflection for the remitted MDD group, compared to control	Yes	Peak extraction
Tucker et al. (2003)	MDD vs. HV	47	Adults	'Spatial Compatibility Task'	Diagnosis x Feedback interaction. Negative feedback conditions elicited a greater negative wave compared to positive in controls, whereas the most negative feedback differed from positive and moderately negative feedback in the depressed group.	Yes	Separated feedback types – no means for loss minus gain provided
Thoma et al. (2015)	MDD vs. HV	34	Adults	Feedback learning tasks: active and observational	The amplitude was reduced in MDD compared to control, across learning and feedback types	Yes	Combined feedback types – no means for loss minus gain provided

3.5 Sensitivity analysis of the EEG data:

To evaluate whether results of the EEG meta-analysis were affected by the presence of influential studies, a sensitivity analysis was conducted using the 'metaninf' command in Stata (58). This was first conduced on all 12 EEG studies (see Table S8), and then separately for the studies with adult (i.e. > age 18) and youth (< 18) samples (see Table S9). Metaninf removes each study in turn and recalculates the random effects meta-analysis. The effect size and confidence intervals on each row of Tables S8 and S9 represent the meta-analysis result when the paper designated on that row was omitted from the analysis. The 'combined' results in these tables are the pooled effect sizes of the meta-analysis with no studies omitted and are consistent with the results reported in the main text. This analysis revealed that, regardless of which study was omitted from the analyses, the results remained consistent. This suggests that the main results reported were not driven by a few influential studies.

TABLE S8: Sensitivity analysis of all studies included in the EEG meta-analysis.

Study omitted		**d**	**95%**	**C.I.**
Liu et al.	2014	0.27	0.05	0.50
Foti et al.	2014	0.36	0.08	0.64
Weinberg & Shankman	2017	0.42	0.14	0.71
Mueller, Panitz, et al.	2015	0.42	0.15	0.69
Webb et al.	2017	0.43	0.15	0.70
Padrao et al.	2013	0.42	0.14	0.69
Bress et al.	2013	0.38	0.10	0.66
Nelson et al.	2016	0.40	0.08	0.72
Bress, Meyer & Hajcak	2015	0.33	0.07	0.59
Bress, Meyer & Proudfit	2015	0.33	0.06	0.59
Bress et al.	2012	0.34	0.07	0.60
Ait Oumeziane & Foti	2016	0.43	0.14	0.72
Combined		0.38	0.12	0.64

TABLE S9: Sensitivity analysis, repeated separately for studies with samples above and below age 18.

Study omitted		d	95%	C.I.
>18 studies				
Liu et al.	2014	0.04	-0.19	0.28
Foti et al.	2014	0.20	-0.27	0.68
Weinberg & Shankman	2017	0.34	-0.21	0.88
Mueller, Panitz, et al.	2015	0.35	-0.13	0.82
Padrao et al.	2013	0.33	-0.15	0.81
Ait Oumeziane & Foti	2016	0.34	-0.22	0.90
Combined		0.26	-0.16	0.68
<18 studies				
Webb et al.	2017	0.63	0.27	0.99
Bress et al.	2013	0.54	0.11	0.96
Nelson et al.	2016	0.59	0.11	1.06
Bress, Meyer & Hajcak	2015	0.42	0.08	0.76
Bress, Meyer & Proudfit	2015	0.41	0.04	0.78
Bress et al.	2012	0.44	0.05	0.82
Combined		0.50	0.15	0.85

3.6 Contradictory findings of behavioural tasks:

To illustrate the inconsistency of behavioral findings in depressed patients in the literature, two paradigms are discussed in greater detail below, the Iowa Gambling Task (IGT) and delay discounting tasks.

The IGT is a laboratory probe developed to measure decision-making under uncertainty and risk (61). Some studies (62-66) suggested that depressed adult participants with MDD adopt a more disadvantageous strategy on the IGT compared to age-matched controls; however, the opposite has also been reported in MDD (67) and in those scoring high on depressive symptoms (68, noted a positive correlation between IGT score and their depression scale). There are also studies that have found no difference when comparing at-risk (69) or depressed (70-72) groups to healthy volunteers.

Similarly conflicting results were found in delay discounting tasks which probe the tendency of people to discount rewards according to how distant they are in time (73). Indeed, significant associations between delay discounting and depression go in different directions. Lempert et al. (74) found that anhedonic individuals tended to choose larger but delayed rewards, whereas Imhoff et al. (75), as well as Pulcu et al. (76), found delay discounting and depression to be significantly correlated.

3.7 Summary of studies employing social and pleasant stimuli:

We identified, and included in the main search, five studies using social/pleasant stimuli in instrumental tasks (as defined in Richards et al 2013) (2, 21, 36, 77, 78) three of which were also included in the fMRI meta-analysis (2, 21, 36).

Brinkman et al (77) used a behavioural approach to examine effort mobilization (measured by cardiovascular reactivity) during a memory task under conditions of social approval in dysphoric vs non-dysphoric university students. They found that dysphoric individuals mobilized less effort than non-dysphoric individuals when anticipating social reward. In another behavioural study (78), the authors compared reaction time (RT) to reward and punishment during the MID and the Affective Incentive Delay task (AID) in healthy and depressed adult outpatients, the latter group split in those with high (HIS) and low suicidal ideation (LSI). In the AID, which employed social scenes and valanced images as stimuli, the HIS group was quicker under the punishment condition than reward condition. In contrast, HC and LSI were quicker under reward condition than punishment condition in the AID. Such pattern of differences was not found in the MID. The same group extended these findings using fMRI in an independent sample of healthy young adults with varying levels of trait anhedonia (2). Trait anhedonia was associated with hypoactivation at the left pulvinar, the left claustrum and the left insula to positive cues during the anticipatory phase of the AID task; no differences were found in the MID. These results suggest that the AID might be more sensitive than the MID in detecting anhedonia, and also groups at higher risk of suicide. A similar study compared neural activations to pleasant images and monetary rewards in adults with MDD and HV (36). The authors found that, compared to HV, MDD patients showed reduced reward network activation to both types of reward, though in different regions: hypoactivation in orbitofrontal and subcallosal cortex for money, and hypoactivation in paracingulate and supplementary motor cortex for images. Interestingly, within the MDD group, hypoactivation was greater for pleasant images than for monetary rewards in the putamen.

Lastly, using a reversal learning paradigm with green smiley faces and red sad faces as outcome, Robinson et al (21) found impaired reversal learning for reward in unmedicated adults with MDD, and this was related to blunted striatial response to unexpected reward.

3.8 Longitudinal fMRI studies:

There was an insufficient number of longitudinal studies (n=9) to conduct a separate meta-analysis (1, 15, 28, 29, 79-83). Five of those studies were conducted as part of treatment trials (1, 15, 28, 82, 83), none of which included randomization, placebo, or other control equivalent. Among the treatment modalities, three studies reported on behavioral activation (BA) and two used escitalopram, whereas five of the studies were observational (1, 29, 79-81). As in the cross-sectional studies, the MID was the most commonly employed task; six out of nine studies used the MID (1, 15, 28, 29, 82, 83). Decreased activation in the striatum when anticipating a reward was a predictor of later onset of depression and increase of symptoms in two of the observational fMRI studies that reported task activation during that phase (rather than during decision making or using a connectivity analysis). The contribution of the frontal cortex to depression, however, was not consistent (29, 79). Four of the five longitudinal observational studies were conducted in adolescents. Two of these employed connectivity measures during win feedback: one found that accumbens-mPFC connectivity was positively correlated with a history of depression (81), while the second reported that caudate-dACC connectivity was decreased in depression (1).

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3.9 Longitudinal EEG studies:

Nelson and colleagues found that blunting of reward feedback at baseline was associated with, and predictive of, greater dysphoria at follow-up in a community-based sample of 444 adolescent girls (48). Similarly, EEG recordings across two time points, two years apart, showed a stable association between blunted FRN and increased depression scores in children and young adolescents (39, 40). These findings were consistent with another study that found low baseline FRN amongst adolescents with increased symptoms of depression at a 21-month follow-up, even after controlling for baseline symptoms (42). No studies in the current review examined longitudinal associations between the FRN and depression in adult participants.

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