

S1 Text

Computational phenotyping of brain-behavior dynamics underlying approach-avoidance in major depressive disorder

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Supplementary Methods

Sample information

Participants were right-handed, reported no medical or neurological illnesses and no current use of psychotropic medications. Healthy controls reported no current or past psychopathology. All participants were assessed by a clinician using the Structured Clinical Interview for the DSM-IV (SCID; (1)) and the Hamilton Depression Rating Scale (HAM-D; (2)). Participants were compensated \$15/hour for their time, \$50 for the MRI session and a \$50 completion bonus.

During the initial screening visit, after the SCID, participants completed a number of self-report questionnaires, including the Beck Depression Inventory (BDI-II; (3)), Snaith Hamilton Pleasure Scale (SHPS; (4)), the Cognitive-Behavioral Avoidance Scale (CBAS; (5)), the Mood and Anxiety Symptom Questionnaire (MASQ; (6)) and the Perceived Stress Scale (PSS; (7)) in order to assess, respectively, depressive symptoms, anhedonic symptoms, behavioral avoidance, subtypes of depressive and anxious symptoms, and perceived stress.

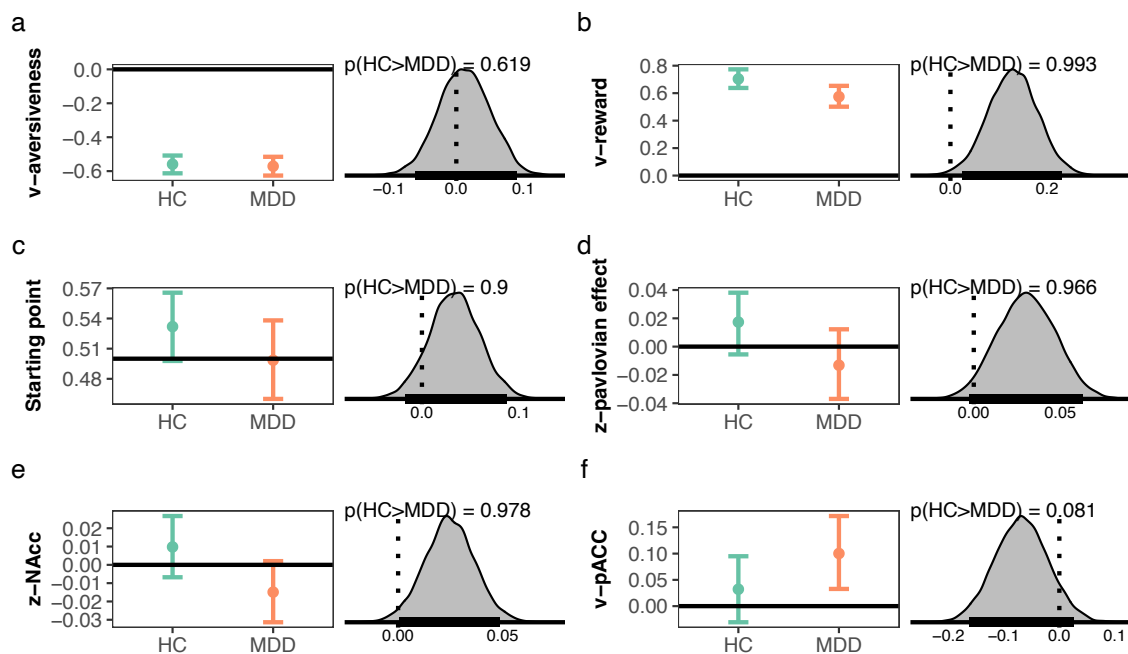


Fig A. Selected results from the computational mixed-effect model. For each coefficient the left plot shows the group posterior distribution for healthy controls (HC) and individuals with major depressive disorder (MDD). The right plot shows the posterior distribution of difference as a measure of the effect of group on each coefficient, and the probability given data that the coefficient is higher in HC than MDD. **A**, weight of aversiveness onto drift rate (v), **B**, weight of reward onto drift rate (v), **C**, estimated relative starting point (z) between

decision thresholds, **D**, impact of Pavlovian effect onto starting point (z), **E**, impact of activity in nucleus accumbens (NAcc) onto starting point (z), **F**, impact of activity in the pACC onto drift rate (v). The results from the mixed-effect model here overlap with the results from the model in Figure 3, in which the two groups were estimated separately.

Table A. Description and fit of tested models.

Model	Reward	Averse	Dreward	Daverse	Conflict	PavlovianBias	DIC
baseline	linear	linear	no	no	no	no	7544
Log(reward)	log	linear	no	no	no	no	7214
Log(averse)	linear	log	no	no	no	no	7569
Dreward	linear	linear	yes	no	no	no	7023
Daverse	linear	linear	no	yes	no	no	7553
Conflict	linear	linear	no	no	yes	no	7501
PavlovianBias	linear	linear	no	no	no	yes	7542
Combined	log	linear	yes	no	yes	yes	6949

Model comparison was performed by comparing a baseline model to a model in which one ‘component’ was modified. The model we report from includes all the ‘components’ that improved fit compared to the baseline model. The function of the impact of reward and aversiveness onto drift rate was assumed to be linear or logarithmic, and were assessed on whether model fit was improved when including a dummy coded variable that indicated whether the offered value of reward (Dreward) or aversiveness (Daverse) was 0 (D=1) or not (D=0). Conflict was measured as the absolute difference in reward and aversiveness and was estimated to influence the decision threshold parameter. PavlovianBias included information on whether approaching (avoiding) offers involved pushing (pulling) the joystick to respond (PavlovianBias = 1) or vice-versa (PavlovianBias = 0). Lower values of DIC indicate better fit to data. DIC = deviance information criterion.

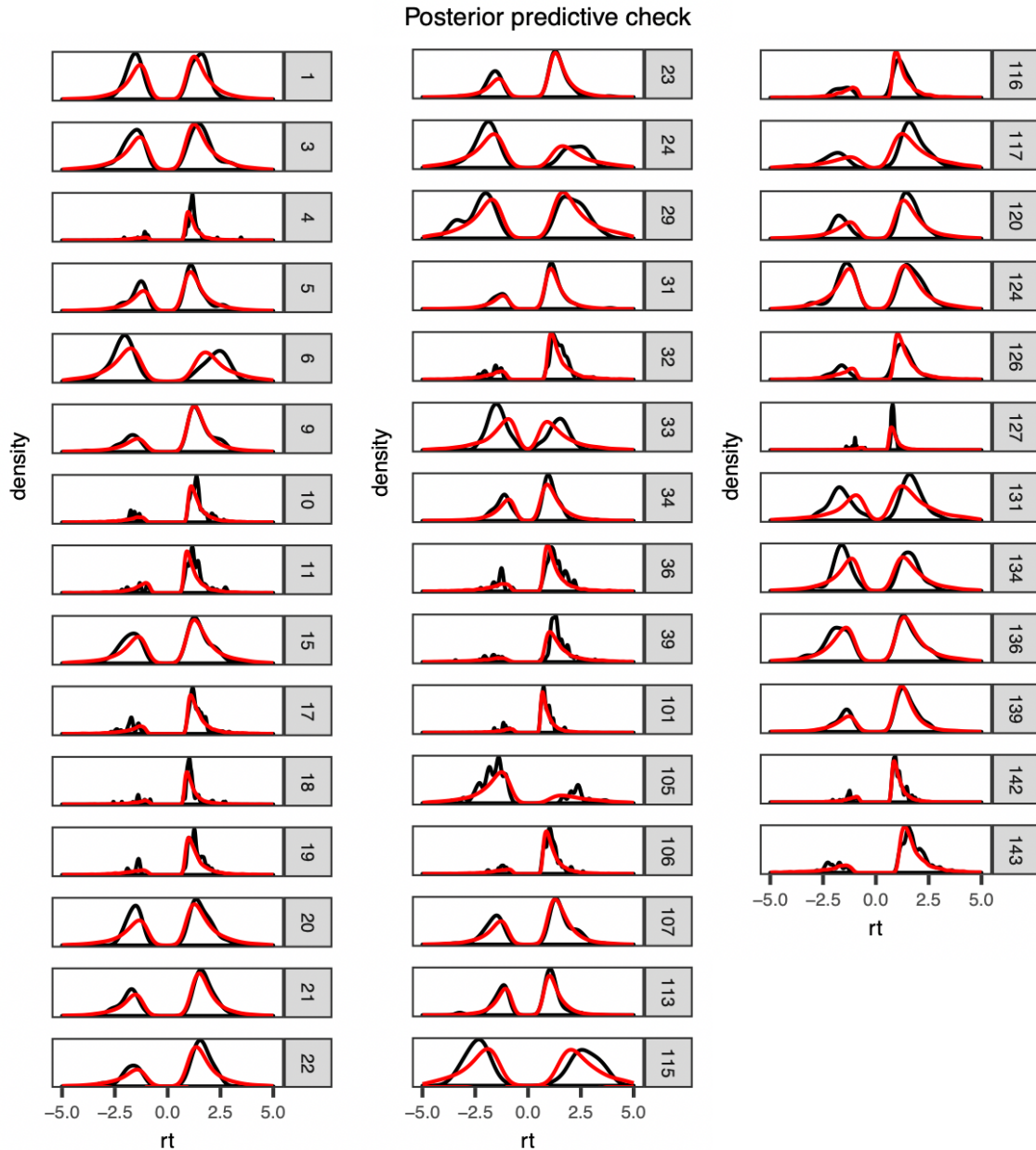


Fig B. Observed (black) and predicted (red) response time distributions across subjects. Avoid-decisions are set to be negative to separate RT distributions for decisions to approach and avoid.

Table B. Posterior distributions for group parameters at follow-up.

parameter	coefficient	Follow up						Original	
		HC			MDD			p(HC>MDD)	p(HC>MDD)
		mean	lower	upper	mean	lower	upper		
threshold (a)	Intercept	2.254	2.027	2.480	2.057	1.868	2.254	0.906	0.467
	conflict	0.219	0.139	0.301	0.119	0.027	0.198	0.955	0.772
non-decision time (t)	Intercept	0.806	0.709	0.919	0.774	0.622	0.935	0.642	0.882
drift rate (v)	Intercept	0.615	0.336	0.855	0.674	0.154	1.183	0.414	0.305
	reward	0.903	0.830	0.982	0.699	0.600	0.800	0.999	0.990
	aversiveness	-0.727	-0.787	-0.662	-0.457	-0.534	-0.373	0.000	0.575
	Dreward	-0.579	-0.780	-0.385	-0.711	-0.974	-0.418	0.762	0.180
starting point bias (z)	Intercept	0.520	0.497	0.540	0.536	0.505	0.571	0.217	0.972
	Pavlovian bias	0.044	0.020	0.066	0.027	-0.003	0.061	0.820	0.971

Lower and upper represent the lower and upper bound of the 95% highest density interval of the posterior distribution. For comparison to results from the original dataset, the rightmost column represents probabilities of group difference from original dataset.

Table C. Multivariate regression for association between clinical measures collected at time of testing and at 6-month follow-up to decision parameters.

BDI (Beck's Depression Inventory)				
<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	44.08	20.97 – 67.19	4.20	0.001
starting_point	14.79	-21.09 – 50.67	0.91	0.384
drift_rate_reward	-10.56	-33.16 – 12.04	-1.03	0.326
starting_point_pavlovian_bias	-26.76	-179.16 – 125.65	-0.39	0.707
starting_point_accumbens	643.41	-1104.28 – 2391.10	0.81	0.435
drift_rate_pACC	-85.98	-356.87 – 184.90	-0.70	0.499
Observations	17			
R ² / R ² adjusted	0.238 / -0.109			

MASQ_AA (Mood and Anxiety Symptom Questionnaire – Anxious Arousal)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	33.23	14.22 – 52.24	3.81	0.002
starting_point	4.18	-27.26 – 35.62	0.29	0.777
drift_rate_reward	-12.82	-34.22 – 8.58	-1.31	0.216
starting_point_pavlovian_bias	33.40	-111.22 – 178.02	0.50	0.624
starting_point_accumbens	-283.20	-1749.36 – 1182.97	-0.42	0.681
drift_rate_pACC	36.93	-184.07 – 257.94	0.36	0.722
Observations	18			
R ² / R ² adjusted	0.128 / -0.235			

**MASQ_GDD (Mood and Anxiety Symptom
Questionnaire – General Distress Depression)**

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	53.43	31.36 – 75.51	5.33	<0.001
starting_point	21.03	-15.87 – 57.94	1.25	0.236
drift_rate_reward	-18.78	-43.92 – 6.36	-1.64	0.128
starting_point_pavlovian_bias	-12.84	-180.67 – 154.98	-0.17	0.869
starting_point_accumbens	119.68	-1664.83 – 1904.20	0.15	0.885
drift_rate_pACC	12.01	-267.30 – 291.32	0.09	0.926
Observations	17			
R ² / R ² adjusted	0.331 / 0.027			

**MASQ_AD (Mood and Anxiety Symptom
Questionnaire – Anhedonic Depression)**

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	96.46	72.11 – 120.81	8.63	<0.001

starting_point	3.65	-36.63 – 43.93	0.20	0.847
drift_rate_reward	-13.00	-40.41 – 14.41	-1.03	0.322
starting_point_pavlovian_bias	-11.70	-196.96 – 173.55	-0.14	0.893
starting_point_accumbens	-98.23	-1976.32 – 1779.86	-0.11	0.911
drift_rate_pACC	11.37	-271.72 – 294.47	0.09	0.932
Observations	18			
R ² / R ² adjusted	0.123 / -0.242			

HAMD (Hamilton Depression Rating Scale)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	13.61	3.94 – 23.28	3.07	0.010
starting_point	-5.12	-21.12 – 10.88	-0.70	0.499
drift_rate_reward	0.72	-10.17 – 11.60	0.14	0.888
starting_point_pavlovian_bias	-7.05	-80.63 – 66.53	-0.21	0.838
starting_point_accumbens	-109.87	-855.84 – 636.10	-0.32	0.754
drift_rate_pACC	20.64	-91.80 – 133.09	0.40	0.696
Observations	18			
R ² / R ² adjusted	0.049 / -0.348			

PSS (Perceived Stress Score)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	44.47	32.51 – 56.43	8.18	<0.001
starting_point	-6.38	-23.18 – 10.41	-0.84	0.421
drift_rate_reward	-14.74	-28.57 – -0.90	-2.34	0.039

starting_point_pavlovian_bias	27.29	-63.05 – 117.62	0.66	0.520
starting_point_accumbens	-216.59	-1011.12 – 577.94	-0.60	0.561
drift_rate_pACC	55.19	-62.95 – 173.33	1.03	0.326
Observations	17			
R ² / R ² adjusted	0.454 / 0.206			

BDI_followup (Beck's Depression Inventory at 6-month followup)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	18.18	-8.46 – 44.81	1.54	0.157
starting_point	-20.93	-67.43 – 25.57	-1.02	0.335
drift_rate_reward	-14.48	-45.60 – 16.64	-1.05	0.320
starting_point_pavlovian_bias	-35.31	-254.62 – 184.00	-0.36	0.724
starting_point_accumbens	-1920.94	-4297.58 – 455.70	-1.83	0.101
drift_rate_pACC	109.64	-217.55 – 436.82	0.76	0.468
Observations	15			
R ² / R ² adjusted	0.347 / -0.015			

MASQ_GDD_followup (Mood and Anxiety Symptom Questionnaire – General Distress Depression at 6 month followup)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	33.99	9.79 – 58.20	3.18	0.011
starting_point	-19.25	-61.52 – 23.01	-1.03	0.330
drift_rate_reward	-20.61	-48.90 – 7.68	-1.65	0.134
starting_point_pavlovian_bias	-98.30	-297.64 – 101.04	-1.12	0.294

starting_point_accumbens	-2054.66	-4214.94 – 105.63	-2.15	0.060
drift_rate_pACC	107.17	-190.23 – 404.57	0.82	0.436
Observations	15			
R ² / R ² adjusted	0.532 / 0.273			

MASQ_AA_followup (Mood and Anxiety Symptom Questionnaire – Anxious Arousal at 6 month followup)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	26.82	9.80 – 43.83	3.56	0.006
starting_point	-14.75	-44.46 – 14.97	-1.12	0.291
drift_rate_reward	-14.81	-34.69 – 5.08	-1.68	0.126
starting_point_pavlovian_bias	16.42	-123.73 – 156.57	0.27	0.797
starting_point_accumbens	-923.69	-2442.46 – 595.07	-1.38	0.202
drift_rate_pACC	132.68	-76.40 – 341.76	1.44	0.185
Observations	15			
R ² / R ² adjusted	0.402 / 0.070			

MASQ_AD_followup (Mood and Anxiety Symptom Questionnaire – Anhedonic Depression at 6 month followup)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	67.54	35.51 – 99.56	4.77	0.001
starting_point	-33.20	-89.12 – 22.71	-1.34	0.212
drift_rate_reward	-0.57	-37.99 – 36.85	-0.03	0.973
starting_point_pavlovian_bias	-175.92	-439.64 – 87.79	-1.51	0.166
starting_point_accumbens	-1792.15	-4650.03 – 1065.73	-1.42	0.190

drift_rate_pACC	25.03	-368.40 – 418.46	0.14	0.889
Observations	15			
R ² / R ² adjusted	0.385 / 0.043			

HAMD_followup (Hamilton Depression Rating Scale at 6 month followup)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	5.03	-11.69 – 21.74	0.68	0.513
starting_point	-21.10	-50.28 – 8.08	-1.64	0.136
drift_rate_reward	-3.57	-23.10 – 15.95	-0.41	0.689
starting_point_pavlovian_bias	-7.25	-144.86 – 130.35	-0.12	0.908
starting_point_accumbens	-1495.25	-2986.47 – -4.04	-2.27	0.050
drift_rate_pACC	83.26	-122.03 – 288.55	0.92	0.383
Observations	15			
R ² / R ² adjusted	0.397 / 0.062			

PSS_followup (Perceived Stress Score at 6 month followup)

<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	26.75	9.41 – 44.09	3.56	0.007
starting_point	-17.99	-48.32 – 12.33	-1.37	0.208
drift_rate_reward	-12.77	-33.47 – 7.92	-1.42	0.192
starting_point_pavlovian_bias	-35.03	-177.27 – 107.22	-0.57	0.586
starting_point_accumbens	- 1607.26	-3222.46 – 7.93	-2.29	0.051
drift_rate_pACC	186.00	-48.49 – 420.49	1.83	0.105

Observations	14			
R ² / R ² adjusted	0.498 / 0.184			
SHAPS_DIM				
<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	29.87	21.88 – 37.86	8.14	< 0.001
starting_point	-8.60	-21.82 – 4.62	-1.42	0.182
drift_rate_reward	2.27	-6.72 – 11.26	0.55	0.592
starting_point_pavlovian_bias	-13.80	-74.58 – 46.99	-0.49	0.630
starting_point_accumbens	29.63	-586.63 – 645.89	0.10	0.918
drift_rate_pACC	25.65	-67.24 – 118.55	0.60	0.559
Observations	18			
R ² / R ² adjusted	0.230 / -0.091			

SHAPS_CAT				
<i>Predictors</i>	<i>Estimates</i>	<i>CI</i>	<i>Statistic</i>	<i>p</i>
(Intercept)	3.58	-3.24 – 10.40	1.14	0.275
starting_point	-7.27	-18.56 – 4.01	-1.40	0.186
drift_rate_reward	1.95	-5.73 – 9.63	0.55	0.590
starting_point_pavlovian_bias	1.58	-50.33 – 53.48	0.07	0.948
starting_point_accumbens	64.85	-461.36 – 591.05	0.27	0.793
drift_rate_pACC	3.68	-75.64 – 82.99	0.10	0.921
Observations	18			
R ² / R ² adjusted	0.226 / -0.097			

Table D. Intraclass correlation coefficient for individual parameters across sessions.

parameter	icc	lbound	ubound	p.value
Intercept decision threshold (a)	0.1945852	-0.0975530	0.4932146	0.1086584
Conflict onto decision threshold (a)	0.2503321	-0.0902381	0.5552156	0.0753136
Non-decision time (t)	0.5989588	0.2546280	0.8013340	0.0008600
Dummy coding reward onto drift rate (v)	0.1725391	-0.1697160	0.4961055	0.1643613
Intercept drift rate (v)	0.6096420	0.3022975	0.8015100	0.0003350
Sensitivity to aversiveness onto drift rate (v)	0.6670888	0.3964795	0.8322043	0.0000375
Reward sensitivity onto drift rate (v)	0.5554038	0.1623472	0.7827145	0.0037499
Intercept starting point (z)	0.0185272	-0.0467882	0.1368059	0.3344647
Pavlovian bias onto starting point (z)	0.1963998	-0.1208797	0.5042825	0.1170539

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