Neurophysiological Profiles of Reward-Sensitivity in Bipolar Spectrum Symptoms

Bipolar disorder is the seventh leading cause of disability worldwide and affects one to two percent of the United States population, according to the World Health Organization (WHO). Past psychological research has linked mood disorders to individual differences in reward-sensitivity, indicating that bipolar disorder is associated with high sensitivity to reward (Nusslock et. al), whereas unipolar depression (without mania) is associated with low sensitivity to reward (Pizzagalli, Jahn, O’Shea, 2005). However, the neurophysiology of reward-sensitivity has been studied more extensively for depressive than bipolar symptoms. For my summer project, I would like to investigate the relationship between individual differences in bipolar symptoms and the neurophysiological profiles of reward-sensitivity. Examining this relationship has the potential to elucidate the pathophysiology of bipolar disorder, identify biological markers that differentiate between this disorder and unipolar depression, and develop treatments. With the Undergraduate Research Grant (URG), I would be able to begin research this summer that I will develop into a high-impact, and ideally, publishable study in the upcoming year for my senior honors thesis.

Bipolar disorder is a severe, chronic illness associated with lower life expectancy and high rates of unemployment, divorce, and suicide (Kasper and Hirschfeld, 2005). It involves both depressive and manic episodes. Depressive episodes include feelings of persistent sadness, low self-esteem, and/or loss of interest in previously enjoyable activities. In comparison, manic episodes include abnormally elevated moods, which may involve periods of irritability or even violence. Unipolar depression (without a history of mania) is characterized exclusively by depressive episodes (Butcher, Mineka, Hooley, 2010). Individual differences in reward-sensitivity have been linked to both unipolar depression and bipolar disorder; unipolar depression is associated with low sensitivity to reward cues, which is reflected in decreased goal-directed behavior and depressed states (Pizzagalli et. al, 2005). In contrast, bipolar disorder is characterized by hypersensitivity to rewarding stimuli, and excessive motivation is reflected in manic symptoms (Nusslock et. al, 2007).

Recently, researchers have begun investigating the neurobiological foundation of abnormalities in reward sensitivity in mood disorders. Studies using functional magnetic resonance imaging (fMRI), a neuroimaging technique that measures changes in blood flow to reflect brain activity, have demonstrated that depression is associated with blunted reward-related brain activity (Pizzagalli et. al, 2009), while bipolar disorder is associated with elevated reward-related brain activity (Nusslock et. al, 2012). In addition to fMRI, researchers also use event-related potentials (ERP) to investigate the biology of mood disorders. ERPs measure neural activity that occurs during cognitive and emotional processing. They are non-invasive and offer excellent temporal resolution, enabling researchers to examine neurophysiological activity milliseconds after the onset of a stimulus (Foti and Hajcak, 2010). Previous research has linked mood-related symptoms to a specific ERP response during a reward-based gambling task. For example, Foti and Hajcak (2009) asked participants to pick between two doors presented on a computer screen, one of which concealed a prize and one of which concealed a negative outcome. Using ERP, they found a specific neurophysiological waveform that peaked at approximately 300 milliseconds after a participant received negative but not positive feedback. This response, called feedback related negativity (FN), has been identified as a typical pattern of neural activity for negative feedback (Foti and Hajcak, 2010). This pattern is now presumed to be an indicator of reward sensitivity (Cohen, Elger, and Ranganath, 2007). Foti and Hajcak (2009) found that depressive symptoms predicted smaller FN magnitude, suggesting that FN
could be a biomarker of depression. However, while FN has been investigated in relation to depressive symptoms, the relationship between FN and bipolar symptoms has yet to be explored.

In the proposed study, we seek to investigate for the first time the relationship between profiles of FN magnitude and bipolar symptomatology. Past research with FN has shown the link between low reward sensitivity and depressive symptoms, but the high reward sensitivity associated with bipolar symptoms has not yet been supported by a positive correlation between elevated bipolar symptoms and the magnitude of FN that we predict in this study. Participants will be 10-15 Northwestern University undergraduates recruited from the Introduction to Psychology summer course or via flyers for payment. Participants will receive $10 per hour plus up to an additional $5 based on task performance from the URG and funds available in Professor Nusslock’s laboratory. Participants will be asked to complete the Mood Spectrum-Self Report-Lifetime (MOOD_SR_L) in order to assess subsyndromal bipolar symptoms (Fagiolini et. al, 1999). Previous research in Professor Nusslock’s Mood Disorders Lab has demonstrated meaningful variability in subsyndromal bipolar symptoms in Northwestern Undergraduates using the MOOD_SR_L. ERP will be recorded during the reward-gambling task used in Foti and Hajcak (2010). Participants will pick between two doors and either gain 50 cents or lose 25 cents. The loss condition, which will elicit an FN response, will occur exactly half the time throughout 40 trials. ERP data will be processed and analyzed using Neuroscan software in Professor Nusslock’s laboratory and the relationship between bipolar symptoms and FN magnitude will be analyzed using bivariate correlation and multiple regressions in SPSS (a statistical computer program). Results will be considered significant if p value <0.05.

The summer will provide sufficient time for me to practice leading the administration of EEG, set up the gambling task in E-Prime (program that runs tasks), pilot the task, and test 10-15 participants. For my senior honors thesis, I hope to continue the study into the academic year ultimately testing 40-50 participants. This work would allow insight into individual differences in abnormal reward-processing associated with bipolar symptoms. In addition, it may aid the identification of a novel biomarker for differentiating between unipolar depression and bipolar disorder and lead to improved diagnosis and treatment for bipolar disorder.

My research experience and coursework has prepared and inspired me to complete an independent project in Professor Nusslock’s Mood Disorders Laboratory. My prior experience conducting ERP studies and processing ERP-related data in this lab will allow me to complete the proposed study. In addition, I have practiced administering behavioral tasks, coding, scoring, and organizing data using Excel, and gained data analysis experience by working at the Oxford University Attention, Brain, and Cognitive Development Lab and an NIMH panic disorder study at Weill Cornell Medical Center. While studying abroad at Oxford, Psychological Disorders, Cognitive Neuroscience, and Behavioral Neuroscience courses informed my understanding of mood disorders and neurobiological research approaches relevant to this study. Finally, I have become familiar with the statistical methods necessary for this project through Statistics and Research Methods classes. Professor Nusslock’s Lab will provide me with the faculty support and resources I need in order to complete an independent summer project.

Using the URG, I would further explore my passion for mood disorders research, expand work I complete this summer into a meaningful senior honors thesis, and prepare for graduate study in clinical psychology. I would like to pursue a PhD to investigate neurobiological and cognitive models of mood disorders or anxiety that may lead to more effective and widely accessible treatments. The URG would provide invaluable experience, helping me to develop into an independent researcher and pursue a career in research.
References


