Prediction Error Reactivity and Its Relation to Reward Expectancy Are Altered in Major Depressive Disorder: Preliminary Findings from the EMBARC Study

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Background

- Neuroimaging research has implicated the ventral striatum and medial frontal regions including anterior cingulate cortex (ACC) in mediating responses to reward expectancy and outcomes.
- Recent findings demonstrate altered reward-related activation in these regions in patients with major depressive disorder (MDD) representing potential neural markers for diagnosis and prediction of treatment response.

Aim

- To compare reward-related neural reactivity in unmedicated patients with MDD and healthy controls using a well-validated card guessing task that allows examination of reward expectancy (RE) and prediction error (PE) responses and their association.

Methods

Participants

80 patients with MDD (54 females, 26 males; Mean age=38.6, *SD*=13.3) and 31 healthy individuals (19 females, 12 males; Mean age=38.4, *SD*=15.7) recruited for a large multi-site study (EMBARC). There were no group differences in age, sex ratio and level of education.

Clinical scales

Hamilton Rating Scale for Depression (HRSD-24)

MDD: *M* = 26, *SD* = 5.7; **HC**: *M* =.8, *SD* = 1.1

Snaith-Hamilton Pleasure Scale (SHAPS)

MDD: *M* = 5.7, SD = 3.3; **HC**: *M* = 1.5, *SD* = 1.3

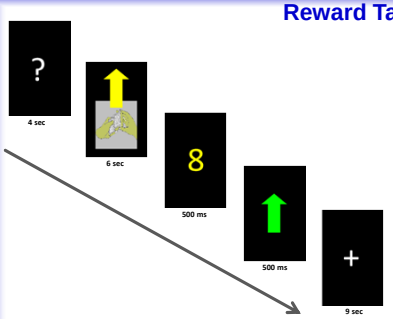
The Spielberger State Anxiety Inventory (STAI-S)

MDD: *M* = 46.8, *SD* = 10.8; **HC**: *M* = 23.8, *SD* = 4.4

Analysis/Image Acquisition

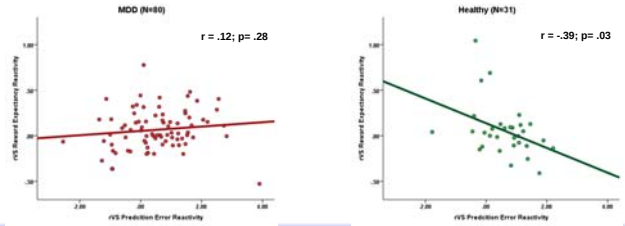
- We conducted ROI analysis focused on the ventral striatum and dACC and correlational analysis examining the relationship between RE and PE reactivity.
- 240 volumes, TR = 2000 ms, TE = 28 ms, Flip Angle = 80º, Matrix = 64 × 64, FOV = 205 mm × 205 mm

Reward Task

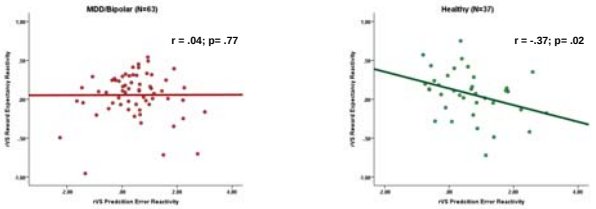


- 24 trials presented in pseudorandom order with predetermined outcomes
- 12 possible win trials
  - 6 win outcomes
  - 6 no change outcomes
- 12 possible loss trials
  - 6 loss outcomes
  - 6 no change outcomes

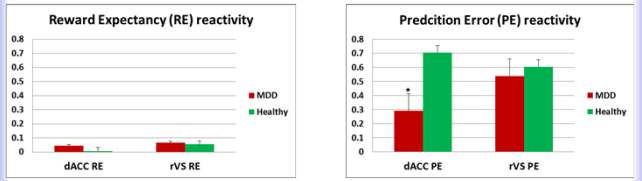
Association between reward expectancy (RE) and prediction error (PE) reactivity in the right ventral striatum (rVS) - EMBARC study



Association between RE and PE reactivity in rVS in a separate sample of medicated patients with mood disorder and healthy controls (Chase et al., 2013)

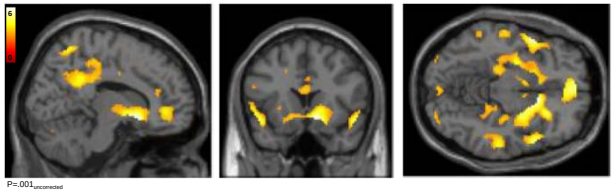


Group comparisons of Reward Expectancy (RE) and Prediction Error (PE) reactivity in the dACC and rVS



* P=.018 (PE rVS reactivity included as covariate)

Whole-brain PE reactivity across all participants (N=111)



P=.001 uncorrected

Summary

- Patients with MDD demonstrate diminished PE reactivity in dACC that may reflect reduced attention to reward outcomes.
- The negative correlation between RE and PE reactivity in the healthy group is consistent with predictions of the temporal difference model. The absence of this association in the MDD group is suggestive of less adaptive contingency learning that may contribute to the development of symptoms.
- The identification of distinct neural responses in a large sample of unmedicated patients provides an important first step in elucidating potential biosignatures of MDD, which may aid prediction of treatment response.

References

1. Chase et al., (2013). *Bipolar Disorders (in press)*.
2. Forbes et al., (2009). American Journal of Psychiatry, 166, 64-73.

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