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Reward-Based Biobehavioral Marker in Anhedonic and Hypomanic/Manic Symptomatology

by

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A thesis
Presented to the faculty of
Towson University
in partial fulfillment
of the requirements for the degree
Master of Arts
Department of Psychology
Towson University
Towson, Maryland 21252
May, 2017
TOWSON UNIVERSITY
OFFICE OF GRADUATE STUDIES

THESIS APPROVAL PAGE

This is to certify that the thesis prepared by Grace-Anna Chaney entitled Reward-Based
Biobehavioral Marker in Anhedonic and Hypomanic/Manic Symptomatology has been approved
by the thesis committee as satisfactorily completing the thesis requirements for the degree
Master of Arts in Experimental Psychology.

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Acknowledgements

First and foremost, I thank God for enabling me to pursue my educational dreams, and for giving me the strength to endure hardships when they arise. Secondly, I thank my family and friends for their unwavering love and support throughout my entire academic journey; I truly could not have done this without you. To my undergraduate professors and mentors, namely Dr. Chad Magnuson, Dr. Carrie Wilmouth, and Dr. Brianne Friberg, I thank you all for igniting in me a passion for empirical inquiry into the mysterious, yet undoubtedly exciting, realm of psychological research. Next, to my present graduate mentor, Dr. Rick Parente, and thesis committee, Dr. Jared McGinley, and Dr. Jacqueline Leventon, for your guidance and words of encouragement and wisdom throughout this process. A special thanks to Dr. Leventon for allowing me to use her electroencephalogram equipment; this project would not have been viable otherwise, so thank you. I also give many thanks to my supervisors, Dr. Vidya Kamath, Dr. Denis Antoine, and Dr. Chiadi Onyike, at Johns Hopkins for their brilliant mentorship, insight, and support. Next, to my friends I have made in the experimental psychology graduate program, thank you so much for letting me constantly commiserate with you, being a continuous source of encouragement, and for our many fond memories we have created during our time at Towson. Lastly, I thank all of the participants for allowing me to apply excessive amounts of gel in their hair, and for taking part in the study in its entirety.
Abstract

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Grace-Anna Chaney

Aberrant reward sensitivity has been an established hallmark of bipolar disorder (BD) and major depressive disorder (MDD), and there is now evidence for a potential biomarker for this abnormality, termed frontal alpha asymmetry. Those with BD exhibit greater relative left hemispheric activity, and those with MDD show greater relative right frontal activity, during challenging, reward-based tasks. The present study utilized a sample of 30 Towson University students and measured their levels of anhedonic and manic symptomatology, the two characteristic symptoms of MDD and BD, respectively. While recording their brain activity via electroencephalogram equipment (EEG), they completed a word unscrambling task that increased in difficulty and was either paired with a potential reward or punishment. Although not significant, positive and negative relationships between the frontal asymmetry index during the hard/reward trials and manic and anhedonic symptomatology, respectively, were revealed, as expected. The present trends are consistent with previous findings for a neural marker of approach motivation in these pathologies, and warrants more extensive inquiry in larger, clinical samples.
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Chapter One:

Introduction

Affective disorders have become increasingly prominent in the United States. Two of the main types of affective disorder, bipolar disorder (BD) and major depressive disorder (MDD), account for 2.6% and 6.7% of the adult population in the U.S every year, respectively, which equates to over 20 million victimized adults (National Institute of Mental Health; Kessler, Chiu, Demler, & Walters, 2005). These statistics are staggering, and they highlight the need for the extensive inquiry and implementation of effective diagnostic and treatment methods. The most commonly diagnosed subtypes of BD are bipolar I and II. The main distinction is that bipolar I is characterized by manic episodes, and bipolar II is characterized by episodes of hypomania (Datto, Pottorf, Feeley, LaPorte, & Liss, 2016). The two main features of MDD are a depressed mood and anhedonic symptoms. Anhedonia is denoted as a loss of interest or pleasure in activities one previously deemed enjoyable (Jesulol, Sharpley, Bitsika, & Agnew, 2015).

The primary distinction between BD and MDD is found in their responsiveness to rewards. The general finding is that hyposensitivity to reward characterizes unipolar depression, while reward hypersensitivity is characteristic of bipolar disorders (e.g., Treadway et al., 2009). In addition to these behavioral disparities, considerable research supports a biological marker of reward-related behavior, entitled approach motivation. Approach motivation is commonly measured via examining electroencephalographic (EEG) activity, specifically examining left versus right frontal activity. Individuals with BD show greater relative left frontal cortical activity, which is indicative of high approach motivation, whereas individuals with MDD show lower relative left cortical...
activity, which is indicative of low approach-related motivation (e.g., Coan & Allen, 2004).

Collectively, behavioral measures of reward sensitivity and this neural marker of approach motivation have potential to be utilized as tools for detecting psychopathology in relation to MD and BDD. Although research on this topic is plentiful, the literature thus far has almost exclusively focused on diagnoses as a whole, and has consequently neglected examining specific symptom profiles of these disorders. An initiative released by The National Institute of Mental Health (NIMH) in 2010 acknowledged this deficit and proposed a call to action to researchers encouraging studies aimed at examining the relationship between biobehavioral dimensions and symptom profiles of various disorders (Insel et al., 2010). The following review of literature delves into the vast scope of research concerned with the etiology of BD and MDD, the role of aberrant reward processing in these disorders, and outlines the various research conducted on frontal asymmetric activity as a biomarker for approach motivation. Finally, the present study will be introduced that proposes a supplemental approach to utilizing established biobehavioral reward-based paradigms to examine the two main symptoms that characterize BD and MDD: hypomania/mania and anhedonia.

Chapter Two:

Literature Review

Current Diagnostic Protocol

The primary aim of the present study is to supplement the existing empirical evidence on biomarkers for psychopathologies, specifically BD and MDD, that could be utilized clinically to assist in the detection and subsequent treatment of these disorders.
Therefore, a brief look into the current diagnostic procedures for BD and MDD is warranted. Currently, only overt, behavioral indicators are considered when deciding on a clinical diagnosis. The Diagnostic and Statistical Manual for Mental Disorders, version five (DSM-V), is the diagnostic assessment tool used among professionals. The manual outlines the criterion that must be met to reach a decided diagnosis, which consists of all established presenting symptoms that characterize each disorder.

**Bipolar Disorder.**

**Bipolar I.** A diagnosis of Bipolar I disorder necessitates the occurrence of at least one manic episode. The following criteria must be met to be defined as a manic episode: 1) a period of an abnormally elevated or irritable mood, aberrant goal-oriented activity or energy levels, that lasts for a minimum of one week and is present for most of the day, almost every day (or for any length of time if a hospitalization is required), 2) three (or more) of the follow symptoms during the mood disturbance that clearly deviate from an individual’s typical behavior: Grandiosity or the inflation of self-esteem, a decrease need to sleep, highly talkative or feeling a pressure to continue talking, racing thoughts or ideas, easily distracted, an increase in goal-oriented activity, or some type of psychomotor agitation (i.e., non-goal-directed activity that has no purpose), a high involvement in activities with great potential for negative repercussions, 3) The mood disturbance is severe enough to result in appreciable impairment in occupational or social functioning, or to require the individual to be hospitalized to prevent them from harming themselves or others, or if there are psychotic symptoms present, 4) The episode cannot be attributed to the physical effects of a substance (e.g., a medication, drug of abuse). Notably, a major depressive episode is not required for a Bipolar I diagnosis (American
Psychiatric Association, 2013).

**Bipolar II.** For a diagnosis of Bipolar II disorder, an individual must meet the criteria for a current or past hypomanic episode, as well as a major depressive episode that is current or has occurred previously (which will be discussed next in the MDD section). A hypomanic episode is characterized by: 1) A period of an abnormally elevated or irritable mood, or increased activity or energy levels, that lasts for a minimum of four consecutive days, and is present for most of the day, almost every day, 2) the same criteria as noted above for Bipolar I in number two, 3) The episode is related to a change in function that is not characteristic of the individual when they are not symptomatic, 4) The alterations in functioning and mood disturbances are observable by others, 5) The episode does not cause noticeable impairments in occupational or social functioning, nor does it require hospitalization, 6) The episode cannot be attributed to the physical effects of a substance (e.g., a medication, drug of abuse) (American Psychiatric Association, 2013).

**Major Depressive Disorder.** To be considered a major depressive episode, at least five of the following symptoms are required to be present at the same time during a two-week period and must be markedly different from an individual’s previous functioning; in addition, one of the symptoms has to be either a depressed mood or a loss of pleasure or interest (i.e., anhedonia): 1) A depressed mood that is present for most of the day, almost every day, 2) A loss of interest or pleasure in activities almost every day, for most of the day, 3) A significant amount of weight loss when one is not dieting or significant weight gain (e.g., at least a change of 5% of one’s body weight in a month), or an increase or decrease in appetite almost every day, 4) inability to sleep or sleeping excessively almost
every day, 5) psychomotor retardation or agitation almost every day (that is observable by others), 6) a loss of energy or fatigue almost every day, 7) feelings of inappropriate or excessive guilt or worthlessness almost every day, 8) a diminished ability to concentrate or think, or indecisiveness, almost every day, 9) recurrent thoughts about death, suicidal ideation with or without a specific plan, or a suicide attempt. In addition, the aforementioned symptoms have to cause a significant amount of distress or impairment in occupational or social functioning, and the episode cannot be attributed to the physiological effects of another medical condition or a substance (e.g., a medication, drug of abuse). Lastly, an individual cannot have a history of a hypomanic or manic episode (American Psychiatric Association, 2013).

Clinical Characteristics of Depression and Bipolar Disorder

Pathophysiological evidence. In an attempt to uncover the etiology of BD and unipolar depression, numerous neuroimaging techniques have been employed. For example, magnetic resonance imaging (MRI) studies have found that individuals with BD show signal hyperintensities (i.e., lesions) in white matter. This finding has been found to be more common in people with BD compared to people with other affective disorders, specifically those with unipolar depression (Dupont, Butters, Schafer, Wilson, Hesselink, & Gillin, 1995). Further, one study found higher rates of these hyperintensities in individuals with bipolar-I disorder than those with bipolar-II (Altshuler, Curran, Hauser, Mintz, Denicoff, & Post, 1995). In addition, neuroimaging studies have also found increased volume in the amygdala, located in the limbic region, as well as ventricular enlargement (Strakowski, Woods, Tohen, Wilson, Douglass, & Stoll, 1993; Jurjus, Nasrallah, Brogan, & Olson, 1993), temporal lobe volume reduction, and larger thalamic
volume in individuals with BD compared to controls (Altshuler, Bartzokis, Grieder, Curran, & Mintz, 1998; Strakowski et al., 1999).

Another fMRI study comparing individuals with MDD and BD revealed anatomical differences at both functional- and whole-brain levels in the anterior cingulate cortex (ACC) and prefrontal networks, such as the ventro/dorsolateral prefrontal cortex (VLPFC, DLPFC) (Hao et al., 2015). Outside of the central nervous system, research has also found changes in activity in the autonomic nervous system in individuals with BD during an emotional elicitation task as measured via electrodermal activity (EDA). The results supported their predictions of an association between pathological mood states and autonomic dysfunction (Greco, Valenza, Lanata, Rota, & Scilingo, 2014). Based on the aforementioned findings, it is clear that there may be structural abnormalities in individuals with affective disorders such as BD and unipolar depression that could potentially be used as unique identifiers of these disorders. However, robust neurological evidence is still needed to further corroborate these findings. The disparities are evident, but the specific outcomes have yet to become reliable enough to definitively utilize them as neuroanatomical markers for these pathologies to use as diagnostic tools (see the review by Bearden, Hoffman, & Cannon, 2001).

**Reward Sensitivity**

A part from neuroanatomical differences in MDD and BD, one particular area of interest regarding the primary characteristics of these disorders, anhedonia and hypomania/mania, respectively, is the altered reward responsiveness found to accompany them. The reward system is associated with a fronto-striatal circuit that is responsive to stimuli that are involved in receiving and anticipating rewards (Depue & Collins, 1999;
Haber & Knutson, 2009). This system is responsible for regulating approach motivation and goal-directed behaviors. It can be activated by both internal (e.g., expecting to get a job promotion) or external (e.g., having a prize-winning opportunity) reward- or goal-relevant events and cues. Both MDD and BD have been found to be associated with aberrant responsiveness to rewards. More specifically, considerable evidence supports that heightened reward processing and sensitivity is an identifying feature of hypomania/mania, while blunted reward processing and sensitivity is associated with unipolar depression (Alloy, Olino, Freed, & Nusslock, 2016). For individuals who have anomalous reward sensitivity, when faced with an environmental event or cue that deactivates or activates their reward system, their reward systems can become activated or deactivated too strongly, which could consequently lead to hypomania/mania or depression, respectively (Alloy et al., 2016).

**Depression.** Hyposensitivity as a main hallmark of anhedonia has been substantiated by numerous studies. For example, one study examined individuals with higher levels of anhedonic symptomatology and found that they showed less willingness to exert effort toward rewards (Treadway et al., 2009). In addition, another study with MDD and healthy controls found that in comparison to controls, the MDD participants were less likely to choose the reward task with high reward/high costs (Treadway et al., 2012). One proposed explanation for differences in the experience of reward for individuals with depression is that an impairment lies in individuals’ ability to convert the likelihood of a reward into motivation (Rizvi, Pizzagalli, Sprouled, & Kennedy, 2016). Further, some research even suggests that it is a marker that is representative of a genetic predisposition to depression (Liu et al., 2015). To support this notion of genetic
involvement, one study compared relatives of individuals with MDD who had subclinical symptoms of depression to a healthy control group and found that these individuals showed a blunted reward bias compared to controls (Liu et al., 2015).

**Bipolar Disorder.** One theory that encompasses the heightened reward sensitivity seen in BD is entitled the Behavioral Approach System (BAS), whose model is used as a measurement tool that reflects individuals’ proneness to respond to reward signals. For example, manic and hypomanic symptoms have been found to be associated with increased BAS activity, with depression being associated with decreased BAS activity. Additional support for this is found in studies examining BAS sensitivity in individuals with BD and those who are prone to exhibiting hypomanic symptoms, which showed that these individuals had elevated BAS scores in comparison to controls (Carver and White, 1994). Further, life events regarding goal-striving behaviors have been found to be associated with increases in hypomanic and manic symptoms, but not episodes of depression (Nusslock et al., 2007).

**Frontal EEG Asymmetry – Neural Index of Approach Motivation**

In addition to the behavioral abnormalities found in reward sensitivity in individuals with BD and MDD, a prodigious amount of research has also found a neural marker reflecting reward-oriented behavior, termed approach motivation. Specifically, studies have found that patterns of asymmetric cortical activity located in frontal regions can distinguish individuals with BD and MDD. For individuals with BD, greater relative left frontal activity is seen, which is reflective of heightened approach motivation, whereas individuals with MDD show lower relative left frontal activity, which is reflective of decreased approach motivation (Insel et al., 2010). This specific area of
focus has become of increasing interest due to an initiative by The National Institute of Mental Health (NIMH) that came out in 2010 entitled Research Domain Criteria (RDoC) (Insel et al., 2010). The aim of this initiative is to further examine the link between symptom profiles and biobehavioral dimensions. Approach motivation is one construct that has received substantial attention, and it falls under the Positive Valence Systems domain of the RDoC. Based on a substantial amount of research, one common way approach motivation is operationalized is through examining electroencephalographic (EEG) activity, specifically examining left versus right frontal activity (Insel et al., 2010).

A myriad of studies published in the last several decades corroborate the link between frontal EEG asymmetry and approach motivation in BD and MDD. According to an approach-withdrawal motivational model, greater relative left frontal EEG activity is indicative of a propensity for engaging or approaching a stimulus, whereas lower relative left EEG activity is indicative of a propensity for decreased approach-related motivation (Coan & Allen, 2004; Davidson, 1995, 1998a,b; Harmon-Jones, 2003a). In addition, according to the BAS theory, if an individual with BD perceives an event as a “challenge” and consequently elicits “approach-motivated perceptions of coping,” BAS should be triggered and symptoms of hypomania or mania may arise. For example, one study showed that individuals who had a high BAS sensitivity displayed asymmetry in the left frontal regions (Black et al., 2014), with another showing a relationship between the BAS and higher left-sided activity in the middle frontal gyrus (Pascalis, Cozzuto, Caprara, & Alessandri, 2013). Individual variation in BAS scores is said to predict positive emotion and approach-related behavior in response to cues of reward (Pascalis et al., 2013).
One area that has received ample attention in frontal EEG asymmetry research is in examining this asymmetry in emotion eliciting tasks. For example, one study found that lower relative left frontal EEG activity during negative movies was predictive of mood deterioration in the following week (Papousek et al., 2014). Further, another study showed that individuals who were prone to hypomanic or manic symptoms had greater relative left frontal activity in response to events meant to evoke anger (Harmon-Jones et al., 2002). Similarly, a study by Harmon-Jones et al. (2002) presented an anger-evoking event and examined if a propensity toward hypomanic and manic symptoms would be associated with heightened relative left frontal EEG activity, and a propensity toward symptoms of depression would be associated with decreased relative left frontal EEG activity during this event, and found that their hypotheses were supported. Finally, individuals who have had life-time depression showed lower relative left frontal EEG activity during various facial expressions in comparison to individuals who have never been depressed (Stewart, Coan, Towers, & Allen, 2011).

Additionally, one compelling finding is that frontal asymmetry has been found to prospectively predict conversion to bipolar I disorder. Nusslock et al. (2012) found that baseline heightened relative left frontal activity prospectively predicted individuals being more likely to convert from bipolar II disorder (hypomania) or cyclothymia (mood disorder characterized by mood shifts, but not as severe as BD) to bipolar I disorder over a follow-up period of 4.7 years. In addition, the results also revealed that relative left frontal activity was significantly heightened in individuals with BD while in a hypomanic episode during the EEG recording, and was related to an earlier age onset of one’s first bipolar episode (Nusslock et al., 2012). In supplement, decreased relative left frontal
activity has been found to be predictive of symptoms of depression in adolescent males one year later (Mitchell & Pössel, 2012).

Further, neurofeedback training has also been found to decrease symptoms of depression and increase relative left frontal EEG asymmetry in individuals with depression after five-weeks (Choi et al., 2011). Further, alpha EEG asymmetry was assessed at mid-frontal and mid-lateral sites in healthy controls and individuals with depression before and after behavioral treatment. Results revealed that individuals with depression had significantly higher alpha EEG asymmetry than control participants during pre-treatment. In addition, increased alpha EEG asymmetry in individuals with depression was significantly associated with higher levels of behavioral inhibition (Gollan et al., 2014).

Finally, one study examined individuals that had a bipolar spectrum diagnosis in comparison to healthy age-matched controls during an anagram task (word unscrambling) that increased in difficulty: easy, medium, and hard (Harmon-Jones et al., 2008). The participants were notified 7-seconds before each trial whether it was going to be an easy, medium, or hard trial, and whether their response would result in a punishment or reward (+50 cents for correct anagrams for the reward conditions, -50 cents for incorrect anagrams in the punishment conditions). Total alpha power was computed and averaged across each difficulty/reward or punishment trials for each of the anticipatory periods. The results revealed that individuals with BD had higher relative left frontal EEG activity during the anticipatory period for the hard/reward trials. Conversely, the control group showed decreased left frontal EEG activity from the medium/reward to the hard/reward trials, but this result was not seen in individuals with BD. Further, self-report measures of
reward sensitivity among participants with BD was related to higher relative left frontal EEG activity in response to the hard/reward trials (Harmon-Jones et al., 2008).

These findings corroborate evidence suggesting that relative left frontal activity may be involved in symptoms of mania, and may be triggered by events that are potentially challenging and rewarding (Harmon-Jones et al., 2008). Healthy individuals showed more adaptive responses to a goal pursuit that was extremely difficult and therefore disengaged, whereas individuals with BD maintained a high motivational state, which is consistent with the characteristic of goal-striving behavior in BD. Harmon-Jones et al. (2008) suggested that this could be an example of how individuals with BD get fixed in the goal pursuit state and do not, or may not be able to, regulate their way out. One suggestion for clinicians is to help their patients understand how goal-striving behavior that is particularly ambitious and manic episode onset are related (Nusslock, Abramson, Harmon-Jones, & Alloy, 2009).

**Reasons for Examining Alpha Bandwidth.** Examining bandwidths is paramount due to how vital neural oscillations are to overall brain functioning; therefore, knowing their functions in healthy individuals and various psychiatric conditions supplements research that tries to ascertain the location of brain functioning abnormalities as they relate to certain pathologies. This could be helpful for both diagnostic purposes and more focused interventions (Buzsaki & Watson, 2012; Uhlhaas & Singer, 2012; Bas, 2013). When assessing frontal asymmetry, the question arises as to what specific bandwidth to examine. In particular, the alpha bandwidth has been the primary focus when computing indices of asymmetry. Alpha rhythms (~8-13 Hz) are the primary oscillations in the conscious, awake brain state whose purpose is to sustain higher cortical functioning and
synchronize activity from other bandwidths (Klimesch et al., 2012). The alpha bandwidth functions through either a power (i.e., amplitude) increase or decrease. Some have suggested that increases in alpha power related to specific tasks is reflective of “top-down inhibitory control of task irrelevant processing,” with alpha power decreases being reflective of releasing inhibition of functioning (Klimesch et al., 2007).

In addition, research has found that BD is linked to alpha activity anomalies during resting state and various tasks (Eidelman-Rothman, Levy, & Feldman, 2016). Further, aberrant alpha patterns have also been linked to anxiety disorders, post-traumatic stress disorder, and obsessive compulsive disorder during resting state in response to certain emotional and cognitive tasks (Eidelman-Rothman et al., 2016). Furthermore, studies examining alpha activity have found greater alpha power during certain phases of tasks such as before stimulus presentation, which was interpreted as being reflective of active inhibition that was irrelevant to the task information, in addition to reflecting a state indicating cognitive readiness for an imminent task (Eidelman-Rothman et al., 2016). Perhaps most importantly, and as evidenced by the previous findings, alpha is of particular interest due to its inverse relationship with cortical activity (Harmon-Jones et al., 2008).

**Relevance and Importance**

It is undoubted that there is no shortage of research on frontal asymmetric cortical activity being associated with MDD and BD. However, a deficit lies in whether specific symptom profiles of these disorders reflect idiosyncratic changes in this neural marker of approach motivation. Almost all studies to date examining frontal asymmetry have exclusively looked at diagnostic categories, thus overlooking the symptoms that
characterize them and where people fall in terms of severity of these symptoms; which could be informative not only for individualized treatment, but also for detecting risk for these disorders. Previous research regarding frontal cortical asymmetry have used dichotomous classifications of depression and BD and thus have been limited in exploring potential variations in asymmetry across different symptom profiles (Jesulol, Sharpley, Bitsika, Agnew, & Wilson, 2015). In addition, Nusslock et al. (2015) posits that asymmetrical frontal activity research is exemplary in its potential for being utilized as a physiological marker that underlies particular symptom clusters (see also Carver & White, 1994).

A couple exceptions do exist, however, but these studies are not without their limitations. For example, one study looked at depression severity and the following symptoms of depression: sadness, worry, anxiety, irritability, and fatigue, using self-report visual analog scales (VAS), during an MRI. Results revealed that fatigue and irritability symptoms were correlated with a reduction in cortical thickness in the right rostral anterior cingulate cortex (rACC) as well as cortical volume (CV) reduction in the ventral lateral prefrontal cortex (VLPFC). In addition, VLPFC CV reduction was related to symptoms of sadness, and worry symptomatology was associated with right VLPFC CV reductions (Lener et al., 2016).

Although these findings are enlightening, this study only illuminated structural differences between various symptoms of MDD, and therefore did not look at functional dissimilarities that can be detected through EEG methodology. In addition, one of the main characteristics of MDD, anhedonia, was not assessed. Not only is anhedonia utilized as a primary diagnostic tool for depression, research has found that examining
anhedonia is promising to understanding MDD due to evidence for anhedonic mechanisms mapping onto specific signaling pathways and neurocircuitry (Der-Avakian & Markou, 2012; Pizzagalli, 2014). Looking at samples with both anhedonic and non-anhedonic individuals would be helpful to elucidate the neurological and behavioral phenotype of unipolar depression with anhedonia. For BD, mania and hypomania as the primary hallmarks for BD-I and II, respectively, is undisputed. Harmon-Jones et al. (2002) did examine hypomanic/manic and depressive symptoms and its relationship to frontal EEG asymmetry, as noted previously; however, this was examined in an anger-evoking task, therefore looking at emotional valence as opposed to approach-related motivation, which has been found to be more pertinent to frontal EEG asymmetry, as discussed below.

Examining frontal asymmetry in reward-based tasks is an area that is not only important due to impairments in reward sensitivity being central to anhedonia and hypomania/mania, but also due to research supporting that the frontal asymmetry index may be more closely linked to tasks assessing motivational direction as opposed to affective valence. For example, Nusslock, Walden, and Harmon-Jones (2015) suggested that frontal EEG asymmetry is more distinctive in facilitating reward and approach-related motivation in comparison to valence-oriented methods, such as assessing positive emotions. Nusslock et al. (2015) noted that examining a motivational based framework instead of a valence-based one rooted in determining whether mechanisms assist inhibitory/withdrawal versus approach propensities is optimal.

Importantly, the need for more symptom-focused inquiries, and therefore the purpose of the present study, is largely predicated on the aforementioned initiative,
RDoC. The main goal of RDoC is to create a classification system for mental illnesses that are rooted in modern neuroscience. This classification system could help engender biomarkers of various psychiatric illnesses that could help facilitate reliable and precise psychiatric assessments. Frontal EEG asymmetry has been found to be integral to the Positive Valence Systems of the RDoC, making it particularly germane. However, its understudied relation to a more motivational-based framework necessitates investigation.

The objective is to identify biological mechanisms specific to both psychiatric disorders in their entirety, as well as specific symptoms of the disorders that could be reflective of biosignatures (Insel et al., 2010). These indices could help predict or detect individual vulnerability to being diagnosed with an emotional disorder. In addition, being cognizant of potential neural markers of these disorders is crucial due to effectively managing depression necessitating individualized approaches that are modified based on specific symptoms that an individual displays (Mahli et al., 2013). The current study aims to merge the strengths of previous inquiries while addressing the weaknesses that have been repeatedly acknowledged in an effort to enhance the literature in this area that, combined, can hopefully one day aid in the diagnosis of BD and MDD.

The Present Study

The purpose of the present study was to utilize established methods of reward sensitivity (i.e., Behavior Avoidance Scale) and a neural marker of approach motivation (i.e., asymmetric frontal cortical activity), in the main characteristics of BD and MDD, hypomania/mania and anhedonia, respectively, during a reward-based task. After assessing reward responsiveness and severity of hypomanic/manic and anhedonic symptoms, a word unscrambling task was employed. The task and general
methodological approach that was implemented has been utilized in a previous study by Harmon-Jones et al. (2008). The task is called the “anagram task” and involves the unscrambling of words that increase in difficulty from easy, medium, to hard. Seven-seconds prior to the onset of each anagram, the participants were told whether the anagram belonged to a reward or punishment condition, which involved either gaining 50 cents for correctly solving the anagram, or losing 50 cents for incorrectly solving the anagram, respectively.

The electroencephalogram (EEG) recording occurred during this 7-second anticipatory period while participants viewed a fixation point. Following, frontal asymmetry indices were computed through log transforming the alpha power values and subsequently taking the natural log right minus the natural log left alpha power. This index was calculated for each of the anticipatory periods, and then averaged across all trials within each difficulty block. Due to the inverse relationship of alpha power with cortical activity, a higher score on this index indicates greater relative left hemisphere activity (Harmon-Jones et al., 2008).

The hypotheses for the behavioral measure of reward responsiveness were: 1) Higher levels of anhedonia would be associated with lower levels of reward responsiveness, and 2) Individuals with higher levels of manic symptoms would show higher levels of reward responsiveness. For the anagram task with the EEG recording, the hypotheses were: 1) Individuals with higher levels of anhedonia would have lower relative left frontal EEG activity during hard/reward trials, indicating low levels of approach motivation, and 2) Individuals with higher levels of manic symptoms would have higher relative left frontal EEG activity during hard/reward trials, indicating high
levels of approach motivation. The hypotheses regarding the hard/reward trials were proposed due to the findings by Harmon-Jones et al. (2008) that was discussed previously.

Chapter Three:

Methods and Materials

Participants

The participants were comprised of Towson University students; $n = 30$. Inclusion criteria required that participants must be at least 18 years of age, right-handed, have English proficiency, and have no history of epilepsy or neurological disorders. Only right-handed students were eligible to participate due to research suggesting that handedness is indicative of hemispheric dominance, meaning that hemispheric specialization of emotion may differ for left- and right-handed students (Harmon-Jones et al., 2008). Thus, not controlling for handedness could introduce a potential confound when examining hemispheric asymmetry. English proficiency was imperative due to the primary task involving scrambled English words; therefore, necessitating familiarity with a range of English vocabulary. Only one participant reported a history of MDD, and none of the participants reported presently taking any psychotropic medications. The sample demographics are presented in Table 1 below.
Table 1

Sample demographics

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22.03 (2.73)</td>
</tr>
<tr>
<td>Female</td>
<td>90%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
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<tr>
<td>White</td>
<td>50%</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>13.3%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>20%</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>16.7%</td>
</tr>
</tbody>
</table>

Note: Standard deviations are in parentheses.

Procedure

**Questionnaires.** After obtaining consent, the participants completed several questionnaires regarding general demographic information (e.g., age, race) and questions about whether they are native English speakers and the amount of time they have been speaking English. In addition, the participants were asked how familiar they are with anagrams (word unscrambling) on a 5-point scale (1 = Not at all familiar, 5 = Extremely familiar). Lastly, questionnaires assessing anhedonia, hypomania, and mania symptomatology, as well as questions assessing their responsiveness to rewards, were administered.

**Anhedonia.** To assess levels of anhedonia, the Snaith-Hamilton Pleasure Scale, a 14-item self-report paper-pencil questionnaire designed to measure an individual’s ability to anticipate or experience pleasure in the last few days, was administered. The answer choices ranged from “Strongly agree” to “Strongly disagree,” in response to questions such as: “I would find pleasure in my hobbies and pastimes.” For scoring, either of the
“Disagree” choices were scored as a 1, and either of the “Agree” choices were scored as a 0. The 14 items were subsequently summed, with the total score ranging from 0 to 14. Higher total scores were representative of higher levels of anhedonia, with two being the cut-off score that best discriminated “normal” and “abnormal” hedonic tone levels (Snaith, 1995).

**Hypomania/Mania.** For the assessment of hypomanic and manic symptoms, the Goldberg Mania Questionnaire was utilized. This measure consisted of an 18-item computerized questionnaire, with answer choices ranging from “Not at all” to “Very much.” A response of “Not at all” received a 0, “Just a little” a 1, “Somewhat” a 2, “Moderately” a 3, “Quite a lot” a 4, and “Very much” a 5. An example item is: “I have so many plans and new ideas that it is hard for me to work.” The questions referred to feelings and behaviors the participants have experienced in the past week. The established nomenclature for this scale is as follows: “No Mania Likely” for a score between 0-9, “Possibly Mildly Manic, or Hypomanic” is a range of 10-17, 18-21 falls under “Borderline Mania,” 22-35 for “Mild-Moderate Mania,” 36-53 for “Moderate-Severe Mania,” and lastly 54 and up is indicative of the “Severely Manic” classification (Goldberg, 1993). The dispersion of scores and their respective categories are presented in Figure 1 below. Due to a small sample size, these classifications were not utilized in the analyses.
Figure 1. Number of participants in each mania category of the Goldberg Mania Scale

**Reward Responsiveness.** To assess participants’ sensitivity to rewards, the Reward Responsiveness subscale from the Behavioral Avoidance Scale (BAS) was employed. There were 9 items, including 4 filler questions, that ranged from 1-4 (1=Very true for me, 4=Very false for me), with all included items being reverse-scored. An example item is: “When I see an opportunity for something I like I get excited right away.” The responses were subsequently summed, with higher total scores indicating higher levels of reward responsiveness (Carver & White, 2013).

**Anagram Task.** Following the completion of the questionnaires, the participants were prepped for EEG recording (detailed in the next section), and were given onscreen and written instructions describing the upcoming task, a word game involving the
unscrambling of words. The word game, herein referred to as the anagram task, was divided into three successive blocks that increased in difficulty, with the first block containing easy anagrams (e.g., cwo), the second medium anagrams (e.g., rptay), and the third hard anagrams (e.g., latuf), as determined in a previous pilot study (Tresselt & Mayzner, 1966). This task was employed in a previous study by Harmon-Jones et al. (2008), and was used in the present study for replication purposes, as described in detail in the introduction. The only difference was that the present study only used half of the anagrams (30 versus 60) due to monetary restrictions.

Participants were allotted 10 seconds to solve the easy anagrams, 30 seconds for the medium anagrams, and 50 seconds for the hard anagrams, with a 5-second intertrial interval. Each block contained 10 anagrams, and was preceded by four practice trials. Seven seconds before each anagram, the participants were told on the screen whether that anagram belonged to a reward condition, or a punishment condition. For the reward condition, the participants were told that they would win 50 cents for correctly solving the anagram, and would have no loss for getting the anagram incorrect. Conversely, for the punishment condition the participants were told that they would lose 50 cents for getting the anagram incorrect, and would not gain or lose money for getting the anagram correct (Harmon-Jones et al., 2008). In each block, half of the anagrams were in the reward condition, with the other half belonging to the punishment condition. To ensure that all of the participants were actually exerting effort and were motivated to correctly solve the anagrams, they were told that the amount of their compensation was contingent on their performance. Specifically, they were told that they could earn up to $7.50. The participants were debriefed afterwards explaining why it was necessary to deceive them,
and were all given the full amount of $7.50.

**Ratings.** Following each block, participants completed a brief questionnaire assessing their present affective state to control for subjective state during the task. The Self-Assessment Manikin affect questionnaire was utilized, which asked the participants to “indicate to what extent you felt this way during the last block of anagrams,” via a visual analogue scale. The scale displayed various emotions with seven answer choices, ranging from the most negative to the most positive affect, and whose scoring ranged from -4 to +4, accordingly (emotions assessed: happiness, satisfaction, annoyance, contentment, hopefulness, boredom, stimulation, excitement, frenzy, jitter, wakefulness, and arousal). A question about how capable the participant felt about their ability to correctly solve the anagrams in each block was asked on a 5-point Likert scale, with 1 = Very incapable and 5 = Very capable (Harmon-Jones et al., 2008). Further, the participants were asked to rate the perceived difficulty of each block of anagrams (1= Very difficult, 5 = Very easy). The anagram task, including the affect questionnaire and aforesaid ratings, were configured in the presentation software E-Prime 2.0.

**Electroencephalography (EEG) Recording and Processing.**

**Recording.** Directly preceding the anagram task, a LiveAmp BrainVision 32-channel fabric EEG cap (Morrisville, NC), was affixed on the participants’ heads. Electroencephalogram recording commenced following the task instructions during a 7-second period while the participants viewed a fixation point. The EEG was recorded during this period due to research suggesting that approach motivation is activated by anticipating action (Brehm, Wright, Solomon, Silka, & Greenberg, 1983). The electroencephalogram was recorded from lateral frontal, mid-frontal, central, parietal, and
anterior and posterior temporal scalp regions from the corresponding active electrode sites, as done in the aforementioned study by Harmon-Jones et al. (2008).

Eye movements were recorded using electro-oculogram (EOG) to facilitate the assessment of artifacts in the output. EOG was recorded from the suborbit and supraorbit for the left eye. All electrode impedances were inspected to ensure they were under 5000 ohms to minimize noise and enable good signal quality. The conductive gel SuperVisc was used. The BrainVision LiveAmp EEG system that was used has a compact wireless amplifier. The EEG and EOG was amplified with a 60 Hz notch filter and digitized at a sampling rate of 500 Hz onto the hard drive of the designated desktop recording computer. Before beginning recording, a square wave, low-impedance (.5 Hz 100 μV) signal was run and inspected (Harmon-Jones et al., 2008).

**Data Processing.** All data was collected using BrainVision Recorder software and analyzed with BrainVision Analyzer. The EEG and EOG signals were visually scored and the parts of the data that had muscle movements, aberrant eye movements, or other artifact sources were removed from all channels. All epochs (brain activity during a specific time period) that were artifact-free and whose duration was 1.024 seconds were extracted through what is called a Hamming window, a method used as a prevention of spurious estimates when examining spectral power (10% Hamming window was used). Subsequently, a fast Fourier transformation (FFT), a method used to deconstruct a signal from a time domain into a frequency-focused domain, which shows you the voltages that are present at different frequencies, was used for the calculation of the power spectra. The FFT is simply another way to view the same signal (Akin, 2002). As noted previously,
these specific methods are being used to be consistent with past research by Harmon-Jones et al. (2008) for replicability purposes.

**Frontal Asymmetry Index.** The power values were averaged across all epochs (time periods) for each trial. Event markers were manually entered to indicate the onset and offset (i.e., beginning of the trial) of the 7-second anticipatory period. A Logitech webcam was used to identify where the participants were during the task, and to thus accurately record the appropriate event markers as it pertained to the specific task difficulty/condition. The focus was on the power of the alpha bandwidth (8 - 13 Hz) because alpha power has been shown to have an inverse relationship to cortical activity (Cook, O’Hara, Uijtdehaage, Mandelkern, & Leuchter, 1998; Lindsley & Wicke, 1974). To normalize the distributions, the power values were log transformed. To compute an index of frontal asymmetry, the natural log right minus the natural log left alpha power was computed, as done in previous research (Harmon-Jones & Allen, 1998; Tomarken, Davidson, Wheeler, & Doss, 1992). This index was computed for each of the anticipatory periods (the 7-second period before each anagram indicating whether there is a reward or punishment associated with that trial) for the lateral frontal (i.e., F7 and F8) and mid-frontal sites (i.e., F3 and F4), which were later averaged to yield one frontal asymmetry index. The anticipatory periods were then averaged across all trials within each difficulty block. Due to alpha power being inversely associated with cortical activity, a higher score on this index was indicative of greater relative left hemisphere activity (Harmon-Jones et al., 2008).
**Figure 2. Methodology of the Anagram Task and EEG Recording**

**Chapter Four:**

**Results**

**Manipulation Checks**

To account for potential influences of past exposure to anagram-related tasks, frequency of anagram usage was assessed, which indicated that, overall, participants had minimal experience with anagrams ($M = 2.10$, $SD = .92$). Next, to ensure the participants’ perception and the intended difficulty for each block was congruent, perceived task difficulty, as well as perceived capability, was assessed following each block. As expected, the easy trials were rated as being the least difficult ($M = 4.32$, $SD = 1.06$), the medium trials moderately difficult ($M = 2.75$, $SD = .80$), and the hard trials very difficult ($M = 2.00$, $SD = .98$). The same trends emerged for perceived capability for each of the trials. Overall, the participants felt the most capable on the easy trials ($M = 4.14$, $SD = .85$), moderately capable on the medium trials ($M = 3.11$, $SD = 1.03$), and the least capable during the hard trials ($M = 2.11$, $SD = 1.03$).
**Reward Sensitivity**

First, totals on both the Snaith Hamilton Personality Scale ($M = 1.10, SD = 1.32$) and the Behavior Avoidance Scale (BAS) ($M = 24.57, SD = 6.86$) were computed. A Pearson correlation was then utilized to examine whether higher levels of anhedonia were associated with lower levels of reward responsiveness. The results did not yield a significant relationship, $r (28) = -0.075, p = .34$. Next, totals on the Goldberg Mania Questionnaire ($M = 29.40, SD = 13.25$) computed, and a Pearson correlation was also used to assess whether individuals with hypomanic and manic symptoms show higher levels of reward responsiveness, and did not reveal a significant relationship, $r (28) = 0.064, p = .368$.

**Effect of Symptom Severity, Task Difficulty, and Reward on Frontal Alpha Asymmetry**

The foremost hypothesis concerned whether disparities in frontal alpha activity would emerge as task difficulty increased and was accompanied with a positive outcome (i.e., reward), depending on profiles of anhedonic and hypomanic/manic symptom severity. Specifically, whether those with more manic symptomatology would show greater relative left frontal activity, and those with higher levels of anhedonia would show lower relative left frontal activity. Therefore, a Pearson correlation was utilized to assess whether individuals with higher levels of anhedonia exhibit lower relative left frontal EEG activity during hard/reward trials for frontal sites. The mid-frontal and lateral frontal total alpha power values were averaged, and therefore one frontal asymmetry index was computed and subsequently used for analysis ($M = -.13, SD = 1.75$). Only 24 of the 30 participants’ EEG data was used in the analyses due to poor data quality from
excessive artifacts, etc., during the hard/reward trials. The one-tailed bivariate Pearson correlation did not reveal a significant relationship, \( r (22) = -.183, p = .196 \). In addition, to examine whether individuals with hypomanic/manic symptoms exhibited higher relative left frontal EEG activity during hard/reward trials, a one-tailed bivariate Pearson correlation was employed; however, similarly, a significant relationship did not emerge, \( r (22) = .132, p = .269 \).

**Secondary Analyses**

**Total Latency and Total Correct by Difficulty Block.** To assess possible performance differences on the anagram task, total latency to solve anagrams in each difficulty block and the number correctly solved based on anhedonic and hypomanic/manic symptoms was assessed. As displayed in Table 2, overall, latency was shortest for the easy trials, comparatively longer for the medium trials, and the longest for the hard trials, as expected. For the total number correctly solved in each difficulty block, as anticipated, collectively, participants solved more easy anagrams correctly, followed by the medium and hard anagrams, as indicated in Table 2.

**Table 2**

*Total correct and total latency to solve anagrams by difficulty block.*

<table>
<thead>
<tr>
<th></th>
<th>Easy</th>
<th>Medium</th>
<th>Hard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Correct</td>
<td>9.10 (2.09)</td>
<td>6.37 (2.81)</td>
<td>3.13 (2.24)</td>
</tr>
<tr>
<td>Total Latency (in seconds)</td>
<td>17.57 (19.69)</td>
<td>76.58 (86.03)</td>
<td>147.37 (162.23)</td>
</tr>
</tbody>
</table>
**Self-Reported Emotions.** To assess subjective mood state during the anagram task, an affect questionnaire was employed after each difficulty block that targeted a variety of emotions (e.g., pleasantness, satisfaction, contentment, wakefulness). As seen in Table 3, the general trend was that positive affect (e.g., happiness, satisfaction) decreased as the task increased in difficulty, while other self-reported emotions gradually decreased (e.g., boredom). In addition, self-reported feelings of stimulation and arousal increased as the task progressed and the anagrams consequently became more difficult.

Table 3

*Self-reported emotions on the Self-Assessment Manikin by difficulty block.*

<table>
<thead>
<tr>
<th></th>
<th>Easy</th>
<th>Medium</th>
<th>Hard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happy</td>
<td>-.07 (1.44)</td>
<td>-.29 (1.30)</td>
<td>-1.18 (1.66)</td>
</tr>
<tr>
<td>Pleased</td>
<td>-.57 (1.85)</td>
<td>-.57 (1.37)</td>
<td>-1.71 (1.61)</td>
</tr>
<tr>
<td>Satisfied</td>
<td>.11 (1.97)</td>
<td>-.46 (1.62)</td>
<td>-1.53 (1.89)</td>
</tr>
<tr>
<td>Content</td>
<td>.75 (1.71)</td>
<td>.07 (1.49)</td>
<td>-.64 (1.79)</td>
</tr>
<tr>
<td>Hopeful</td>
<td>1.04 (1.35)</td>
<td>.14 (1.32)</td>
<td>-.68 (1.77)</td>
</tr>
<tr>
<td>Relaxed</td>
<td>.86 (2.24)</td>
<td>.04 (1.53)</td>
<td>-1.00 (2.00)</td>
</tr>
<tr>
<td>Stimulated</td>
<td>-1.46 (1.77)</td>
<td>.21 (1.81)</td>
<td>.14 (1.90)</td>
</tr>
<tr>
<td>Excited</td>
<td>-1.29 (1.49)</td>
<td>-.29 (1.70)</td>
<td>-.43 (1.83)</td>
</tr>
<tr>
<td>Frenzied</td>
<td>-.79 (1.79)</td>
<td>-.04 (1.73)</td>
<td>-.32 (2.00)</td>
</tr>
<tr>
<td>Jittery</td>
<td>-.14 (1.67)</td>
<td>0 (1.74)</td>
<td>-.21 (2.08)</td>
</tr>
<tr>
<td>Wide awake</td>
<td>-.36 (2.21)</td>
<td>-.04 (2.19)</td>
<td>-.93 (2.24)</td>
</tr>
<tr>
<td>Aroused</td>
<td>-1.04 (1.99)</td>
<td>-.57 (2.06)</td>
<td>-.43 (2.08)</td>
</tr>
</tbody>
</table>

Note: Scale is from -4 to 4, with -4 being indicative of the most negative affect.
Chapter Five: Discussion

Frontal Asymmetry Findings

Overall, no significant findings were unveiled for the correlations between the mania and anhedonia scores with either the reward sensitivity measure, nor the frontal asymmetry index for the hard/reward trials. However, though not significant, the directional relationship of the results was consistent with the conceptual framework of the BAS dysregulation theory. The BAS model states that individuals who exhibit more manic symptomatology should exhibit greater relative left frontal activation during challenging, goal-oriented tasks that have the potential for a positive outcome (i.e., the hard anagram trials in the reward condition). Due to the a priori hypothesis that higher scores on the mania scale would reflect a higher asymmetry index, a one-tailed analysis was performed, and the positive direction of the correlation coefficient was consistent with this model.

Similarly, the aforementioned model would suggest that greater anhedonic symptomatology would reveal greater relative right hemispheric activity, which would be represented by lower asymmetry indices. The present findings revealed that scores on the anhedonia scale produced a negative relationship, as predicted, which indicated that greater anhedonic symptomatology was associated with a lower frontal asymmetry index. However, since these relationships did not reach statistical significance, additional findings that reveal patterns of activation consistent with the BAS model would provide support for the notion that challenges coupled with potential rewards may lead to greater and lower activation of this system in those with a propensity toward BD and MDD.
symptoms, respectively. Consequently, these results would suggest that asymmetrical frontal activity could serve as a biomarker for bipolar and depressive symptomatology, such as mania and anhedonia, accordingly. However, these assertions cannot yet be made due to the lack of statistical significance and small sample size in the present study. Therefore, any inferences drawn from the current findings should be cautiously weighed, with further evidence needed to make substantive, reliable claims, especially in relation to its clinical implications.

Further, due to the mid-frontal and lateral frontal sites being merged into one frontal asymmetry index, it is unclear whether there is differential activation at these sites. Therefore, the findings from Harmon-Jones et al. (2008), which unveiled significant group differences in left frontal activation at the lateral frontal sites, was not able to be reproduced, and therefore these findings could not be further validated. In addition, the mean self-reported emotions during the anagram task varied as would be expected based on the difficulty of the trials. Therefore, although not statistically confirmed, safe assumptions can be made that the participants’ subjective ratings, which reflected present affective state, were relatively homogenous; thus, eliminating the potential for differences in state-dependent changes in cortical activity that could produce heterogeneity not attributed to varying levels of symptomatology.

**Relevance and Clinical Utility**

This research is particularly germane because, for BD, increased goal-striving activity is one of the main predictors of onset of hypomanic or manic symptomatology. Thus far, much of the research has focused on environmental factors that predict the onset and severity of BD, with the overarching conclusion being that one’s environment
leads to a dysregulated temperament that can result in developing full-blown BD (Harmon-Jones et al., 2008). However, it is clear that psychosocial processes are not the only predictor of BD onset, and repeated evidence for biological markers for psychopathologies such as BD provide incontrovertible support for the notion that examining biological processes in BD is paramount. Similarly, greater anhedonic symptoms are associated with a greater likelihood of developing MDD, as well as being reflective of the degree of illness severity. In light of the repeated evidence for neurological markers in these disorders, overlooking this facet of BD and MDD pathology would be negligent and detrimental to the advancement of better detection and diagnostic methods that can be clinically implemented.

The empirical inquiry regarding the etiology of MDD and BD has been relatively vast, yet the investigation into how symptom profiles of these disorders reflect both behavioral and biological outcomes is almost nonexistent. Exclusively examining diagnostic groups in their entirety does not enable the examination of how these potential biological markers change as a function of symptom severity. Therefore, the present study serves as not only another foundation for redirecting this area of research toward a more biological focus, but also serves as a platform to advocate for more extensive investigation into biomarker research in ubiquitous psychiatric conditions, such as the affective disorders, MDD and BD.

As noted in a previous section, there are numerous behavioral symptoms that characterize these disorders that are utilized as part of the diagnostic procedure. Supplementing these overt measures of dysfunction with covert, objective markers of pathology could be instrumental in facilitating diagnosis, and perhaps more importantly,
detecting vulnerability, to these disorders. The agenda is not to make the established behavioral hallmarks of these psychopathologies obsolete, but rather to augment accurate and early diagnosis and detection. Therefore, continued empirical support for this frontal asymmetry index as a neural marker of BD and MDD could be a promising start to re-conceptualizing diagnostic protocol through the integration of overt and covert indicators.

**Limitations**

The primary limitation of this study is the small sample size. Due to unforeseen setbacks, the desired sample size was not attained. In addition, this is not a clinical sample, so the results derived from this group of individuals must be interpreted carefully and direct clinical application should be cautiously inferred until more evidence is obtained. Further, the scores on the Goldberg Mania Scale, which assessed mania symptomatology, were unusually high. This is proposed to be because this is a sample of college students, and therefore some of the questions may not have been tapping into clinical pathology, but rather situational influences (e.g., insufficient sleep was attributed to a high workload, as opposed to being an indicator of mania). Lastly, the event markers that were utilized to record the onset and offset of the 7-second anticipatory periods between the fixation points and the onset of the anagrams were input manually; therefore, this presented a potential hindrance to temporal accuracy of the brain activity associated with each anticipatory period.

**Future Research**

Going forward, subsequent empirical inquiries in this realm of research should ideally include clinical samples who have a pre-existing diagnosis of MDD or BD. Preferably, examining the symptom severity of anhedonia and hypomania/mania in those
with current MDD or BD diagnoses, respectively, would conceivably provide the most reliable evidence for the salience of these symptoms and their neurological origins. Larger sample sizes should also be employed to optimize power and external validity. In addition, formulating and executing other challenging and reward-based tasks would be advantageous for it would be useful to see if these findings are global, or merely task-specific.

**Conclusion**

The present study supplements past literature by addressing symptom profiles of two prominent disorders and examines how previously discovered biomarkers and reward responsiveness vary as a function of symptom severity. The anticipated directional relationship between the frontal asymmetry indices for the hard/reward trials for the mania and anhedonia scores, support the notion that biomarkers and psychosocial factors should be examined in conjunction, to better inform which indicators can be utilized to detect vulnerability to MDD and BD onset. Examination of the interplay between underlying biological mechanisms and psychosocial stressors is scarce, and therefore warrants continued investigation. Overarchingly, the primary aim of this study was to give support to the idea that psychopathology should not be categorically isolated, for this does not accurately encapsulate the individual variability within these disorders. Beyond the potential promise of uncovering a biological correlate for BD and MDD that could be utilized for detection of these disorders, failure to acknowledge the neurological underpinnings that drive these illnesses presents a potential impedance to effective treatment and positive long-term outcomes.
For example, behavioral observation of an individual suspected to be at risk for developing a psychiatric illness, may be congruent with present diagnostic criteria; therefore, standard therapeutic and psychopharmacological interventions may be implemented. However, adhering to a singular treatment approach overlooks an individual’s idiosyncratic symptom profile that underlies the presentation of both their overt and covert processes. Therefore, the goal of the present study was to give credence to not only a neural marker that could be used to detect illness onset, but also one that could be used in conjunction with behavioral presentation to construct tailored treatment regimens. Thus, continued adherence to this conceptual framework, along with optimization of methodology and sample composition, will permit the scientific validation and resulting credibility that is necessary for empirical, and consequential clinical, advancement.
The IRB has approved your protocol "Reward-Based Biobehavioral Marker in Anhedonic and Hypomanic/Manic Symptomatology" effective 1/2/2017.

Your IRB protocol can now be viewed by your faculty advisor in MyOSPR. For more information, please visit: http://www.towson.edu/academics/research/sponsored/myospr.html

If you should encounter any new risks, reactions, or injuries to subjects while conducting your research, please notify IRB@towson.edu. Should your research extend beyond one year in duration, or should there be substantive changes in your research protocol, you will need to submit another application.

We do offer training and orientation sessions for faculty/staff, please sign up for one of the sessions: http://fusion.towson.edu/WWW/signupGeneric/index.cfm?type=OSPR

Check back to that registration site frequently – we’ll post additional sessions for January and spring semester soon.

Regards,
Towson IRB
Appendix B

INFORMED CONSENT FORM

PRINCIPAL INVESTIGATOR:  Grace-Anna Chaney

PHONE: (540) 312-8875

EMAIL: gchane2@students.towson.edu

Purpose of the Study:
This study is designed to see if those who report more of a decreased interest in everyday activities and those who show more goal-striving behavior show more brain activity in one hemisphere in relation to the other during a word unscrambling task.

Procedures:
Participants will be given questionnaires asking about various behaviors that relate to one’s interest in daily activities and behaviors toward various rewards. Another questionnaire will ask about basic demographic information, such as age, ethnicity, English proficiency, etc., as well as other information relevant to the study such as current medication taken. Participants will then be seated in front of a Desktop computer and an electroencephalography (EEG) cap will be affixed on their heads. They will then perform a task, which requires unscrambling words increasing in difficulty from easy, medium, to hard.

Risks/Discomfort:
For the EEG task, minor discomfort may be experienced when the EEG cap is affixed on the participants' heads, however the overall procedure is non-invasive and should not cause any more than minimal discomfort. All of the procedures pose minimal risk.

Should any of the questions or procedures become distressing to you, the study will be
terminated immediately.

**Benefits:**
There are no direct benefits to you for participating in this study other than course credit received and monetary compensation depending on your performance on the word unscrambling task (you can receive up to $7.50 in a Visa gift card or cash). This study is clinically relevant because two symptoms, lack of interest in daily activities and goal-striving behavior (i.e., anhedonia and hypomania/mania), are characterized by abnormal responsiveness to rewards via a particular biomarker (i.e., frontal hemisphere asymmetry) and are related to two prevalent psychological disorders (Major Depressive Disorder and Bipolar Disorder, respectively). This could be used to distinguish, prevent, and/or predict vulnerability to these, and similar, disorders.

**Alternatives to Participation:**
Participation in this study is voluntary. You are free to withdraw or discontinue participation at any time.

**Cost Compensation:**
Participation in this study will involve no costs to you. As noted previously, you will be paid based on your performance on the word unscrambling task. You can earn up to $7.50 in a Visa gift card or cash.

All information collected during the study period will be kept strictly confidential. You will be identified through identification numbers. No publications or reports from this project will include identifying information on any participant. If you agree to join this study, please sign your name below.

_____ I have read and understood the information on this form.
I have had the information on this form explained to me.

Subject's Signature

Witness to Consent Procedures

Principal Investigator
Appendix C

Demographics

Please answer the following questions about yourself and your background. Some questions may be personal, so please note that all of this information will be kept COMPLETELY confidential and your anonymity will be ensured. You also have the right to skip any question(s), or parts of a question, if you choose.

1. Age (in years): _______________

2. Sex: Male / Female

3. Please specify your ethnicity (circle).
   - White
   - Hispanic or Latino
   - Black or African American
   - Native American or American Indian
   - Asian / Pacific Islander
   - Other: _____________

4. Are you right or left-handed? Right / Left

5. Are you a native speaker of English (i.e., did you learn English as a first language)?
   Y / N

6. If not, how long have you been speaking English? ______

7. Do you have any history of epilepsy or neurological disorders? Y / N

8. Do you take any medications? If so, please list the name(s) of the medication(s) and reason(s) for taking it.
   Y / N
If yes, name of medication: ____________________
Reason for taking it: _______________________

9. Have you ever been diagnosed with Major Depressive Disorder (MDD) or Bipolar Disorder (I or II)?
   Y / N

If yes, which one? ________________________

Other psychiatric diagnosis(es): ________________________________

10. How frequently do you use anagram-based tasks (i.e., word unscrambling), either currently or in the past?

    1  2  3  4  5

1 = Never, 5 = A great deal
Appendix D

Behavior Avoidance Scale (BAS)

Instructions:
Each item of this questionnaire is a statement that a person may either agree with or disagree with. For each item, indicate how much you agree or disagree with what the item says. Please respond to all the items; do not leave any blank. Choose only one response to each statement. Please be as accurate and honest as you can be. Respond to each item as if it were the only item. That is, don't worry about being "consistent" in your responses. Choose from the following four response options:

1 = very true for me

2 = somewhat true for me

3 = somewhat false for me

4 = very false for me

1. A person's family is the most important thing in life. _____
2. When I'm doing well at something I love to keep at it. _____
3. When I get something I want, I feel excited and energized. _____
4. I often wonder why people act the way they do. _____
5. When I see an opportunity for something I like I get excited right away. _____
6. How I dress is important to me. _____
7. When good things happen to me, it affects me strongly. _____
8. It would excite me to win a contest. _____
9. It's hard for me to find the time to do things such as get a haircut. _____
**Scoring:**

Responses summed. Higher scores indicate higher levels of reward responsiveness.

**Reference:**

Appendix E

Goldberg's Mania Scale

Instructions:

The 18 items below refer to how you have felt and behaved **DURING THE PAST WEEK.** For each item, indicate the extent to which it is true, by checking the appropriate box next to the item.

0 = Not at all 1 = Just a little 2 = Somewhat 3 = Moderately 4 = Quite a lot 5 = Very much

1. My mind has never been sharper. 0 1 2 3 4 5
2. I need less sleep than usual. 0 1 2 3 4 5
3. I have so many plans and new ideas that it is hard for me to work. 0 1 2 3 4 5
4. I feel a pressure to talk and talk. 0 1 2 3 4 5
5. I have been particularly happy. 0 1 2 3 4 5
6. I have been more active than usual. 0 1 2 3 4 5
7. I talk so fast that people have a hard time keeping up with me. 0 1 2 3 4 5
8. I have more new ideas than I can handle. 0 1 2 3 4 5
9. I have been irritable. 0 1 2 3 4 5
10. It's easy for me to think of jokes and funny stories. 0 1 2 3 4 5
11. I have been feeling like "the life of the party." 0 1 2 3 4 5
12. I have been full of energy. 0 1 2 3 4 5
13. I have been thinking about sex. 0 1 2 3 4 5
14. I have been feeling particularly playful. 0 1 2 3 4 5
15. I have special plans for the world. 0 1 2 3 4 5
16. I have been spending too much money. 0 1 2 3 4 5

17. My attention keeps jumping from one idea to another. 0 1 2 3 4 5

18. I find it hard to slow down and stay in one place. 0 1 2 3 4 5

Comments:

__________________________________________________________________________

__________________________________________________________________________

Medication:

__________________________________________________________________________

__________________________________________________________________________

Scoring:

• 0-9, No Mania Likely

• 10-17 Possibly Mildly Manic, or Hypomanic

• 18-21, Borderline Mania

• 22-35, Mild-Moderate Mania

• 36-53, Moderate-Severe Mania

• 54 and up, Severely Manic

Reference: The Goldberg Mania Questionnaire was developed by Ivan Goldberg, M.D.
Appendix F

The Snaith-Hamilton Pleasure Scale (SHAPS)

Instructions:

This questionnaire is designed to measure your ability to experience pleasure in the last few days. It is important to read each statement very carefully. Tick one of the boxes [ ] to indicate how much you agree or disagree with each statement.

1. I would enjoy my favorite television or radio program:
   - Strongly disagree [ ]
   - Disagree [ ]
   - Agree [ ]
   - Strongly agree [ ]

2. I would enjoy being with my family or close friends:
   - Strongly disagree [ ]
   - Disagree [ ]
   - Agree [ ]
   - Strongly agree [ ]

3. I would find pleasure in my hobbies and pastimes:
   - Strongly disagree [ ]
   - Disagree [ ]
   - Agree [ ]
   - Strongly agree [ ]

4. I would be able to enjoy my favorite meal:
   - Strongly disagree [ ]
Disagree [ ]
Agree [ ]
Strongly agree [ ]

5. I would enjoy a warm bath or refreshing shower:

Strongly disagree [ ]
Disagree [ ]
Agree [ ]
Strongly agree [ ]

6. I would find pleasure in the scent of flowers or the smell of a fresh sea breeze or freshly baked bread:

Strongly disagree [ ]
Disagree [ ]
Agree [ ]
Strongly agree [ ]

7. I would enjoy seeing other people’s smiling faces:

Strongly disagree [ ]
Disagree [ ]
Agree [ ]
Strongly agree [ ]

8. I would enjoy looking smart when I have made an effort with my appearance:

Strongly disagree [ ]
Disagree [ ]
Agree [ ]
Strongly agree [ ]

9. I would enjoy reading a book, magazine or newspaper:

   Strongly disagree [ ]
   Disagree [ ]
   Agree [ ]
   Strongly agree [ ]

10. I would enjoy a cup of tea or coffee or my favorite drink:

    Strongly disagree [ ]
    Disagree [ ]
    Agree [ ]
    Strongly agree [ ]

11. I would find pleasure in small things, e.g. bright sunny day, a telephone call from a friend:

    Strongly disagree [ ]
    Disagree [ ]
    Agree [ ]
    Strongly agree [ ]

12. I would be able to enjoy a beautiful landscape or view:

    Strongly disagree [ ]
    Disagree [ ]
    Agree [ ]
    Strongly agree [ ]
13. I would get pleasure from helping others:

   Strongly disagree [ ]
   Disagree [ ]
   Agree [ ]
   Strongly agree [ ]

14. I would feel pleasure when I receive praise from other people:

   Strongly disagree [ ]
   Disagree [ ]
   Agree [ ]
   Strongly agree [ ]

**Scoring:**

Either of the Disagree responses receives a score of 1 and either of the Agree responses receive a score of 0. The SHAPS is scored as the sum of the 14 items so that total scores ranged from 0 to 14. A higher total SHAPS score indicated higher levels of anhedonia. A cut-off score of 2 provides the best discrimination between “normal” and “abnormal” level of hedonic tone.

**Reference:**

Appendix G

ANAGRAM TASK

EASY BLOCK (EVEN) - INSTRUCTIONS:

“Unscramble the letters to form a word. There may be more than one answer for each scrambled word, so type in the first answer that comes to mind. Accuracy is important in this task. This first block will consist of anagrams that are at an EASY level of difficulty. You will have 10 seconds to solve each one.”

TASK INSTRUCTIONS CONTINUED

“How each anagram may affect your earnings will be displayed prior to each one. There are two possibilities for how your answer will affect your amount. The first type (+50¢) gives you a chance to increase your amount. If you answer it correctly you will win 50 cents and if you get it wrong you won’t win or lose any money. For the second type (-50¢), you only have the chance to avoid losing money. If you get the anagram wrong, you will lose 50 cents but if you get it right you won’t win or lose any money. The first four anagrams are for practice and will not affect your earnings.”

RULES

1. Use of scratch paper is not allowed.

2. Every letter must be used and each letter can be used only once per word. For example, medo can not be doomed, but only dome.

3. No abbreviated words are allowed. For example, medo can not be demo because demo is an abbreviation of the word demonstration.
4. No proper names are allowed.

5. For example, xlae can not be alex, but only axle.

**PRACTICE ANAGRAMS FOR EASY BLOCK (EVEN)**

EASY PRACTICE

onw

EASY PRACTICE

cwo

EASY PRACTICE

pna

EASY PRACTICE

tca

**ANAGRAMS FOR EASY BLOCK (EVEN)**

EASY -50¢

atp

EASY +50¢

hte

EASY +50¢

amr

EASY -50¢

yug

EASY +50¢

aet
EASY -50¢
byo
EASY -50¢
pti
EASY +50¢
rde
EASY +50¢
aws
EASY -50¢
aex

EASY BLOCK (ODD) - INSTRUCTIONS:
“Unscramble the letters to form a word. There may be more than one answer for each scrambled word, so type in the first answer that comes to mind. Accuracy is important in this task. This first block will consist of anagrams that are at an EASY level of difficulty. You will have 10 seconds to solve each one.”

TASK INSTRUCTIONS CONTINUED
“How each anagram may affect your earnings will be displayed prior to each one. There are two possibilities for how your answer will affect your amount. The first type (+50¢) gives you a chance to increase your amount. If you answer it correctly you will win 50 cents and if you get it wrong you won't win or lose any money. For the second type (-50¢), you only have the chance to avoid losing money. If you get the anagram wrong,
you will lose 50 cents but if you get it right you won’t win or lose any money. The first four anagrams are for practice and will not affect your earnings."

**RULES**

1. Use of scratch paper is not allowed.

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3. No abbreviated words are allowed. For example, medo can not be demo because demo is an abbreviation of the word demonstration.

4. No proper names are allowed.

5. For example, xlae can not be alex, but only axle.

**PRACTICE ANAGRAMS FOR EASY BLOCK (ODD)**

**EASY PRACTICE**

ow

**EASY PRACTICE**

cwo

**EASY PRACTICE**

pna

**EASY PRACTICE**

Tca
ANAGRAMS FOR EASY BLOCK (ODD)

EASY +50¢
atp
EASY -50¢
hte
EASY -50¢
amr
EASY +50¢
yug
EASY -50¢
aet
EASY +50¢
byo
EASY +50¢
pti
EASY -50¢
rde
EASY -50¢
aws
EASY +50¢
aex
MEDIUM BLOCK (EVEN) - INSTRUCTIONS:
“Unscramble the letters to form a word. There may be more than one answer for each scrambled word, so type in the first answer that comes to mind. Accuracy is important in this task. This first block will consist of anagrams that are at an MEDIUM level of difficulty. You will have 30 seconds to solve each one.”

TASK INSTRUCTIONS CONTINUED
“How each anagram may affect your earnings will be displayed prior to each one. There are two possibilities for how your answer will affect your amount. The first type (+50¢) gives you a chance to increase your amount. If you answer it correctly you will win 50 cents and if you get it wrong you won't win or lose any money. For the second type (-50¢), you only have the chance to avoid losing money. If you get the anagram wrong, you will lose 50 cents but if you get it right you won’t win or lose any money. The first four anagrams are for practice and will not affect your earnings.”

RULES
1. Use of scratch paper is not allowed.
2. Every letter must be used and each letter can be used only once per word. For example, medo cannot be doomed, but only dome.
3. No abbreviated words are allowed. For example, medo cannot be demo because demo is an abbreviation of the word demonstration.
4. No proper names are allowed.
5. For example, xlae cannot be alex, but only axle.
PRACTICE ANAGRAMS FOR MEDIUM BLOCK (EVEN)

MEDIUM PRACTICE
rbscu

MEDIUM PRACTICE
gawno

MEDIUM PRACTICE
bnloe

MEDIUM PRACTICE
ulipp

ANAGRAMS FOR MEDIUM BLOCK (EVEN)

MEDIUM +50¢
hecab

MEDIUM -50¢
hicar

MEDIUM -50¢
aohrc

MEDIUM +50¢
rptay

MEDIUM -50¢
ekrle

MEDIUM +50¢
MEDIUM BLOCK (ODD) - INSTRUCTIONS:

"Unscramble the letters to form a word. There may be more than one answer for each scrambled word, so type in the first answer that comes to mind. Accuracy is important in this task. This first block will consist of anagrams that are at an MEDIUM level of difficulty. You will have 30 seconds to solve each one."

TASK INSTRUCTIONS CONTINUED

"How each anagram may affect your earnings will be displayed prior to each one. There are two possibilities for how your answer will affect your amount. The first type (+50¢) gives you a chance to increase your amount. If you answer it correctly you will win 50 cents and if you get it wrong you won't win or lose any money. For the second type (-50¢), you only have the chance to avoid losing money. If you get the anagram wrong, you will lose 50 cents but if you get it right you won’t win or lose any money. The first four anagrams are for practice and will not affect your earnings."
RULES

1. Use of scratch paper is not allowed.

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4. No proper names are allowed.

5. For example, xlae cannot be alex, but only axle.

PRACTICE ANAGRAMS FOR MEDIUM BLOCK (ODD)

MEDIUM PRACTICE
rbscu

MEDIUM PRACTICE
gawno

MEDIUM PRACTICE
bnloe

MEDIUM PRACTICE
ulipp

ANAGRAMS FOR MEDIUM BLOCK (ODD)

MEDIUM -50¢
hecab

MEDIUM +50¢
HARD BLOCK (EVEN) - INSTRUCTIONS:

“Unscramble the letters to form a word. There may be more than one answer for each scrambled word, so type in the first answer that comes to mind. Accuracy is important in this task. This first block will consist of anagrams that are at an HARD level of difficulty. You will have 50 seconds to solve each one.”
**TASK INSTRUCTIONS CONTINUED**

“How each anagram may affect your earnings will be displayed prior to each one. There are two possibilities for how your answer will affect your amount. The first type (+50¢) gives you a chance to increase your amount. If you answer it correctly you will win 50 cents and if you get it wrong you won't win or lose any money. For the second type (-50¢), you only have the chance to avoid losing money. If you get the anagram wrong, you will lose 50 cents but if you get it right you won’t win or lose any money. The first four anagrams are for practice and will not affect your earnings.”

**RULES**

1. Use of scratch paper is not allowed.

2. Every letter must be used and each letter can be used only once per word. For example, medo cannot be doomed, but only dome.

3. No abbreviated words are allowed. For example, medo cannot be demo because demo is an abbreviation of the word demonstration.

4. No proper names are allowed.

5. For example, xlae cannot be alex, but only axle.

**PRACTICE ANAGRAMS FOR HARD BLOCK (EVEN)**

**HARD PRACTICE**

yenpo

**HARD PRACTICE**

eodnw
HARD PRACTICE

gsrua

HARD PRACTICE

latuf

ANAGRAMS FOR HARD BLOCK (EVEN)

HARD -50¢
oarlb

HARD -50¢
jutan

HARD +50¢
datir

HARD +50¢
tinga

HARD -50¢
tanbo

HARD +50¢
hugol

HARD -50¢
aitop

HARD -50¢
rigon

HARD +50¢
gt nao
HARD +50¢
aocrb

**HARD BLOCK (ODD) - INSTRUCTIONS:**

“Unscramble the letters to form a word. There may be more than one answer for each scrambled word, so type in the first answer that comes to mind. Accuracy is important in this task. This first block will consist of anagrams that are at an **HARD** level of difficulty. You will have 50 seconds to solve each one.”

**TASK INSTRUCTIONS CONTINUED**

“How each anagram may affect your earnings will be displayed prior to each one. There are two possibilities for how your answer will affect your amount. The first type (+50¢) gives you a chance to increase your amount. If you answer it correctly you will win 50 cents and if you get it wrong you won’t win or lose any money. For the second type (-50¢), you only have the chance to avoid losing money. If you get the anagram wrong, you will lose 50 cents but if you get it right you won’t win or lose any money. The first four anagrams are for practice and will not affect your earnings.”

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1. Use of scratch paper is not allowed.
2. Every letter must be used and each letter can be used only once per word. For example, medo cannot be doomed, but only dome.
3. No abbreviated words are allowed. For example, medo cannot be demo because demo is an abbreviation of the word demonstration.

4. No proper names are allowed.

5. For example, xlae cannot be alex, but only axle.

**PRACTICE ANAGRAMS FOR HARD BLOCK (ODD)**

HARD PRACTICE
yenpo
HARD PRACTICE
eodnw
HARD PRACTICE
gsrua
HARD PRACTICE
latuf

**ANAGRAMS FOR HARD BLOCK (ODD)**

HARD +50¢
oarlb
HARD +50¢
jutan
HARD -50¢
datir
HARD -50¢
tinga
HARD +50¢
tanbo
HARD -50¢
hugol
HARD +50¢
aitop
HARD +50¢
rigon
HARD -50¢
gtnao
HARD -50¢
aocrb
Appendix H

Self-Assessment Manikin (SAM)

Instructions:

Please indicate to what extent you felt this way during the last block of anagrams.

For example, use the extreme happy rating if the reaction was one of feeling “happy, pleased, satisfied, contented, hopeful, relaxed,” and use the other extreme if you felt “unhappy, annoyed, unsatisfied, melancholic, despairing, or bored” (Bradley & Lang, 1994).
Scoring:

Each scale is on 9-point rating scale ranged from -4 to +4, with 0 representing the center segment of the scale (Bradley & Lang, 1994).

Reference:

Appendix I

Perceived Capability and Difficulty

1. How capable did you feel about your ability to correctly solve the anagrams in this block?

   1  2  3  4  5

   1 = Very incapable, 5 = Very capable

2. How difficult did you find this block of anagrams?

   1  2  3  4  5

   1= Very difficult, 5 = Very easy

Reference:

Appendix J

Debriefing Form

Being told that you would be paid based on your performance on the word unscrambling task was important not only for consistency purposes due to replicating a previous study (Harmon-Jones et al., 2008), but also because a hypothetical reward, or a reward that does not depend on your performance, may not produce the same effects in frontal asymmetry. Therefore, it was necessary to initially deceive you into thinking your reward was commensurate with how well you unscrambled the words.

If there are any questions, comments, or concerns regarding the study, please contact Grace-Anna Chaney at gchane2@students.towson.edu or Dr. Rick Parente at FParente@towson.edu. If any distress or discomfort arose as a result of the study, please contact the Towson University Counseling Center at (410) 704-2512.
Appendix K

I, ________________________, have been given $7.50 in the form of a Visa gift card or

   (Print Name)

cash for participation in the present study.

____________________________________________________________________
Participant Signature   (Print Name)   Date

____________________________________________________________________
PI Signature            (Print Name)   Date
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DEGREE AND DATE TO BE CONFERRED: Master of Arts, 2017

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2017  M.A., Experimental Psychology. Towson University, Towson, MD

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2015  Psychology Student of the Year
2014 – 2015  President/Vice President of the Psi Chi Honor Society
2013  Invited applicant to the Alpha Lambda Delta Honor Society

PROFESSIONAL MEMBERSHIP

2015 – Present  Psychonomic Society, Student Member
2014 – 2015  Psychology Community, Vice President and Treasurer
2013 – 2015  Virginia Psychological Association, Student Member
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2015 – Present  Research Program Assistant, Medical Psychology Clinic
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**PRESENTATIONS**


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MANUSCRIPTS


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- **Physiological Lab Procedures**: BIOPAC 150/Acqknowledge 4.4 system: electrocardiography (ECG, heart rate variability), electrodermal activity (EDA), respiration belt. BrainVision actiCHamp: electroencephalogram (EEG) equipment.
- **Other Research Software**: E-Prime, Comprehensive Meta-Analysis, Qualtrics