Accounting for dynamic fluctuations across time when examining test-retest reliability: analysis of a reward paradigm in the EMBARC study

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Introduction:

• The extant neuroimaging literature describing the test-retest reliability of different paradigms is highly inconsistent.

• In previous work using functional magnetic resonance imaging (fMRI) of a reward paradigm, we have examined the neural response in ventral striatum (VS) to positive prediction errors – events when an outcome is more rewarding than was expected.

•However, although variation in activation between sessions will lead to lower reliability estimates, it may be *predictable* insofar as it accords with theoretical models of functioning in reward systems, such as the temporal difference model (1). This model provides an overarching account of prediction error activation in the VS.

• This possibility is significant when evaluating reward-related biomarkers of treatment response or disease progression.

Methods:

• Forty control participants were tested twice, one week apart, in one of four sites (UT Southwestern; University of Michigan; Massachusetts General Hospital; Columbia University: 10 participants per site). Three participants were excluded: one due to a missing time 1 scan, one due to severe ghosting, and one due to a very low signal to noise ratio (SNR: 41). All included individuals had SNR of >80.

• All participants performed a reward-related guessing task (2) while whole brain fMRI data were acquired at 3Tesla (TR/TE=2000/28). Data analysis was performed using SPM8.

• Following a previous study (3), two main contrasts were evaluated using parametric modulators: a regressor reflecting signed prediction errors (PE) and a regressor reflecting reward expectancy (RE). These regressors were included in the first level model.

• A functionally-defined mask of the VS (3) was used for region of interest analysis. Statistics are reported for the right VS, but similar findings were observed on the left.

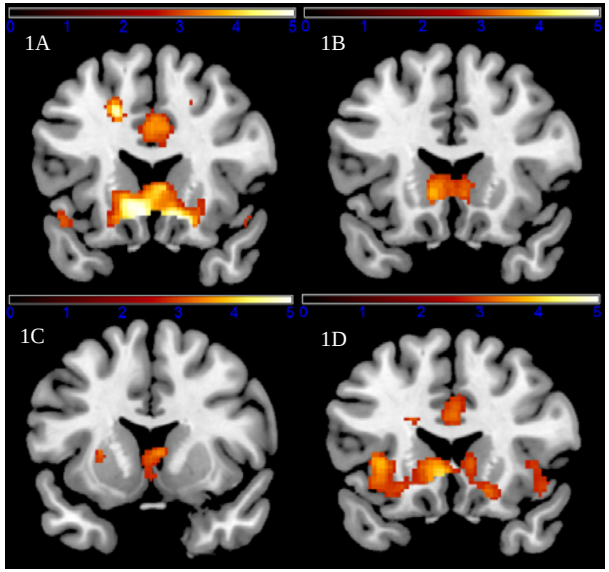
Results:

• Significant VS PE-related activity was observed at session 1 (t=5.65, p<0.001: fig 1A, 2A) but not session 2 (t=1.50, p=0.14: fig 1B, 2A), and the magnitude of reduction was significant (t=3.060, p=0.004).

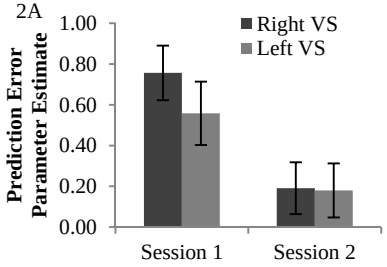
• Significant VS RE-related activity was observed at session 2 (t=2.74, p=0.009: fig 1C, 2B) but not session 1 (t<1: fig 1D, 2B).

• Across participants, increases in VS RE-related activity from time 1 to 2 were associated with decreases in VS PE-related activity from time 1 to time 2 across participants (fig 3: r=-0.39, p=0.016).

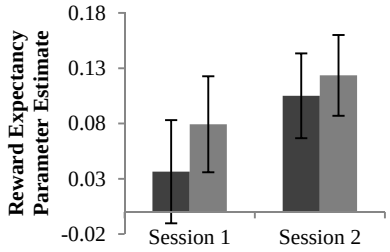
• ICCs in VS were very low (RE: 0.20; PE: 0.00). No significant correlations between session 1 and 2 were observed (p's>0.2). By contrast, ICCs in the visual cortex were much greater (left 0.52; right 0.36).



2A



2B



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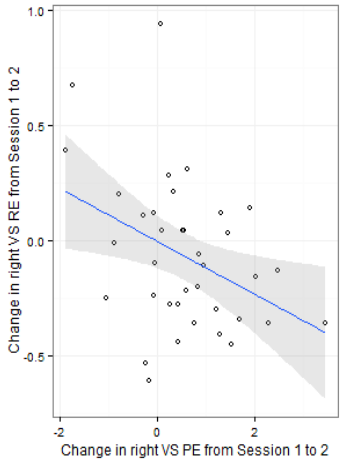

Conclusion:

• Conventional measures of reliability (e.g. ICCs) cannot distinguish between lawful, dynamic changes and noisy signal.

• Reward-related VS activations have poor ICCs, yet follows predictions of temporal difference models of reward learning.

• Significant prediction VS-error related activation coupled to the outcome diminished from time 1 to time 2, whereas VS-reward expectancy related activation coupled to a predictive cue increased.

•These findings have implications for psychopharmacological studies in individuals with depression and the development of reward-related biomarkers: the predictable dynamics of the brain must be acknowledged in order to monitor and evaluate the progression of illness or treatment response.

References: 1. O'Doherty et al Neuron 2003; 2. Forbes et al American Journal of Psychiatry 2009; 3. Chase et al Bipolar Disorders (in press)

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