Neuroscience and Psychiatry

Mood Instability and Reward Dysregulation—A Neurocomputational Model of Bipolar Disorder

Liam Mason, PhD, DClinPsy; Eran Eldar, PhD; Robb B. Rutledge, PhD

Classically, bipolar disorder is seen as a relapsing-remitting condition with episodes of dizzying and capricious highs (manic episodes) that are clearly separated from melancholic lows and inertia (depressive episodes) and interspersed with remission. Yet, in the clinical setting, the picture is often far more complicated. Bipolar disorder lies on a spectrum with subtypes that are defined by arbitrary and often unfulfilled criteria for the severity and duration of mood episodes, which leads to high rates of “unspecified” diagnoses. “Mixed affective” episodes, in which depressive and manic symptoms co-occur, are the norm rather than the exception. Mood instability also persists out of episode, causing as much impairment as within-episode symptoms and muddying the classically episodic presentation.

These complexities challenge existing models of bipolar disorder and broader psychobiological frameworks that describe the relationship between mood and behavior. A prominent theory proposes that bipolar disorder arises from the dysregulation of a “behavioral activation system” that drives positive affect, confidence, and the approach of rewarding stimuli, and temporary increases and decreases in this system result in mania and depression, respectively. However, a plausible neurobiological mechanism for these temporary changes is lacking. There is fundamental disagreement about the core pathophysiology of bipolar disorder. Some research supports a “reward hypersensitivity” account, but other research suggests that reward sensitivity is fundamentally blunted. In contrast to existing models that do not make quantitative predictions, we argue that a new computational approach, based on a dynamic understanding of the 2-way relationship between mood and reward sensitivity, can provide insight into the mechanisms by which patients with bipolar disorder transition between relapse and recovery, as well as explain mixed affective states and pervasive mood instability.

The application of computational approaches to the study of emotion and decision making provides new ways to relate momentary changes in mood and behavior to well-defined neural circuits. Recent studies have found that mood fluctuations are highly contingent on reward prediction error signals that are represented by activity in the ventral striatum, a region that is involved in goal-directed behavior. These signals encode how rewarding an outcome is expected to be (Figure, A). For example, positive surprises (eg, winning £100 [$132] on a scratch card) elicit striatal activity and a positive mood state. This then biases how subsequent rewards are perceived, increasing their perceived value when mood is elevated (and conversely decreasing perceived value when mood is low). Expectations that guide future decisions are updated based on these mood-biased reward prediction errors. A moderate mood bias helps individuals adapt quickly to an environment that is changing, either for better or for worse. However, if mood strongly biases reward perception, as we propose occurs in bipolar disorder, the result is recursive cycles that cause mood, expectations, and behavior to escalate to extremes (Figure, A). Importantly, the same elevated mood bias parameter leads to hypersensitivity to rewards when mood is high and hypo sensitivity to rewards when mood is low, reconciling previously contradictory accounts of bipolar disorder. Empirical support for the model comes from the finding that trait differences in propensity toward elevated moods were explained by the degree to which mood induction biased reward valuation, as inferred from changes in striatal responses and preference for options encountered when mood was elevated (Figure, B).

Our neurocomputational model makes several predictions about how mood changes will escalate, resolve, and reverse in bipolar disorder. We predict that a stronger mood bias parameter that amplifies normal mood fluctuations in response to rewards will be associated with less time in remission and more severe mood episodes (Figure, C). We also predict that high mood bias parameters are a risk factor for developing bipolar disorder, consistent with findings that this parameter correlates with trait measures of bipolar disorder vulnerability (Figure, B). The mood bias parameter, being stable for a given individual, should also be similar across euthymic, depressed, and manic phases. Through amplification of normal mood fluctuations, the model also accounts for the mood instability that occurs both during episodes and residually between mood episodes. For example, as mood episodes progress, expectations become increasingly discrepant with the objective value of outcomes. Surprises that run counter to the valence of the episode become increasingly likely, causing mood and behavior to fluctuate (Figure, C). This greater variability in prediction errors might also account for mood lability in mixed affective states, which could be readily tested using computational modeling.

Another parameter within the model is the learning rate, which determines how quickly expectations are updated based on reward prediction errors. Learning rate asymmetries may explain the dominance of a positive or negative mood (eg, in patients with unipolar mania and bipolar II) (Figure, C). Further, an increasing learning rate may explain why episode frequency can increase across the course of the disorder, at least for some patients (“kindling”). In a changeable environment, it is advantageous to increase the rate of learning to adapt behavior. The volatility that results from repeated relapses and their sequelae could strengthen the belief that further changes are likely, warranting an increased learning rate to adapt to these changes. However, an increased learning rate would also increase spontaneous mood instability, increasing the likelihood of further mood episodes. Alternatively, a gradual increase in mood bias parameters could also lead to kindling. Testing which parameter provides a better explanation (eg, by comparing model parameters among patients with bipolar disorder in early and later stages)
is important because these explanations imply different underlying neural circuitry and interventions.

Model parameters provide a way of quantifying mood disturbances in a mechanistic way. By quantifying mood and behavior in relation to well-defined neural circuits, this computational approach strongly accords with the dimensional approach that is advocated by the Research Domain Criteria framework. Although the proposed model accounts for how positive and negative life events increase the likelihood of mood episodes, the etiology of individual differences in this parameter remains unaddressed. In addition to illuminating multiple poorly understood features of bipolar disorder, this computational approach provides an inroad for improving the diagnosis and treatment of mood instability across psychiatric disorders.

ARTICLE INFORMATION

Author Affiliations: Max Planck University College London Centre for Computational Psychiatry and Ageing Research, University College London, London, England (Mason, Eldar, Rutledge); Wellcome Trust Centre for Neuroimaging, University College London, London, England (Eldar, Rutledge).

Corresponding Author: Liam Mason, PhD, DClinPsy, Max Planck University College London Centre for Computational Psychiatry and Ageing Research, University College London, London, England (l.mason@ucl.ac.uk).

Published Online: October 11, 2017. doi:10.1001/jamapsychiatry.2017.3163

Conflict of Interest Disclosures: None reported.

Funding/Sponsor: Dr Rutledge receives research support from a Career Development Award from the Medical Research Council. Dr Eldar receives research support from grant O9584/2/11/Z from the Wellcome Trust Cambridge–University College London Mental Health and Neurosciences Network. The Max Planck University College London Centre is a joint initiative supported by University College London and the Max Planck Society. No other disclosures were reported.

Role of the Funder/Sponsor: The funding organizations had no role in the preparation, review, or approval of the manuscript or decision to submit the manuscript for publication.

Additional Contributions: We thank Peter Dayan, PhD, Gatsby Computational Neuroscience Unit, University College London, for helpful comments and discussions arising from an earlier version of this paper. He was not compensated for his contribution.

REFERENCES


