Data supplement for Rappaport et al., Brain Reward System Dysfunction in Adolescence: Current, Cumulative, and Developmental Periods of Depression. Am J Psychiatry (doi: 10.1176/appi.ajp.2019.19030281)

SUPPLEMENTAL METHODS

Participants

Of the 131 participants, 3 had 14 waves of depression symptom data, 17 had 13 waves, 25 had 12 waves, 36 had 11 waves, 18 had 10 waves, 12 had 5-9 waves, and 20 had <5 waves of data. Moreover, of the 131 participants, 24% met criteria for a current diagnosis of MDD or MDD not otherwise specified, and 49% met criteria for a lifetime diagnosis of MDD. SES was significantly negatively correlated with cumulative and current depression (r = -0.23, p = 0.01; r = -0.28, p < 0.01, respectively). For cumulative and current depression there were no sex differences ($F(1,129) = 0.773$, p = 0.381; $F(1,127) = 0.088$, p = 0.767, respectively) nor race differences ($F(2,128) = 2.354$, p = 0.099; $F(2,128) = 1.635$, p = 0.199, respectively).

Depression severity measures

All diagnostic interviews were audiotaped and reviewed for reliability using established methods previously reported (1). Inter-rater reliability among clinicians was high for a diagnosis of depression (κ = 1.0; ICC = 0.98). In calculating cumulative depression severity, a depression severity score was created by calculating the total number of core symptoms from the major depressive disorder (MDD) module endorsed by the caregiver and/or child during each assessment. Then the area under the curve of the trajectory of these symptoms over their time in the study was calculated.

Procedure

An event-related card-guessing task was used to assess neural reactivity to anticipation and receipt of reward feedback (2–5). For each trial, participants were asked to guess whether a card (represented by a “?”) was “high” or “low” using a button press (4000ms) and told that they would either win or lose money or neither win or lose money depending on their guess. After guessing, participants received one of four cues (2000ms) indicating they were likely to win (Win cue), lose (Lose cue), either win or lose (Mixed cue), or likely to get neutral feedback indicating no change (Neutral cue). If no response was made, participants viewed a fixation cross for the remainder of the trial. Following the cue, participants saw a fixation cross (jittered 0, 2000, or 4000ms), before receiving feedback (2000ms) that they either won money (Reward outcome), lost money (Loss outcome), or neither won nor lost money (None outcome), followed by a fixation cross (jittered 2000, 4000, or 6000ms). At the end of the task, participants were informed that they had “won” $17. In total there were two runs of 36 trials each presented in a pseudorandom order lasting about 8.5 minutes each, including 12 trials each of the Win and Lose cues, 6 trials each of the Mixed and Neutral cues, 11 trials each of the Reward and Loss

outcomes, and 14 trials of the None outcome per run. Participants with fewer than five Reward or Loss trials in a run were excluded from analyses (n=2).

fMRI Analyses

Functional magnetic resonance imaging data were collected on a Siemens PRISMA 3T scanner with a 32-channel head coil. Participants completed T1- and T2-weighted structural scans (0.8mm^3) in addition to 17 minutes of task-based blood-oxygen-level-dependent (BOLD) scanning across four scans. Task-based scans were acquired using a T2*-weighted multiband EPI sequence with no gaps between slices (Multiband[MB]=7, 72 axial slices per volume, 2.4mm isotropic voxels, TE=33.1 ms, TR=720 ms, FOV=216 mm, flip=52˚, 715 volumes per run for a total of 1430 volumes). T_1-weighted structural scans were acquired in the sagittal plane using a magnetization-prepared rapid gradient-echo (MP-RAGE) three-dimensional sequence (TR=2400 ms, TE=2.22 ms, flip angle=8°, 166 slices, field of view=300 x 320 mm, voxel size=0.8x0.8x0.8 mm). Functional magnetic resonance imaging data were run though the Human Connectome Project minimal preprocessing pipelines (6,7). Functional data were corrected for PRISMA scanner gradient distortions, readout distortions and bias field correction using opposing pair spin-echo field maps and rigid body alignment to a single band reference image. Data were co-registered to within subject T1 and resampled to MNI152 2mm istotropic voxels using a single-step resample. Data were finally normalized to a grand mean of 10000. Further preprocessing and analysis was conducted using Analysis of Functional Neuroimages (AFNI) (8). Spatial smoothing with a 6-mm smoothing kernel (FWHM) and linear trend removal were conducted. Each participant's fMRI data was quality controlled by assessing activation in M1 (Brodmann's area 4) to the beginning of the trial while they selected either 'high' or 'low', and in V1 (Brodmann's area 17) to mean activation across all types of cues and across all types of outcomes to assure proper alignment of functional scans with anatomical scans. Percent of relative root mean square (RMS) realignment estimates >0.3 and relative RMS mean (mm) were extracted. Participants with greater than 0.20 root mean square (RMS) realignment estimates were excluded from all analyses (n=8). Cluster contiguity was defined as voxels sharing a face (NN=1 in AFNI) with positive and negative clusters separated ("bisided" in AFNI).

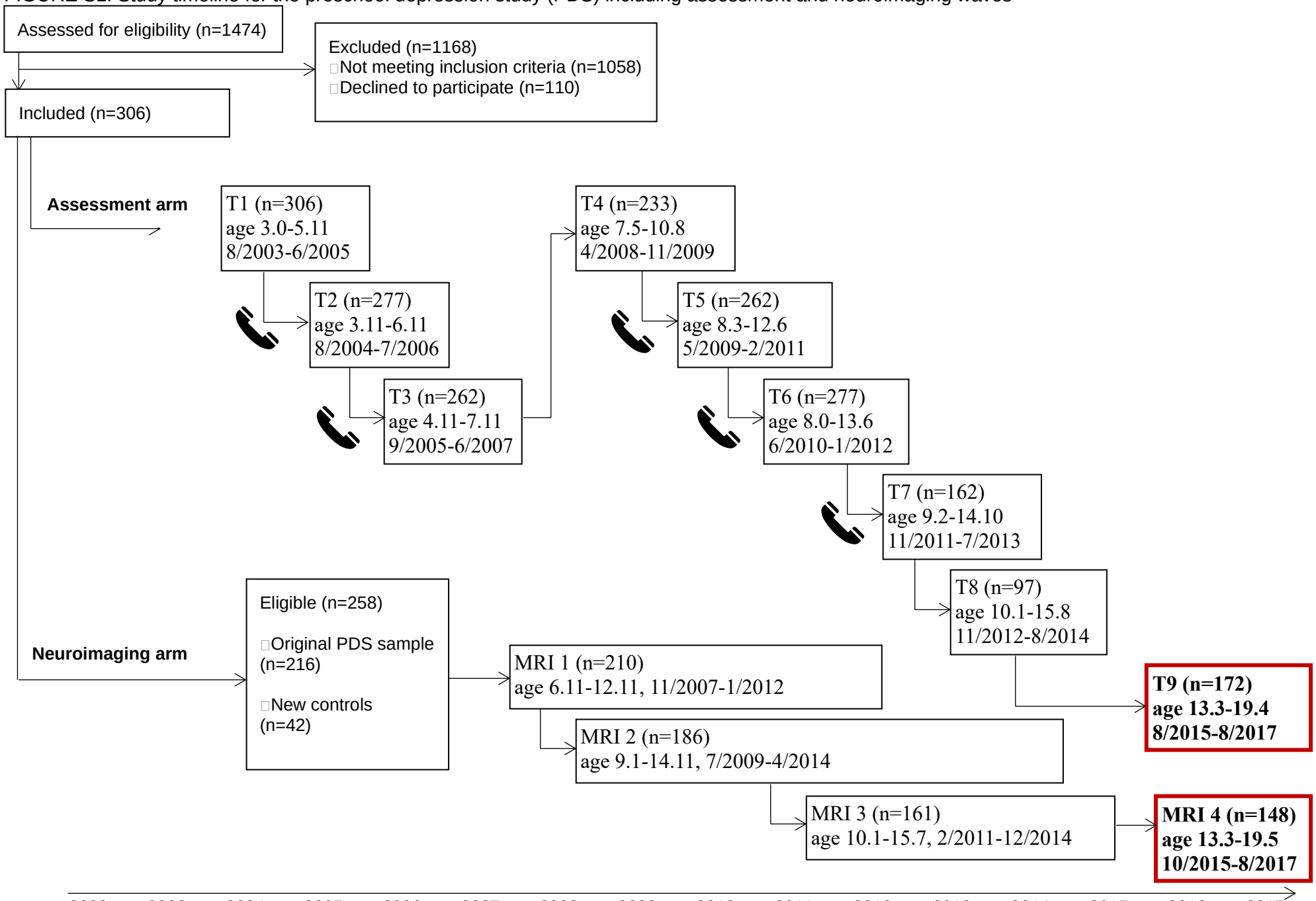
Psychotropic Medications

Use of psychotropic medications in the past 48 hours was added to analyses to determine whether results changed substantially, but was not entered as a covariate in the initial analyses due to concerns that it would overcorrect for participants experiencing severe levels of depression, who are more likely to be using psychotropic medications to manage their symptoms. In fact, both current and cumulative depression severity significantly related to use of psychotropic medications (β = 0.139, 95% CI = (0.088, 0.190), $p < 0.001$; (β = 0.120, 95% CI = (0.068, 0.171), $p < 0.001$, respectively). Findings did not meaningfully differ when accounting for psychotropic medication use (Supplemental Materials Tables S5–S8 and Figure S5).

Regions of interest

The cortical ROIs were determined based on cortical parcellations from the DD Desai atlas (9): the dorsal anterior cingulate cortex (ACC) was defined as ctx_G_and_S_cingul-Ant, the rostral ACC as ctx_G_and_S_cingul-Mid-Ant, the insula as G_insular_short, S_circular_insula_ant, and S_circular_insula_sup. The subcortical ROIs were determined based on subcortical parcellations from the Talairach Daemon atlas: the caudate was defined as the Caudate Head, the putamen as the Putamen, and the nucleus accumbens as the Nucleus Accumbens (10).

FIGURE S1. Study timeline for the preschool depression study (PDS) including assessment and neuroimaging waves

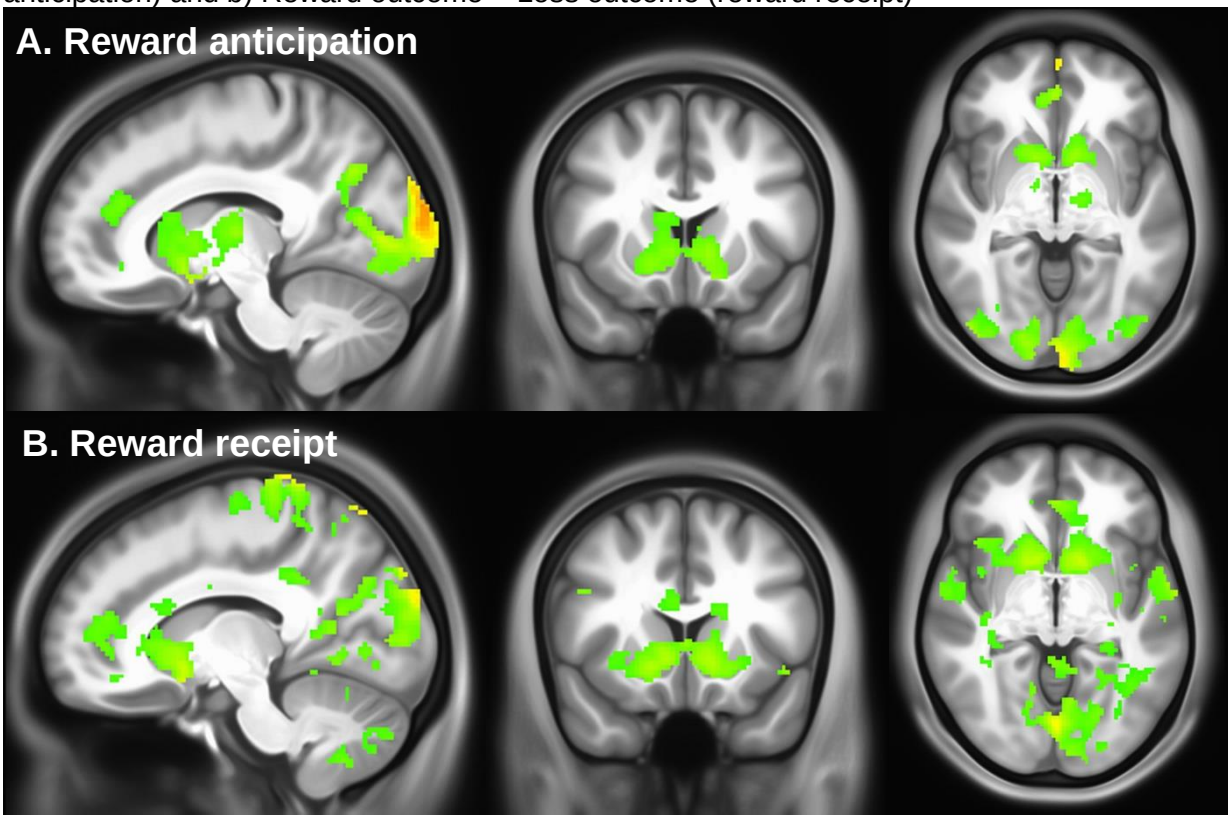


Phone icon indicates when semi-annual wave was conducted between formal annual behavioral assessments. In cases when subjects participated in an MRI but not a recent behavioral assessment, depression symptoms were assessed on the day of the MRI in the same manner as in the behavioral assessment (i.e., a semi-structured interview). As depicted, there were up to 14 possible assessment waves when depression symptoms were collected using semi-structured interviews (i.e. PAPA, CAPA, or KSADS). Reward task was collected at MRI 4 and current depression severity (CDI-2) at the concurrent Behavioral assessment T9.

SUPPLEMENTAL RESULTS

Head motion (i.e. mean relative root mean square of realignment estimates) was significantly associated with average response to reward receipt in the rACC (p = 0.050) and cumulative depression severity (p = 0.046); however motion was not significantly associated with average response in all others ROIs for reward feedback and reward anticipation, and not significantly associated with current, preschool, school age, and adolescent depression severity.

FIGURE S2. Average group-level BOLD response to a) Win cue > Lose cue (reward anticipation) and b) Reward outcome > Loss outcome (reward receipt)



Blood-oxygen-level-dependent (BOLD) response overlaid on T1-weighted structural brain image. Images are centered at x=12, y=14, z=-4 (MNI coordinates).

Depression severity and neural response to reward receipt

See Table S1 for associations between cortico-striatal circuit and ROIs and depression severity. See Table S2 for whole brain associations between BOLD signal to reward receipt and current depression severity. Whole brain analyses did not reveal any significant clusters of activation during reward receipt that were correlated with cumulative depression severity.

Associations between depression severity during distinct developmental periods and neural response to reward anticipation

Analyses of the subsample followed since preschool were mostly consistent with those of analyses of the full sample, with two exceptions: school age depression severity no longer predicted mean activity in the cortico-striatal circuit, caudate, or putamen (see Table S10). Analyses that included psychotropic medication as a covariate were consistent with those of analyses of the full sample, with two exceptions: school age depression severity no longer predicted mean activity in the caudate or putamen (see Table S7).

Result for brain response to reward receipt

TABLE S1. Current and cumulative depression severity predicting BOLD response to reward receipt in *a priori* ROIs in the full sample

		Regions of Interest						
		Cortico-striatal	**NAcc**	**Caudate**	**Putamen**	**Insula**	**dACC**	**rACC**
Current	β	-0.053	-0.039	-0.071	0.014	-0.077	-0.062	-0.027
	95% CI	-0.235, 0.130	-0.219, 0.141	-0.254, 0.112	-0.167, 0.196	-0.258, 0.104	-0.248, 0.125	-0.211, 0.156
	p	0.568	0.877	0.877	0.877	0.877	0.877	0.877
Cumulative	β	-0.020	-0.072	-0.072	0.102	-0.030	-0.024	0.019
	95% CI	-0.201, 0.160	-0.249, 0.105	-0.252, 0.108	-0.078, 0.281	-0.213, 0.154	-0.208, 0.160	-0.164, 0.201
	p	0.823	0.841	0.841	0.841	0.841	0.841	0.841

β represent standardized regression coefficient estimates; *p* values for individual ROIS (i.e. not cortico-striatal) are FDR corrected for multiple comparisons. Associations at $p < .05$ bolded. Covariates of non-interest included in all models.

TABLE S2. Current depression severity associations with BOLD signal to reward receipt in whole brain analysis

Brain region	**Cluster Size (# of 2mm^3 voxels)**	**MNI coordinates**		
		x	y	z
Current depression severity				
Right precentral gyrus	105	-48	-16	60
Left precuneus	72	-26	-42	42
Right superior frontal gyrus	66	26	58	-2
Left precentral gyrus	34	-44	-12	50
Left precentral gyrus	30	-38	-22	52
Left superior temporal gyrus	24	-52	-10	4
Left middle temporal gyrus	23	-52	-70	12
Right cingulate gyrus	23	26	-36	42
Left thalamus	18	-14	-24	2
Right middle temporal gyrus	14	50	-66	6
Left superior temporal gyrus/insula	11	-50	-38	16
Left uncus	10	-30	-8	-40
Right parahippocampal gyrus	10	44	-20	-20
Left postcentral gyrus	10	-28	-24	36

MNI coordinates correspond to peak activation within each cluster. Clusters significant at $p < .005$ (uncorrected) and at least 10 voxels. c– clusters showing positive correlations with depression severity

Results for brain response to reward anticipation

TABLE S3. Separate analyses for current, cumulative, preschool, school age, and adolescent depression severity predicting BOLD response to reward anticipation in the full sample

		Regions of Interest						
		Cortico-striatal	**NAcc**	**Caudate**	**Putamen**	**Insula**	**dACC**	**rACC**
Current	β	-0.136	**-0.296**	-0.181	-0.095	-0.002	0.033	-0.043
	95% CI	-0.312, 0.040	**-0.470, -0.122**	-0.355, -0.007	-0.270, 0.081	-0.184, 0.180	-0.148, 0.214	-0.226, 0.140
	p	0.129	**0.006**	0.126	0.576	0.984	0.864	0.864
Cumulative	β	**-0.304**	**-0.278**	**-0.274**	**-0.250**	-0.180	**-0.256**	**-0.207**
	95% CI	**-0.481, -0.128**	**-0.457, -0.100**	**-0.452, -0.097**	**-0.428, -0.071**	-0.361, 0.002	**-0.434, -0.077**	**-0.388, -0.027**
	p	**0.001**	**0.008**	**0.008**	**0.010**	0.052	**0.010**	**0.030**
Preschool	β	**-0.178**	-0.099	**-0.138**	**-0.187**	**-0.129**	**-0.160**	**-0.154**
	95% CI	**-0.297, -0.06**	-0.221, 0.022	**-0.257, -0.019**	**-0.306, -0.068**	**-0.251, -0.006**	**-0.281, -0.039**	**-0.276, -0.033**
	p	**0.004**	0.107	**0.036**	**0.015**	**0.047**	**0.026**	**0.026**
School Age	β	**-0.172**	-0.134	**-0.168**	**-0.168**	-0.099	-0.135	-0.123
	95% CI	**-0.306, -0.039**	-0.268, -0.001	**-0.299, -0.036**	**-0.299, -0.037**	-0.236, 0.037	-0.271, 0.000	-0.259, 0.014
	p	**0.012**	0.074	**0.038**	**0.038**	0.151	0.074	0.093
Adolescent	β	**-0.151**	**-0.185**	-0.135	-0.086	-0.070	-0.111	-0.106
	95% CI	**-0.274, -0.029**	**-0.307, -0.064**	-0.258, -0.012	-0.210, 0.038	-0.195, 0.055	-0.234, 0.013	-0.23, 0.018
	p	**0.016**	**0.019**	0.094	0.208	0.270	0.139	0.139

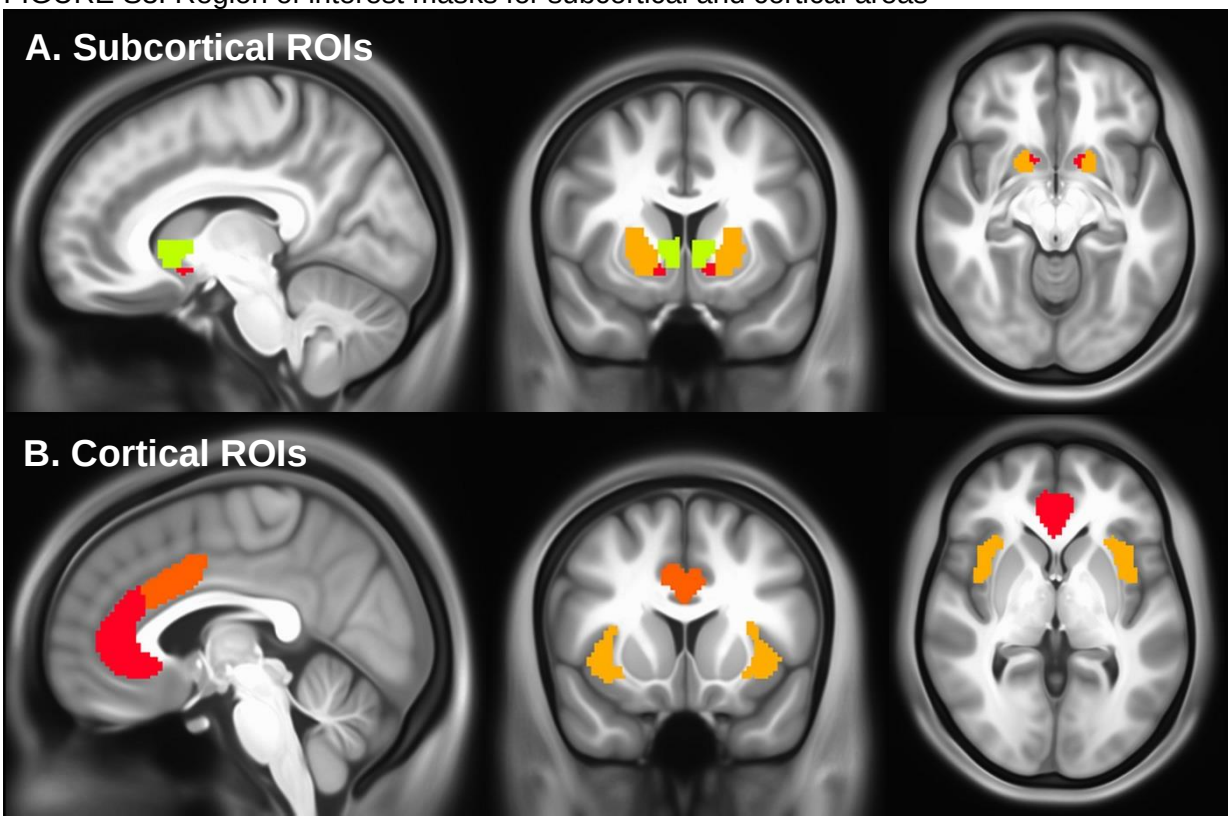
β represent standardized regression coefficient estimates; *p* values for individual ROIs (i.e. not cortico-striatal) are FDR corrected for multiple comparisons. Associations at $p < .05$ bolded. Covariates of non-interest included in all models.

TABLE S4. Preschool, school age, and adolescent depression severity simultaneously (i.e., in same model) predicting BOLD response to reward anticipation in the subsample followed since preschool

Regions of Interest	Developmental period	β	95% CI	*p*
Cortico-striatal Circuit	**Preschool**	**-0.156**	**-0.3, -0.012**	**0.034**
	School Age	-0.003	-0.174, 0.168	0.972
	Adolescence	-0.104	-0.239, 0.031	0.129
Nucleus accumbens	Preschool	-0.064	-0.21, 0.081	0.381
	School Age	-0.008	-0.181, 0.165	0.928
	Adolescence	**-0.154**	**-0.29, -0.018**	**0.027**
Caudate	Preschool	-0.105	-0.25, 0.041	0.156
	School Age	-0.035	-0.208, 0.138	0.687
	Adolescence	-0.078	-0.215, 0.058	0.256
Putamen	**Preschool**	**-0.176**	**-0.322, -0.029**	**0.019**
	School Age	-0.011	-0.186, 0.164	0.901
	Adolescence	-0.028	-0.166, 0.109	0.683
Insula	Preschool	-0.128	-0.278, 0.022	0.093
	School Age	0.014	-0.165, 0.193	0.876
	Adolescence	-0.036	-0.176, 0.105	0.616
Dorsal ACC	Preschool	-0.140	-0.288, 0.008	0.064
	School Age	-0.013	-0.189, 0.163	0.883
	Adolescence	-0.068	-0.206, 0.071	0.335
Rostral ACC	**Preschool**	**-0.156**	**-0.304, -0.008**	**0.040**
	School Age	0.042	-0.135, 0.218	0.642
	Adolescence	-0.094	-0.233, 0.044	0.180

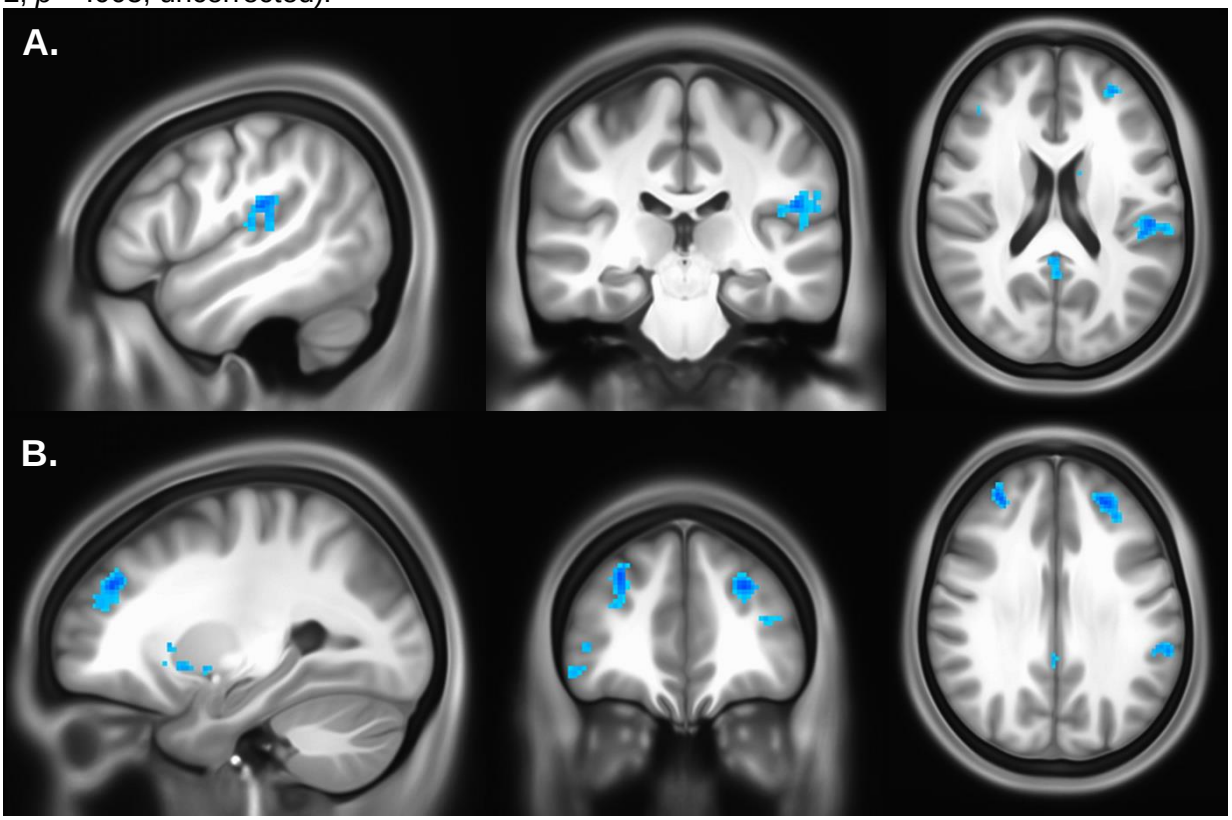
Associations at $p < .05$ bolded. Covariates of non-interest included in all models.

FIGURE S3. Region of interest masks for subcortical and cortical areas



Images in panel A are centered at x= –10, y= –10, z= –10, and images in panel B are centered at x= –4, y= –13, z= 1 (radiological coordinates). Panel A: yellow-green–caudate, pink–nucleus accumbens, gold–putamen. Panel B: pink–rostral ACC, orange–dorsal ACC; gold–insula

FIGURE S4. BOLD response to reward anticipation in striatum associated with cumulative depression severity in the full sample from whole brain analysis (clusters not depicted in Figure 2; $p < .005$, uncorrected).



Images in panel a are centered at x = –50, y = –26, z = 20, and images in panel b are centered at x = –26, y = 42, z = 30 (MNI coordinates).

Results with Psychotropic medication included as a covariate

TABLE S5. Current and cumulative depression severity simultaneously (i.e., in same model) predicting BOLD response to reward anticipation in *a priori* ROIs in the full sample with psychotropic medication use included as a covariate

Regions of Interest	Depression severity	*β*	95% CI	*p*
Cortico-Striatal Circuit	Current	0.027	-0.184, 0.238	0.800
	Cumulative	**-0.299**	**-0.508, -0.089**	**0.006**
Nucleus accumbens	**Current**	**-0.225**	**-0.439, -0.011**	**0.039**
	Cumulative	-0.15	-0.363, 0.062	0.164
Caudate	Current	-0.065	-0.277, 0.147	0.547
	Cumulative	**-0.222**	**-0.433, -0.011**	**0.039**
Putamen	Current	0.044	-0.169, 0.256	0.686
	Cumulative	**-0.245**	**-0.457, -0.034**	**0.024**
Insula	Current	0.108	-0.114, 0.329	0.337
	Cumulative	**-0.24**	**-0.46, -0.020**	**0.032**
Dorsal ACC	**Current**	**0.220**	**0.007, 0.434**	**0.043**
	Cumulative	**-0.382**	**-0.594, -0.170**	**0.001**
Rostral ACC	Current	0.126	-0.095, 0.347	0.261
	Cumulative	**-0.221**	**-0.441, -0.002**	**0.048**

Associations at $p < .05$ bolded. Covariates of non-interest included in all models.

TABLE S6. Preschool, school age, and adolescent depression severity simultaneously (i.e., in same model) predicting BOLD response to reward anticipation in *a priori* ROIs in the subsample followed since preschool with psychotropic medication use included as a covariate

Regions of Interest	Developmental period	*β*	95% CI	*p*
Cortico-striatal Circuit	**Preschool**	**-0.156**	**-0.301, -0.011**	**0.035**
	School Age	-0.002	-0.176, 0.173	0.985
	Adolescence	-0.101	-0.249, 0.047	0.177
Nucleus accumbens	Preschool	-0.065	-0.211, 0.082	0.383
	School Age	-0.007	-0.183, 0.170	0.940
	Adolescence	**-0.152**	**-0.301, -0.002**	**0.047**
Caudate	Preschool	-0.105	-0.251, 0.041	0.157
	School Age	-0.031	-0.207, 0.145	0.729
	Adolescence	-0.069	-0.219, 0.080	0.358
Putamen	**Preschool**	**-0.176**	**-0.323, -0.029**	**0.020**
	School Age	-0.008	-0.186, 0.170	0.933
	Adolescence	-0.021	-0.172, 0.129	0.779
Insula	Preschool	-0.128	-0.278, 0.023	0.096
	School Age	0.005	-0.177, 0.187	0.955
	Adolescence	-0.054	-0.208, 0.100	0.488
Dorsal ACC	Preschool	-0.139	-0.287, 0.009	0.066
	School Age	-0.026	-0.205, 0.153	0.775
	Adolescence	-0.094	-0.245, 0.057	0.220
Rostral ACC	**Preschool**	**-0.157**	**-0.305, -0.009**	**0.038**
	School Age	0.059	-0.120, 0.237	0.514
	Adolescence	-0.058	-0.209, 0.093	0.444

Associations at $p < .05$ bolded. Covariates of non-interest included in all models.

TABLE S7. Independent regressions with current, cumulative, preschool, school age, and adolescent depression severity predicting BOLD response to reward anticipation in *a priori* ROIs in the full sample with psychotropic medication use included as a covariate

		Regions of Interest						
		Cortico-striatal	**NAcc**	**Caudate**	**Putamen**	**Insula**	**dACC**	**rACC**
Current	β	-0.100	**-0.289**	-0.159	-0.061	0.005	0.058	0.032
	95% CI	-0.297, 0.096	**-0.484, -0.094**	-0.354, 0.036	-0.257, 0.136	-0.198, 0.209	-0.145, 0.261	-0.171, 0.235
	p	0.315	**0.024**	0.325	0.860	0.958	0.860	0.907
Cumulative	β	**-0.321**	**-0.277**	**-0.287**	**-0.265**	**-0.223**	**-0.307**	-0.180
	95% CI	**-0.518, -0.125**	**-0.476, -0.078**	**-0.484, -0.089**	**-0.463, -0.067**	**-0.424, -0.022**	**-0.504, -0.110**	-0.381, 0.021
	p	**0.002**	**0.013**	**0.013**	**0.014**	**0.036**	**0.013**	0.079
Preschool	β	**-0.170**	-0.088	**-0.128**	**-0.182**	**-0.132**	**-0.163**	**-0.138**
	95% CI	**-0.291, -0.050**	-0.211, 0.035	**-0.250, -0.007**	**-0.304, -0.061**	**-0.257, -0.008**	**-0.286, -0.040**	**-0.26, -0.015**
	p	**0.006**	0.161	**0.046**	**0.022**	**0.046**	**0.030**	**0.046**
School Age	β	**-0.165**	-0.121	-0.160	-0.164	-0.109	-0.147	-0.100
	95% CI	**-0.306, -0.025**	-0.261, 0.019	-0.299, -0.022	-0.302, -0.026	-0.253, 0.034	-0.289, -0.005	-0.243, 0.043
	p	**0.022**	0.136	0.070	0.070	0.160	0.086	0.169
Adolescent	β	**-0.152**	**-0.186**	-0.134	-0.078	-0.090	-0.134	-0.079
	95% CI	**-0.290, -0.014**	**-0.323, -0.049**	-0.272, 0.005	-0.217, 0.062	-0.23, 0.051	-0.273, 0.005	-0.218, 0.06
	p	**0.032**	**0.050**	0.116	0.273	0.273	0.116	0.273

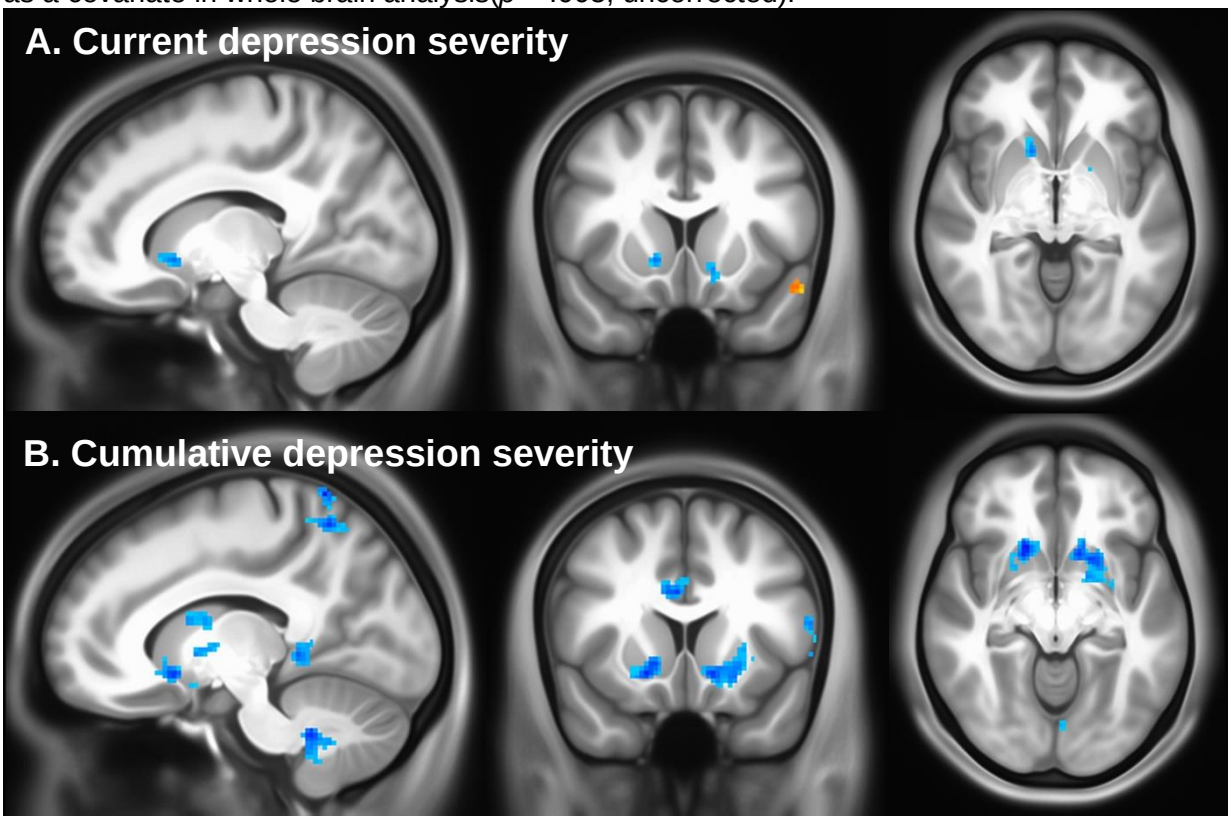
β represent standardized regression coefficient estimates; *p* values for individual ROIs (i.e. not cortico-striatal) are FDR corrected for multiple comparisons. Associations at $p < .05$ bolded. Covariates of non-interest included in all models.

TABLE S8. Current and cumulative depression severity associations in a whole brain analysis with BOLD response to reward anticipation with psychotropic medication use included as a covariate

Brain region	Cluster Size (# of 2mm^3 voxels)	MNI coordinates		
		x	y	z
Current depression severity [b]				
Right cerebellum [c]	45	26	-84	-44
Left medial frontal gyrus [c]	33	-18	-6	58
Left inferior temporal gyrus [c]	27	62	-32	-20
Right cerebellum [c]	26	54	-70	-32
Right nucleus accumbens	24	14	14	-4
Left superior temporal gyrus [c]	18	-48	14	-16
Left middle occipital gyrus [c]	16	-16	-104	16
Left medial globus pallidus	16	-18	2	-8
Right parietal lobule	16	32	-50	58
Left nucleus accumbens	15	-12	12	-8
Left medial frontal gyrus [c]	14	-12	28	-12
Left superior frontal gyrus [c]	13	-32	34	38
Left pons	13	-8	-20	-44
Right parahippocampal gyrus [c]	11	32	-14	-26
Left culmen [c]	10	-10	-32	-16
Cumulative depression severity [a]				
Right anterior cingulate [e]	680	4	12	28
Left inferior parietal lobule (insula) [e]	608	-54	-28	28
Left nucleus accumbens [e]	520	-8	6	-14
Left posterior cingulate [e]	505	-2	-44	12
Right postcentral gyrus	273	46	-40	60
Right postcentral gyrus	268	62	-20	38
Right cuneus	236	18	-76	12
Left cerebellum	226	-20	-40	-40
Left postcentral gyrus	207	-12	-54	72
Left postcentral gyrus	189	-42	-42	64
Right caudate	187	16	20	-4
Left inferior frontal gyrus	164	-54	12	14

MNI coordinates correspond to peak activation within each cluster. a– cumulative depression severity cluster significant at $p < .005$ (uncorrected) and at least 150 voxels; b– current depression severity clusters significant at $p < .005$ (uncorrected) and at least 10 voxels. c– clusters showing positive correlations with depression severity; e- clusters significant at corrected $p < .05$

FIGURE S5. BOLD response to reward anticipation in striatum associated with cumulative depression severity and current depression severity with psychotropic medication use included as a covariate in whole brain analysis($p < .005$, uncorrected).



Images in panel A are centered at x= 14, y= 14, z= -4, and images in panel B are centered at x= -12, y= 14, z= -8 (MNI coordinates).

Results in the subsample followed since preschool

TABLE S9. Current and cumulative depression severity simultaneously (i.e., in same model) predicting BOLD response to reward anticipation in *a priori* ROIs in the subsample followed since preschool

Regions of Interest	Depression severity	*β*	95% CI	*p*
Cortico-Striatal Circuit	Current	0.060	-0.147, 0.266	0.566
	Cumulative	**-0.340**	**-0.559, -0.121**	**0.003**
Nucleus accumbens	**Current**	**-0.223**	**-0.433, -0.013**	**0.038**
	Cumulative	-0.137	-0.360, 0.086	0.225
Caudate	Current	-0.03	-0.237, 0.177	0.775
	Cumulative	**-0.239**	**-0.459, -0.019**	**0.033**
Putamen	Current	0.092	-0.118, 0.302	0.385
	Cumulative	**-0.298**	**-0.521, -0.075**	**0.009**
Insula	Current	0.136	-0.084, 0.357	0.224
	Cumulative	**-0.246**	**-0.480, -0.012**	**0.039**
Dorsal ACC	**Current**	**0.259**	**0.047, 0.472**	**0.017**
	Cumulative	**-0.407**	**-0.632, -0.182**	**0.001**
Rostral ACC	Current	0.126	-0.093, 0.346	0.256
	Cumulative	**-0.318**	**-0.55, -0.085**	**0.008**

Associations at $p < .05$ bolded. Covariates of non-interest included in all models.

TABLE S10. Independent regressions with cumulative, current, preschool, school age, and adolescent depression severity predicting BOLD response to reward anticipation in *a priori* ROIs in the subsample followed since preschool

		Regions of Interest						
		Cortico-striatal	**NAcc**	**Caudate**	**Putamen**	**Insula**	**dACC**	**rACC**
Current	β	-0.099	**-0.287**	-0.141	-0.047	0.021	0.069	-0.022
	95% CI	-0.285, 0.088	**-0.470, -0.104**	-0.325, 0.042	-0.234, 0.141	-0.174, 0.216	-0.125, 0.264	-0.218, 0.174
	p	0.297	**0.015**	0.386	0.828	0.828	0.828	0.828
Cumulative	β	**-0.318**	**-0.265**	**-0.268**	**-0.264**	-0.184	**-0.273**	**-0.249**
	95% CI	**-0.516, -0.120**	**-0.465, -0.065**	**-0.467, -0.069**	**-0.468, -0.061**	-0.391, 0.022	**-0.477, -0.07**	**-0.454, -0.044**
	p	**0.002**	**0.017**	**0.017**	**0.017**	0.080	**0.017**	**0.021**
School Age	β	-0.140	-0.101	-0.130	-0.137	-0.083	-0.128	-0.092
	95% CI	-0.281, 0.000	-0.243, 0.040	-0.270, 0.009	-0.279, 0.006	-0.227, 0.062	-0.271, 0.015	-0.237, 0.052
	p	0.051	0.238	0.159	0.159	0.259	0.159	0.248
Adolescent	β	**-0.142**	-0.172	-0.113	-0.073	-0.062	-0.105	-0.120
	95% CI	**-0.273, -0.011**	-0.301, -0.043	-0.244, 0.017	-0.208, 0.061	-0.197, 0.073	-0.238, 0.029	-0.253, 0.014
	p	**0.034**	0.057	0.177	0.340	0.363	0.187	0.177

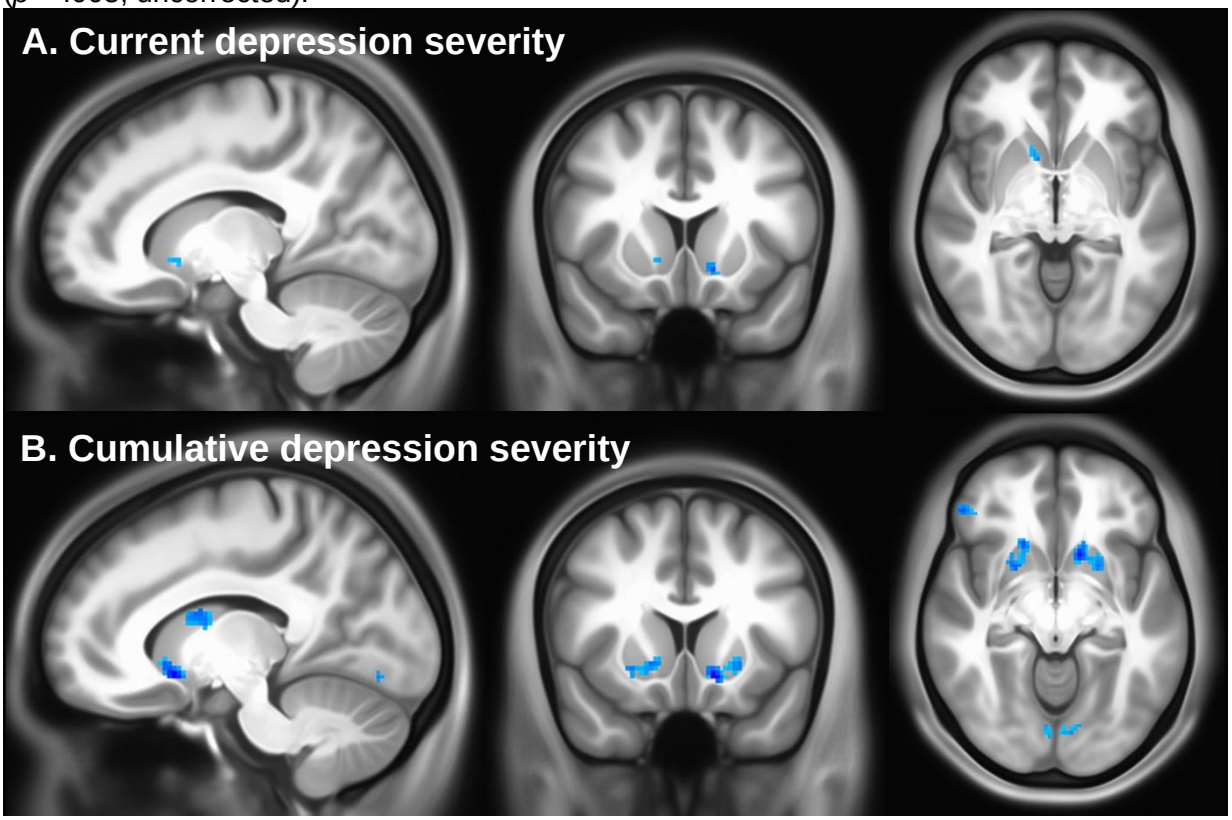
β represent standardized regression coefficient estimates; *p* values for individual ROIs (i.e. not cortico-striatal) are FDR corrected for multiple comparisons. Associations at $p < .05$ bolded. Covariates of non-interest included in all models. Preschool developmental period not included because model only included participants that had been followed since preschool, and therefore results are identical to those in Table S3.

TABLE S11. Current and cumulative depression severity associations in a whole brain analysis with BOLD response to reward anticipation in the subsample followed since preschool using mask of clusters from full sample

Brain region	**Cluster Size (# of 2mm^3 voxels)**	**MNI coordinates**		
		x	y	z
Current depression severity [b]				
Left cuneus [c,d]	35	-14	-102	16
Left middle frontal gyrus [c,d]	28	-16	-0	62
Right nucleus accumbens [d]	20	10	10	-4
Right inferior temporal gyrus [c]	17	62	-32	-22
Left nucleus accumbens [d]	17	-12	14	-8
Left medial frontal gyrus [c]	13	-18	-8	58
Left pons	11	-8	-20	-46
Cumulative depression severity [a]				
Left inferior parietal lobule/insula	210	-56	-36	32
Left nucleus accumbens	163	-12	14	-10
Right lingual gyrus	148	6	-72	-2
Right putamen	146	18	20	-6
Right middle frontal gyrus	142	50	40	-4
Left superior frontal gyrus	124	-28	42	30
Right middle frontal gyrus	106	24	56	24
Left caudate	59	-10	6	16

MNI coordinates correspond to peak activation within each cluster. a– cumulative depression severity cluster significant at $p < .005$ (uncorrected) and at least 50 voxels; b– current depression severity clusters significant at $p < .01$ (uncorrected) and at least 10 voxels. c– clusters showing positive correlations with depression severity. d– current depression severity clusters significant at $p < .005$ (uncorrected) and at least 10 voxels.

FIGURE S6. BOLD response to reward anticipation in striatum associated with cumulative depression severity and current depression severity in the subsample followed since preschool ($p < .005$, uncorrected).



Images in panel A are centered at x= 14, y= 14, z= -4, and images in panel B are centered at x= -12, y= 14, z= -8 (MNI coordinates).

Whole brain analyses using equitable thresholding and clustering (ETAC) (11)

FIGURE S7. BOLD response to reward anticipation in striatum associated with cumulative depression severity and current depression severity from ETAC analyses

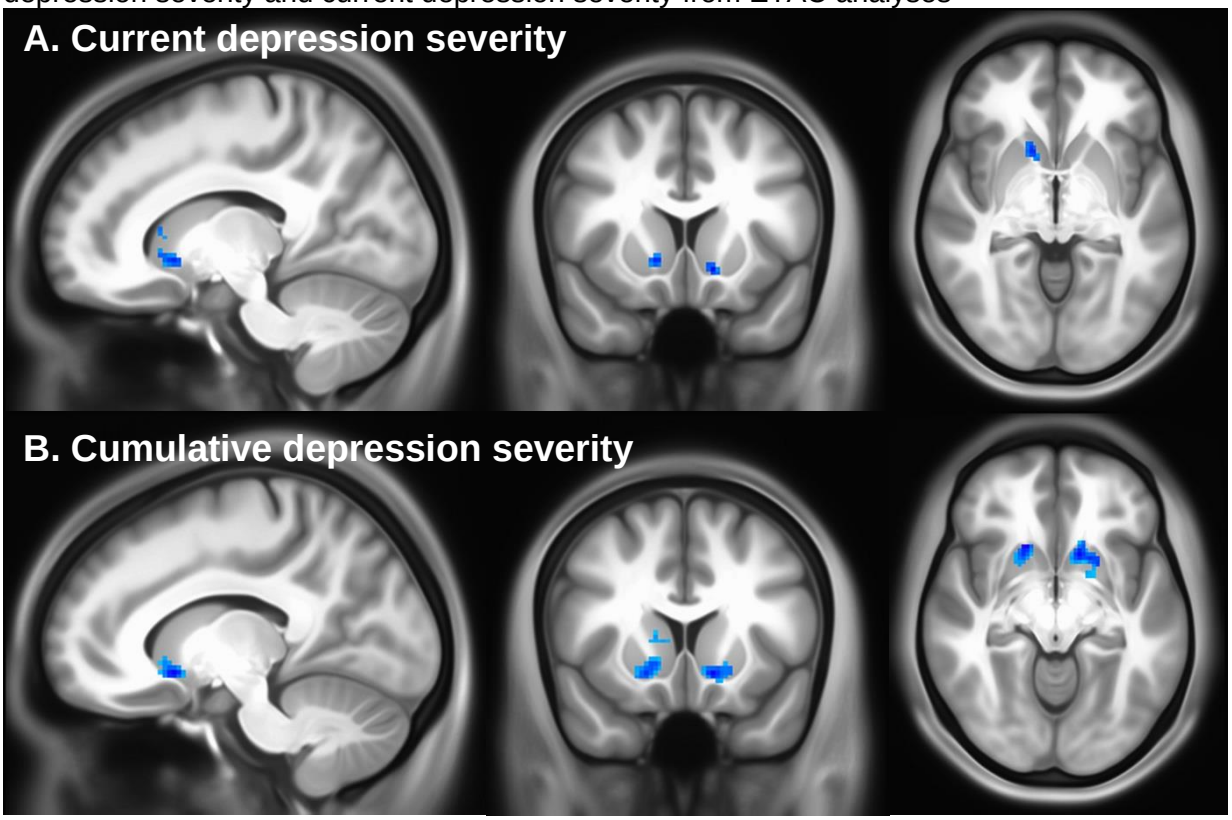


TABLE S12. Current and cumulative depression severity associations in a whole brain analysis with BOLD response to reward anticipation from ETAC analyses

Brain region	**Cluster Size (# of 2mm^3 voxels)**	**MNI coordinates**		
		x	y	z
Current depression severity [a]				
Right ventral striatum	35	14	14	-4
Left cuneus [c]	25	-14	-100	16
Left ventral striatum	19	-12	12	-8
Cumulative depression severity [b]				
Left ventral striatum	153	-12	14	-8
Right putamen	102	18	18	-8
Cingulate gyrus	58	0	-42	26
Right caudate	27	10	16	6
Right putamen	25	22	0	14
Left caudate	24	-2	12	0

MNI coordinates correspond to peak activation within each cluster. a– current depression severity clusters significant at $p < .005$ and at least 10 voxels; b– cumulative depression severity cluster significant at $p < .005$ and at least 20 voxels; c– clusters showing positive correlations with depression severity. All cluster significant using equitable thresholding and clustering method (ETAC).

MANCOVA ANALYSES

Cue type x Current and Cumulative depression severity interactions

Cue Type x Current and Cumulative depression severity

To test for differential associations between depression severity and BOLD to the four different cue types (Win, Lose, Mixed, Neutral), a MANCOVA was conducted that included both cumulative and current depression severity, as well as other covariates of non-interest (age, sex, race, SES). This MANCOVA revealed a significant Cue Type x Cumulative depression interaction for the cortico-striatal circuit ($F(3,119) = 3.06$, $p = 0.031$), and then in follow-up analyses the putamen ($F(3, 119) = 2.78$, $p = 0.044$), and dorsal ACC ($F(3, 119) = 4.61$, $p = 0.004$). The MANCOVA's for caudate and rostral ACC were trend level ($F(3,119) = 2.08$, $p = 0.107$; $F(3,119) = 2.31$, $p = 0.080$, respectively). The same MANCOVA revealed no significant Cue Type x Current depression interactions for the ROIs, though this interaction for the nucleus accumbens was approaching significance ($F(3, 119) = 2.56$, $p = 0.059$). Thus, these MANCOVA results are highly consistent with the multiple regression results for the cortical-striatal circuit, the putamen, the dorsal ACC and to some extent the nucleus accumbens, with partial support for the caudate and rACC.

Cue Type x Cumulative depression severity

Another MANCOVA only including cumulative depression and covariates of non-interest revealed a significant Cue Type x Cumulative depression interaction for the cortico-striatal circuit ($F(3,122) = 3.90$, $p = 0.011$) as a whole, and in follow-up analyses, the caudate ($F(3,122) = 3.60$, $p = 0.016$), putamen ($F(3,122) = 3.14$, $p = 0.028$), nucleus accumbens ($F(3,122) = 3.23$, $p = 0.025$), and dorsal ACC ($F(3,122) = 2.84$, $p = 0.041$), but not the insula ($F(3,122) = 1.48$, $p = 0.224$) or rostral ACC ($F(3,122) = 2.37$, $p = 0.074$). These results are consistent with the MANCOVA model that included both current and cumulative depression. Further they are consistent with the regression analyses reported in the main text other than for the rostral ACC, which was trend level in the MANCOVA analyses, but significant in the regressions.

Cue Type x Current depression severity

Another MANCOVA only including current depression and covariates of non-interest revealed a significant Cue Type x Current depression interaction only for the nucleus accumbens ($F(3,122) = 4.84$, $p = 0.003$), and not for the cortico-striatal circuit ($F(3,122) = 0.82$, $p = 0.483$), caudate ($F(3,122) = 1.493$, $p = 0.220$), putamen ($F(3,122) = 0.385$, $p = 0.764$), insula ($F(3,122) = 0.095$, $p = 0.963$), dorsal ACC ($F(3,122) = 0.155$, $p = 0.927$), or rostral ACC ($F(3,122) = 1.609$, $p = 0.191$). There were no significant main effects of cumulative depression for any of the ROIs. Again, these results are generally consistent with the MANCOVA model that included both current and cumulative depression. Further they are consistent with the regression analyses reported in the main text.

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