ASSESSING APPROACH MOTIVATION IN DEPRESSED INDIVIDUALS WITH A HISTORY OF CONCUSSION

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DEDICATION

This dissertation is dedicated to my beloved husband.

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ASSESSING APPROACH MOTIVATION IN DEPRESSED INDIVIDUALS WITH A HISTORY OF CONCUSSION

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Depression is the leading cause of disability worldwide. Anhedonia, a core symptom of depression, has been described as a lack of pleasure or interest, though it is a much more complex process than simply lack of pleasure. Anhedonia is made up of anticipation, motivation, enjoyment, and learning related to rewards. When an individual's motivation is impaired, reward perception is blunted as the drive to work for it is reduced. This "approach motivation" is generally subserved by the ventral striatum and orbitofrontal cortex, two areas which can be affected in a variety of neurologic conditions, including traumatic brain injury, as these subcortical structures can be affected by pathophysiological sequalae of trauma. To explore this concept, we examined data from a large ongoing study of adult depression (Dallas 2K). A total of 110 participants with depression with (n=40) and without a history (n=70) of self-reported concussion were tested on a measure of approach motivation, the Energy Expenditure for Rewards Task (EEfRT). We also analyzed depression symptom severity and the relationship between anhedonia severity to approach motivation on the EEfRT. Results revealed no significant differences between depressed adults with and without a history of concussion on approach motivation. Exploratory analyses revealed differences between high and low

depression severity groups, such that high depression severity participants were less likely to select low probability/high reward tasks, but this was irrespective of concussion history. Though the main study results were nonsignificant, exploratory analyses present an opportunity for future direction of studies related to approach motivation and cognition in co-morbid depression and concussion.

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ANCOVA – Analysis of Covariance

D2K- Dallas 2K longitudinal study

EEG – Electroencephalogram

EEfRT- Effort Expenditure for Rewards Task

ERP- Evoked Response Potentials

fMRI – Functional Magnetic Resonance Imaging

LFA- Left Frontal Activity

LOC – Loss of Consciousness

MDD- Major Depressive Disorder

MRI- Magnetic Resonance Imaging

mTBI – Mild Traumatic Brain Injury

OFC- Orbitofrontal Cortex

PCS- Post-concussive syndrome

PHQ-9- Patient Health Questionnaire-9

TBI – Traumatic Brain Injury

TECH – Texas Evaluation of Concussion History

CHAPTER ONE
Introduction

Depression is the leading cause of disability worldwide, with a major depressive episode occurring in 7.1% individuals during their lifetime. Factors that increase the likelihood of a major depressive episode include female gender, age 18-25, and identifying with more than one race. Sixty-three percent of those with a major depressive episode describe their impairment as severe, and 35% of people with a major depressive episode do not receive treatment (NIMH, 2019). Despite ongoing research efforts, the complexities of depression limit our understanding of its mechanisms. In order to offer more effective treatment solutions, further research is needed to better comprehend the neurobiological underpinnings of the disorder.

Major depression is diagnosed by the presence of a constellation of symptoms, of which depressed mood and loss of interest or pleasure (anhedonia) serve as hallmark indicators (American Psychiatric Association, 2013). Depression can manifest in typical or atypical fashion, which poses a significant challenge to treatment. For example, one person with depression may have a depressed mood and fatigue, poor sleep, psychomotor slowing, and difficulty with concentration, whereas another may have anhedonia as the core symptom along with fatigue, loss of appetite, suicidality, and feelings of guilt or worthlessness; both presentations warrant a major depressive disorder (MDD) diagnosis, but may necessitate different treatments. Anhedonia (the loss of interest or pleasure), one of the hallmark indicators of depression, is considered a key psychopathological endophenotype in MDD (Craske, 2016; Hasler et al., 2004) and its presence predicts a worse course of MDD in adults (Spijker, Bijl, de Graaf, & Nolen, 2001; Wardenaar, Giltay, van Veen, Zitman, & Penninx, 2012). Anhedonia is particularly important to examine, not only because of its implications within depression, but

also because of its complexity. The pursuit and experience of pleasure involves the following: a desire or wanting of a reward, expectation or anticipation of a reward, motivation to obtain the desired reward, effort used to sustain energy to attain the award, and enjoyment of the reward (Der Avakian, 2016). These elements of reward can be divided into two different domains of pleasure. While one domain is related to obtaining pleasure (motivation), the other is related to enjoyment (or consumption) of pleasure. Research suggests that reward impairments related to motivation are more deeply rooted in depression compared to the impairment of enjoyment of reward (Treadway & Zald, 2011). Dopamine is implicated in the motivational aspect of pleasure, which is an entirely different system than consummatory pleasure that is driven by opioids. When motivation to obtain rewards is diminished, depression may emerge or worsen because there is no driving force to seek out pleasure. There are disease processes that are known to disrupt the dopamine pathway, such as schizophrenia, drug addiction, and Parkinson's disease (Bressan & Crippa, 2005; Holcomb & Rowland, 2007; Moran et al., 2019), which is implicated in deficits in motivation (Barch, 2005; McGuigan, 2019). If impairment in motivation is inherent in these dopamine-related diseases, it is possible that a defect to the dopamine pathway by means of pathophysiological disturbance such as excitatory-inhibitory balance, axonal dysfunction, or inflammation (Giza, Grico, & Prins, 2018) resulting from mild traumatic brain injury (mTBI), could influence motivation. Depressive symptoms are not uncommon following mTBI and can appear soon after injury or emerge later, and premorbid mood disorders can contribute to onset of depressive disorder after concussion (Yrondi, Brauge, LeMen, Arbus, & Pariente, 2017). Most symptoms of concussion, such as headache, dizziness, and fatigue often remit within a few days to a month (Lovell et al., 2006), though some individuals experience

persistent symptoms (Vanderploeg, Curtiss, Luis, & Salazar, 2007). There are multiple theories related to persistent post-concussive symptoms, but there is a lack of clarity because of the overlapping nature of the symptoms in multiple other conditions. Since depression can be seen following mTBI/concussion (Scholten et al., 2016), and because motivation is often impaired in depression, it could be hypothesized that motivation impairment may also play a role in persistence of post-concussive symptoms.

One aspect of reward impairment that merits greater attention in depression is *approach motivation*, as this is a potentially modifiable treatment target. Research suggests that depressive symptoms in adults are associated with deficits in motivation for pleasurable stimuli, as well as impairments in ability to modulate behavior for it (approach motivation) (Romer-Thomsen et al., 2015; Whitton, Treadway, & Pizzagalli, 2015). Standard behavioral depression treatments such as behavioral activation will be more challenging if a person's approach motivation is impaired, as they will be less likely to seek out reward. If a person has depression and a history of concussion, it is unknown whether their approach motivation may be further impacted. Further understanding of how motivation is expressed in depression, as well as in depression with concussion/mTBIs, may help clarify the impact of reward behavior. This research is designed to further contribute to the field of evidence-based understanding of mental illness by examining the behaviors related to motivation in the context of depression and concussion.

Review of the Literature

DEPRESSION

Major depressive disorder (MDD) affects more than 300 million people globally, and approximately 7% of adults and 13% of adolescents within the U.S. within a given year (NIMH,

2016). Depression is currently ranked as the leading cause of disability worldwide. The financial burden of depression has risen, increasing from $173.2 billion in 2005 to $210.5 billion in 2010, an increase of 21.5% over this period (Greenberg et al., 2015). This is due to the increase in MDD prevalence from 13.8 million in 2005 to 15.4 million in 2010, with the largest increase in the 50+ age range. The financial burden of this disease is largely due to loss of work and health care costs (Greenberg et al., 2015).

Not only are the financial implications significant, but the effects of depression on an individual's life can be overwhelming. Individuals with depression often describe numbness, disconnection, and a lack of enjoyment of their lives. Depression leads to a heightened risk of suicide, as hopelessness and more severe pathology are associated with increased suicidal ideation (Hawton, Comabella, Haw, & Saunders, 2013), as does substance use and psychosis (Bachmann, 2018),

Symptoms of depression include a down or depressed mood, loss of pleasure or interest (anhedonia), change in sleep/appetite/activity, difficulty paying attention and concentrating, feelings of guilt and worthlessness, thoughts of death/suicidality, and fatigue (American Psychiatric Association, 2013). Depression is difficult to treat and has an approximately 30% remission rate (Trivedi et al., 2006), and those who require more treatment steps tend to have higher relapse rates (Rush et al., 2006). Earlier onset of MDD is associated with greater impairment (Zisook et al., 2007), which makes early detection and intervention of greater importance.

ANHEDONIA

One of the hallmark symptoms of depression is anhedonia (American Psychiatric Association, 2013), which is likely to be present among individuals entering a depressive episode (Iacoviello et al., 2010) and affects approximately 37% of those with depression (Pelizza & Ferrari, 2009). Anhedonia is considered a key psychopathological endophenotype in MDD (Craske at al., 2016; Hasler et al., 2004) and its presence predicts a worse course of MDD (Spijker, Bijl, de Graaf, & Nolen, 2001; Wardenaar, Giltay, van Veen, Zitman, & Penninx, 2012). Further, anhedonia is a predictor of non-response to selective serotonin reuptake inhibitors (SSRI) (McMakin et al., 2012; Rush et al., 2009), thus inhibiting the most prevalent pharmacological treatment. Anhedonia was once modestly described as an inability to experience pleasure (Ribot, 1986), though this criterion has expanded to include a significantly broader system of processes. Anhedonia is a sum of its parts, including desire or wanting of a reward, expectation or anticipation of a reward, motivation to obtain the desired reward, effort used to sustain energy to attain the award, and enjoyment of and learning about the reward (Der Avakian, 2016). Generally, the reward cycle can be categorized by anticipation, motivation, consuming, and learning, known as the reward processing system (Schultz, 2015).

REWARD

Dysfunction in reward anticipation has been identified as a significant contributor to depression (Treadway & Zald, 2011). Treadway and Zald (2011) suggested that anhedonia during the course of a major depressive episode is indicative of an impairment to the cost/benefit decision making due to over-estimation of effort required to obtain reward, under-estimation of the benefits, or a failure of cost/benefit analysis, which influences one's motivation to pursue the reward. Several other studies have suggested that MDD symptoms are associated with reduced

reward anticipation (Chentsova-Dutton & Hanley, 2010; McFarland & Klein, 2009; Sherdell, Waugh, & Gotlib, 2012). Costello (1972) explained that depression, from a behavioral perspective, is due to a loss of reward or a loss of interest in the environment. Further, Alloy (2016) posits that individuals have trait-like individual characteristics that make them vulnerable to depression, including hyposensitivity to reward. Validating this point, both adults and youth experiencing depressive episodes report reduced pleasure sensitivity and increased anhedonia in comparison to individuals without depression (Fawcett, Clark, Scheftner & Gibbons, 1983; Luby, Mrakotsky, Heffelfinger, Brown, & Spitznagel, 2004). Experimental evidence suggests that depressive symptoms in adults are associated with deficits in motivation for pleasurable stimuli, as well as the ability to modulate behavior for it, more so than the absence of pleasure when confronted with pleasurable stimuli (Romer-Thomsen et al., 2015, Whitton, Treadway, & Pizzagalli, 2015).

Bakker et al. (2017) utilized real-time data to assess reward as it plays out in daily life using a device that semi-randomly beeps, inviting participants to fill out a short questionnaire on mood, context, and behavior related to positive affect, reward anticipation, and active behavior. The participants (N=133) were age 16-25 and two-thirds had subclinical depressive symptoms. Results showed that more reward anticipation was associated with more positive affect, which in turn predicted higher active behavior. This was the case in the opposite direction as well, with reduced reward anticipation being associated with negative affect and reduced activity. The associations that were not significant between reward anticipation and active behavior were the ones that were moderated by the total depression scale score, suggesting that higher depression

severity is associated with deficits in how reward anticipation and active behavior influence one another (Bakker et al., 2017).

Approximately four decades ago, the "anhedonia hypothesis" was coined by Wise and colleagues (Wise et al., 1978; Wise, 1982) to describe the role of dopamine as a mediator between the pleasure produced by drugs and food, which, when suppressed or impaired, reduces the perception of pleasure. However, since this initial publication, several other alternative dopamine theories arose, including the reward prediction theory (Schultz, Dayan, & Montague, 1997; Schultz, 2002) in which dopamine serves as the signal for incongruency between the reward that was received versus the reward that was expected. The incentive salience theory suggested dopamine's role was to provide information about the perceived incentive value of rewarding stimuli (Berridge, 1996; Berridge & Robinson, 1998). Recent research has revealed that these theories do not fully account for the complexity of the interaction of neural systems that constitute the pleasure experience, as this is a complex construct. Der-Avakian et al. (2016) discussed the linear processes that must take place prior to an experience of pleasure; one must anticipate or expect a future reward, determine the potential value of said reward, evaluate the cost to obtain the reward, become motivated to seek to obtain it, and to learn from prior experience to repeat pleasurable approach behaviors again. Within this process, any dysfunction of the reward system can take place, which may *clinically* appear as "anhedonia." It may be of importance to correctly distinguish the aspect of failure within the pleasure process to then facilitate appropriate treatment, as different aspects of the reward system impact different neural substrates. Approach motivation is of particular interest in this study, due to lack of desire to work for a reward, potentially complicating standard depression treatments.

APPROACH MOTIVATION

Approach motivation, or effort expenditure for reward, appears to involve specific neural circuity (Der-Avakian & Markou, 2012). Approach motivation is driven by dopaminergic circuity (Salamone & Correa, 2012; Schultz, 2016; Treadway et al., 2012) and rewards such as foods and sweet tastes activate the mesolimbic dopamine system in animal studies (Berridge, 1996, Kelley and Berridge 2002; Salamone et al., 2003). The wanting phase of reward dominates the appetitive state, or anticipation of a reward, while enjoyment occurs during the consummatory phase when confronted with the reward (Romer-Thomsen, Whybrow, & Kringelback, 2015), such as listening to a favorite song or eating something desirable. In animal studies exploring effort-based decision making, dopamine interference has predicted an animal's choice of a low-cost, low-reward food, versus a high-cost, high-reward food (Denk et al., 2005; Salamone, Correa, Farrar & Mingote, 2007). Stimulation of dopamine through pharmacological means increases high cost, high reward choices (Bardgett, Depenbrock, Downs, Points, & Green, 2009). Conversely, consummatory pleasure is generally facilitated by opioid driven processes (Barbano & Cador, 2007; Schneider, Heise, & Spangel, 2010), meaning that the enjoyment of food, or a song, or artwork is driven by opioids, whereas dopamine is implicated in the pursuit of those rewards. Both anticipation and consumption of reward are important aspects of anhedonia, though for the purpose of this study, the focus is on the anticipatory pleasure system, namely approach motivation.

The implicated neuronal correlates of the pleasure system include the ventral striatum and orbitofrontal cortex (OFC). The ventral striatum appears to play a central role in obtaining primary and secondary rewards, such as food and money, respectively. To illustrate, 20 healthy

controls and 32 euthymic bipolar I (N=17) and bipolar II (N=15) patients underwent a neuroimaging reward paradigm during functional MRI scanning, structural scanning, and completed psychometric and clinical assessments, and results suggested that higher self-reported reward sensitivity has been associated with elevated ventral striatum activity during reward anticipation (Caseras, Lawrence, Murphy, Wise & Phillips, 2013). The OFC is implicated in assessing the probability of those rewards (Haber & Knutson, 2010), as the ventral striatum receives its main input from the OFC and anterior cingulate cortex. A meta-analysis of 22 functional magnetic resonance imaging (fMRI) studies examining reward-related processing in 341 MDD patients and 367 healthy controls revealed that individuals with depression tended to show reduced ventral striatum response to monetary and other positive stimuli for both anticipation and receipt of rewards (Zhang, Chang, Guo, Zhang, & Wang, 2013). Ultimately, these works provide evidence for reward hyposensitivity and related constructs as correlates of depression. However, as noted by Alloy (2016), these studies do not address whether this hyposensitivity is a trait that is independent of a depressive episode and precedes the development of the disorder, or whether it is an effect of the depression. Studies examining behavioral measures of reward sensitivity have generally supported the sensitivity as mood-dependent, with no differences found between never-depressed controls and those with remitted depression (Westheide et al., 2007; Yang et al., 2014). However, there have also been studies that provide evidence for mood-independent influences on reward functioning using fMRI when depressive episodes are remitted (Dichter, Kozink, McClernon, & Smoski, 2012; Schiller, Minkel, Smoski, & Dichter, 2013; Takahashi et al., 2009).

In general, individual differences in left frontal activity (LFA) were demonstrated to be connected with the mesolimbic dopaminergic neural pathways in healthy adults utilizing dopamine antagonists (Wacker, 2013). Hughes, Yates, Morton, and Smillie (2014) examined the effects of LFA on behavioral output related specifically to approach behavior, rather than solely as a neural component affecting mood states or expectations of behavior. Utilizing EEG to determine LFA, they measured approach behavior utilizing the proportion of hard-task choices on the Effort Expenditure for Rewards Task (EFfRT) (Treadway et al., 2009), a task designed to measure approach motivation and the focal task in the current study, suggesting that LFA is linked to behavioral pursuit of reward. More significant LFA was associated with increased willingness to choose the harder task, and thus expend greater energy to achieve a larger reward. Further elucidating this idea, Tomer (2014) found that asymmetry of D2 dopamine receptor binding capacity within frontal and striatal brain regions predicted sensitivity to reward and punishment. More specifically, greater left asymmetry (greater left frontal activity) was correlated with reward responsiveness and behaviors like reward approach, whereas greater right asymmetry was associated with withdrawal-like affect. In a study by Shankman, Klein, Tenke, and Bruder (2007), frontal and parietal EEG activity were assessed while depressed and non-depressed participants completed a gambling task, resulting in differences in left frontal asymmetry. There were no group differences on frontal EEG activation; however, the early onset depression group displayed left frontal asymmetry. Offspring of depressed parents demonstrated greater right, relative to left, frontal activation in infant samples (Thibodeau, Jorgensen, & Kim, 2006). Though there are mixed findings, the result of a meta-analysis suggests that depression is

characterized by heightened right activation (Thibodeau et al., 2006) and is better characterized by the withdrawal-affect (Alloy, 2016), leading individuals to pursue reward less frequently. Further, evoked response potentials (ERPs) have also been used to analyze neurophysiological correlates of depression. Essentially, an ERP is an electroencephalograph (EEG) with embedded electrical potentials that occur in preparation for or in response to internal or external events (Alloy, 2016). Feedback-related negativity (FRN), as part of ERP, has recently gained support as an indicator of sensitivity to reward referred to as *reward positivity* evidenced by mesocortico-limbic reward circuit activation (Proudfit, 2015). Thus, an elevated FRN has been associated with elevated reward sensitivity, and reduced FRN with decreased reward sensitivity. Liu et al. (2014) and Keren et al. (2018) reported that depressed individuals had a blunted FRN relative to individuals without depression.

The reward system is multifaceted and complex. Though a full understanding of its networks is yet to be understood, an important consideration of reward is how it is impacted when there is an additional insult, such as concussion, in addition to a diagnosis of depression. Concussions are relatively common occurrences, and for a subset of individuals, depression arises or worsens as a consequence (Yrondi, Brauge, LeMen, Arbus, & Pariente, 2017). Due to the relationship in brain regions implicated in both depression and concussion, and the potential for post-concussive symptoms such as depression to develop, this relationship was further evaluated in regard to approach motivation.

CONCUSSION

Concussion or mild traumatic brain injury (mTBI), is a head trauma that is characterized by confusion, disorientation, and sometimes loss of consciousness (LOC), accounting for 92% of

TBI events in the general population (Leibson et al., 2011). Following acute injury to the brain, a state of disarray caused by a neurometabolic cascade can lead to a variety of symptoms (McCrea, 2008). Generally, a mTBI is considered to be a transient process that one quickly recovers from (McCrea, 2008). Most symptoms of concussion, such as headache, dizziness, and fatigue often remit between a few days to a month (Lovell et al., 2006), with a typical time course to remission of 10-14 days (Giza, Grico, & Prins, 2018; McCrory et al., 2017). However, approximately 10-20% of individuals experience a range of more persistent symptoms following concussion (Vanderploeg, Curtiss, Luis, & Salazar, 2007) including headache, dizziness, irritability, double vision, tinnitus, memory problems, anxiety, impaired concentration, and depression. These non-remitting symptoms have previously been known as post-concussive syndrome (PCS) (Carroll et al., 2004). PCS is based entirely on self-report and its cardinal symptoms are common to other medical and psychological disorders, making PCS especially difficult to quantify. There are multiple theories as to why symptoms sometimes persist following concussion, especially since objective evidence is lacking. The majority of patients with mTBI have unremarkable findings on neuroimaging (Silverberg, Guhaime, & Iaccarino, 2020) and there are no sensitive biomarkers for concussion. When depression/anxiety symptoms are paired with acute post-traumatic stress, a greater incidence of PCS at 3-month follow-up occurs (Meares et al., 2011), however. Ponsford et al. (2012) found that pre-morbid and current psychiatric symptoms (especially anxiety), paired with life stressors and pain, predicted worse PCS at follow-up in 123 mTBI patients and 100 trauma patient controls assessed in the emergency department and followed up 1 week and 3 months postinjury. This information suggests that stress and psychiatric symptoms have a profound effect on PCS, perhaps creating a cycle of symptom influence. Further, a recent study

utilizing subjective and objective neuropsychological data to assess post-concussive symptoms (Stillman, Madigan, Torres, Swan, & Alexander, 2019) found that depression was the most significant predictor of subjective cognitive impairment. Finally, Iverson et al. (2017) examined 7617 articles related to delayed concussion recovery, finding that the most consistent predictor of slower recovery from concussion was the severity of a person's acute and subacute symptoms, including headaches and depression. Further, individuals with mental health premorbidity appear to be at greater risk for having persistent symptoms (Iverson et al., 2017).

The subjective nature of PCS makes it especially difficult to understand. Few studies have demonstrated the effect that mood symptoms, especially premorbid depression (Solomon, Kuhn, & Zuckerman, 2016; Vargas et al., 2015; Garden and Sullivan 2010), have on concussion recovery. From a psychological perspective, incorrectly attributing cognitive and psychological symptoms to concussion, rather than a dispositional state such as depression, may be a significant contributor to PCS. As an example, Mittenberg, DiGiulio, Perrin, & Bass (1995), examined symptoms experienced by healthy volunteers and individuals with head injuries. Both groups were asked to rate current symptoms (cognitive, affective, and somatic), as well as symptoms they experienced after their head injury. For the control group, they were asked to imagine symptoms after a head injury. The individuals with head injury reported 60% fewer symptoms pre-injury compared to the base rate in the healthy controls, though both groups reported a high degree of symptoms that were experienced or imagined after a head injury. In a similar study of individuals with depression and healthy controls, the tendency to under-estimate pre-injury problems and misattribute symptoms to head injury was observed once again (Gunstad & Suhr, 2001). Misattribution is a phenomenon that is consistently seen in patients with

prolonged concussion symptoms (Ferguson, Mittenberg, Baone, & Schneider, 1999; Gunstad & Suhr, 2001; Iverson, Lange, Brooks, & Rennison, 2010; Mittenberg et al., 1992), and frequently depression and prolonged concussion symptoms are so entwined that it is difficult to understand which precipitates the other. Although neuroimaging does not always suggest structural brain injury, prolonged symptoms following concussion may be due to any combination of neurological and psychological factors. These factors can include alterations in white matter integrity and cerebral perfusion, but also emotional distress prior to and after the event, and perception of illness (Ontario Neurotrauma Foundation, 2013).

CONCUSSION, DEPRESSION, AND REWARD

It is estimated that within 12 months post-TBI (all severities), up to 50% of patients may have an onset of MDD (Scholten et al., 2016). Alhilali, Delic, Gumus, and Fakhran, (2015) utilized diffusion-tensor imaging in post-concussive patients experiencing depression, anxiety, and irritability compared to those not experiencing prolonged concussion symptoms. They found that white matter injury patterns were seen for anxiety and depression (but not irritability), suggesting that physiological changes in the brain following concussion may account for the increase in mood symptoms, although pre-morbid imaging was not available to determine whether these white matter tracts were previously compromised. Notably, injury to the nucleus accumbens was implicated in time to recovery in patients with depression, suggesting potential for a dysfunctional reward circuit. A study by Chen et al. (2017) on dopamine interference following TBI in rodent models discovered that exposure to TBI was associated with major changes in the release and reuptake of dopamine within the nucleus accumbens.. The alterations were most severe 1-2 weeks post-injury and the extent of the abnormalities was correlated with

injury severity (Chen et al., 2017). Lastly, Cannella et al. (2020), found that TBI in rats induced changes including decreased dendritic complexity and reduced spine density in areas of the brain essential for reward perception and processing. They also demonstrated that these changes may affect expression of dopamine-associated genes.

For post-concussive patients experiencing mood symptoms, the comorbidity leads to lower levels of life-satisfaction (Emanuelson et al., 2003; Stalnacke, 2007) and health-related quality of life (King & Kirwilliam, 2013), as well as a reduced return to work (Chu et al., 2017; Nolin & Heroux, 2006). Though we cannot yet determine whether depression influences post-concussive symptoms or whether concussion influences depressive symptoms, one of the goals of the present study was to evaluate the relationship of both depression and concussion history on an aspect of reward behavior that could be inherent to both, potentially worsening the reward impairment when both are present.

SUMMARY

An impairment to one's approach motivation is believed to impact pleasurable, or hedonic experiences, thus leading to a hallmark symptom of depression known as anhedonia (Bakker et al., 2017). Anhedonia contributes to the profile of depression and minimizes the efficacy of treatments (McMakin et al., 2012; Rush et al., 2009). The approach aspect of anhedonia is influenced by dopamine within the reward pathways, specifically the ventral striatum and orbitofrontal cortex (Caseras, Lawrence, Murphy, Wise & Phillips, 2013; Zhang, Chang, Guo, Zhang, & Wang, 2013). A concussion can lead to alterations in white matter and cerebral perfusion (Ontario Neurotrauma Foundation, 2013) and in rats, decreased dendritic complexity and reduced spine density in areas essential for reward perception and processing (Cannella et al., 2020), though less is understand about how this presents clinically. Depression

and concussion present a complex relationship which further exploration may enhance outcomes for those affected by both.

While depression and concussion treatments have improved over the years and more options are available, the rates of remission and successful treatment have not followed the same path, and the role of anhedonia remains largely unknown. Once we understand the nature of depression and concussion, and how they influence one another and influence clinical outcomes, better treatments can be adapted. This study aimed to evaluate the effect that current depression and a history of concussion have on one's willingness to expend effort, with a focus on anhedonia and its relationship to expenditure of effort. By elucidating the relationship between depression, concussion, and approach motivation, it is possible that more targeted treatments could be developed in order to assist these individuals with motivation.

AIMS AND HYPOTHESES

Aims and Hypotheses

Primary Aims

Aim 1a. Determine the difference in effort outcomes (proportion of hard-task selection) on an approach motivation task for participants with depression and positive concussion history, versus participants with depression and no concussion history. Depression was defined as a PHQ-9 score of 10 or greater during the time of the EEfRT administration, and evidence of a mood disorder based on clinical interview upon entry into the D2K study.

Hypothesis 1. Participants with depression and history of concussion will show greater impairment to their approach motivation as reflected by their willingness (decision) to select hard-tasks (overall proportion of hard-task selection on the EEfRT), regardless of

probability of winning or amount of earnings than those with depression and no concussion history.

Aim 1b. Identify the difference in approach motivation as it relates to the presence of prolonged concussive symptoms in those depressed participants with concussion history.

Hypothesis 1b. Participants with depression and concussion with no prolonged symptoms (symptoms persisting for 2+ weeks after concussion) will be willing to expend greater effort for rewards (overall proportion of hard-task selection), than those with depression and concussion with prolonged symptoms.

Aim 2. Characterize the relationship between impairment in approach motivation on the EEfRT and level of depression severity, as measured by PHQ-9 scores, in those depressed participants with a history of concussion.

Hypothesis 2. Participants with a depression diagnosis and history of concussion will show a negative relationship between their willingness to expend effort for rewards (overall proportion of hard-task selection) and the severity of depressive symptoms (as measured by the PHQ-9).

Exploratory Aim:

Investigate the relationship between self-rated anhedonia, as measured by the PHQ-9, and willingness to expend effort for rewards (overall proportion of hard-task selection).

Hypothesis. Severity of endorsement of the anhedonia item on the PHQ-9 will significantly negatively correlate with willingness to expend effort for rewards on the EEfRT.

CHAPTER TWO

Methodology

Participants

Existing data from an ongoing 10-year natural history, longitudinal, prospective study known as Dallas 2K (D2K) (Trivedi et al., 2020) conducted at the Center for Depression Research and Clinical Care at UT Southwestern Medical Center was used from November 2016 to April 23, 2020. Current study participants included male and female subjects age 18 or older, of any race/ethnicity. All D2K participants must speak, read, and understand English and have a lifetime or a current diagnosis of a mood disorder. The sample for the current study was selected from the D2K population due to presence of a mood episode/disorder (as evidenced by a clinically elevated PHQ-9 score (10 or greater) and corroborated with a major depressive episode/disorder or mood disorder diagnosis) along with a history of concussion based upon the Texas Evaluation of Concussion History (TECH), and Effort Expenditure for Rewards Task (EFfRT) task outcomes. Of 111 participants that met criteria for this study, 41 were in the depression/no concussion group, and there were 70 in the depression with concussion history group (see Figure 1. Consort Diagram). Baseline demographic information was collected via participant self-report and included age, biological sex, highest obtained education, and race. In addition, psychiatric diagnoses from the participant's D2K record was obtained based upon a standard semi-structured diagnostic interview.

Measures

Effort Expenditure for Rewards Task *(EFfRT)*

The task which assessed participant's approach motivation level is the Effort Expenditure for Rewards Task (EFfRT), a computer software game which highlights a participant's motivation to achieve reward through a monetary and skill-based activity.

The EEfRT is a multi-trial game in which individuals select tasks based on easy or hard difficulty to obtain monetary rewards (Treadway et al., 2009). Participants receive actual money

for their game earnings. For each trial, participants use button presses within a specified amount of time to raise the level of the "bar" to the "top" within the prescribed time (e.g. filling a container with virtual stacking blocks). Hard tasks involve 100 presses with the non-dominant little finger within 21 seconds, whereas easy tasks include 30 button presses with the dominant-hand index finger in 7 seconds. Easy task trials allot the patient $1.00 if successfully completed whereas harder tasks have ranges of monetary reward. Harder task winnings offer have a reward magnitude of $1.24 to $4.30. Participants are not guaranteed the reward if they complete the task; some trials are "win" trials and others are "no win," in that the participant will not win any money even if it is successfully completed. Participants are provided information regarding the probability that the trial is a "win" trial (88%, 50%, and 12%). Probabilities are applied to both easy and hard tasks with equal probability proportions across the experiment (low versus hard).

All participants are presented with the same task order. Each task begins with a fixation cross (looks like a plus sign) for 1 second, followed by task information including probability of winning and monetary reward for 5 seconds. Participants learn in the instructions that if they do not choose a task within the 5 second time frame, the difficulty level is randomly selected for them. They have one second before the task begins. Following completion of the task, there is a 2 second screen providing information on successful or unsuccessful completion. If the task was successfully completed, the screen was followed with another 2 second screen sharing whether they won money for that task (reward feedback). Generally, easy-task trials take 15 seconds and hard task trials 30 seconds.

Participants are given explanation that they will receive a base compensation amount for participation, and in addition, two of their "win" trials would be randomly selected at the end of the task in which they would receive the actual amount won on those two trials. They are given

20 minutes to complete as many trials as they can. Hard task trials take approximately twice the amount of time of the easy tasks. Participants are told that the more hard tasks attempted towards the beginning, the less likely they would be to play high value, high probability tasks that appear during the end. Participants have to make the decision within 5 seconds, which helps ensure that their choices are a reflection of their willingness to expend effort and not a formal calculation of an optimal response (Treadway et al., 2009). For the purposes of the current study, and following prior literature, willingness to expend effort was defined by willingness to perform the hard tasks, expressed as a proportion of the number of chosen hard tasks to the overall completed tasks.

Additional variables available for analysis from the EEfRT task include proportion of easy-task choices (how often a participant selected the easier task), proportion of no-choice selection (how often they did not make a choice), completion rate (whether the task was completed or not), and average response time (how quickly they responded in making a choice).

Also available are different probability structures within the EEfRT task that assess various dimensions of reward responding, including: low probability/low reward task options, low probability/high reward task options, overall low probability options, medium probability/low reward, medium probability/high reward, overall medium probability options, high probability/low reward, high probability/high reward, and overall high probability options. The proportions allow the evaluator to examine how often the participant selected each task, whether the person is more incented by probability or reward, or the combination of both, and whether the participant is making thoughtful decisions (e.g. is there a pattern to their decision making). These additional analyses provide further information regarding the different

impairments to reward behavior and the cost/benefit analysis integral to motivation (Treadway & Zald, 2011).

PHQ-9

The nine-item Patient Health Questionnaire (PHQ-9) was used to assess depression severity. The PHQ-9 scores each of the 9 DSM-IV criteria as "0" (not at all) to "3" (nearly every day) self-reported by the patient. PHQ-9 scores of 5, 10, 15, and 20 generally represent mild, moderate, moderately severe, and severe depression, respectively (Kroenke et al., 2001). The PHQ-9 has good predictive value, as validated in a sample of 3,000 primary care patients. The vast majority (93%) with no depressive disorder had a PHQ-9 score less than 10, while most patients (88%) with major depression had scores of 10 or greater. Scores less than 5 almost always signify the absence of a depressive disorder and scores of 5 to 9 primarily represent patients with no depression or subthreshold depression (Kroenke et al., 2001). For the purpose of this study, a threshold score of 10 or greater was used.

Concussion History Tool

The Texas Evaluation of Concussion History (TECH) is a self-report questionnaire identifying concussion history and corresponding sequalae. Items are structured to assess nature of the injury, details of the impact and loss of consciousness, and related symptoms and symptom timeline. In tandem with the depressive symptomatology assessment (PHQ-9) and clinical data, this information was used to define the concussion and no-concussion groups which were the main focus of the study.

Statistical Analyses

All statistical analyses were carried out using IBM SPSS Statistics version 26.0. The level of significance was set at $\alpha=.05$ (two-tailed).

Baseline Demographics and Characteristics

To test for potential effects of main demographic and clinical characteristics, independent sample t-tests were conducted on age, education, race, and PHQ-9 score, while sex frequencies were characterized using chi-square between the concussed/non-concussed MDD groups. There were no differences observed; age, $t(109) = -.777$, $p = .896$, PHQ-9 score, $t(109) = -1.337$, $p = .101$. sex, x^2 $(1, N = 110) = 3.626$, $p = .057$, though it appeared that there was a trend for sex. Next, Pearson correlations were conducted on age and PHQ-9 status across the sample, while an independent sample t-test was conducted to compare males versus females on the willingness to expend effort. No relationship was observed between willingness to expend effort and age, $r = -.156$, $n = 111$, $p = .101$, mean PHQ-9 score, $r = .062$, $n = 111$, $p = .515$, education, $r = .007$, $n = 111$, $p = .945$, and race, $r = .132$, $n = 111$, $p = .172$, but they did differ on sex, $t(108) = -2.01$, $p = .047$. Males ($M = .37$, $SD = .18$) chose more hard-tasks overall than females ($M = .29$, $SD = .20$). Sex was used as a covariate throughout the analyses based on these results. Age was also used as a covariate due to the theoretical possibility that cognitive ageing and motor ability could potentially influence willingness to expend effort on harder tasks (Salthouse, 1991).

Primary Aims

Aim 1a.

A univariate ANCOVA was utilized to compare willingness to expend effort on the EEfRT task between depressed individuals with and without history of concussion (depression/no concussion n= 70; depression/concussion n= 40), controlling for age and sex.

Aim 1b.

A univariate ANCOVA was conducted to evaluate the relationship between the presence of prolonged concussion symptoms (depression with prolonged concussion symptoms n=14, depression with no prolonged symptoms n=26) and willingness to expend effort measured by the EEfRT using proportion of hard-task choices. One participant was excluded due to missing sex data. The independent variable, prolonged concussion symptoms, included two levels: history of concussion symptoms remitting within two weeks or less, and prolonged concussion symptoms lasting more than two weeks. The dependent variable was the proportion of hard-task choices selected on the EEfRT. The original proposal included prolonged symptoms lasting for a month or longer; however, due to sample limitations of too few participants with over a month of prolonged symptoms, as well as literature that suggests an average 10-14-day recovery for mTBI (McCrory et al., 2017), the selection threshold was lowered from one month to two weeks.

Aim 2.

A Pearson correlation was used to examine the relationship between PHQ-9 score severity and overall proportion of hard-task choices on the EEfRT in the group of depressed, concussed participants (n=111).

Exploratory Aim

Aim 3.

Exploratory:

A chi-square analysis was conducted to evaluate whether severity of anhedonia endorsement on the PHQ-9 (n=111) was related to willingness to expend effort on the EEfRT. The two independent variables were level of endorsement of anhedonia (loss of

pleasure or interest), grouped into low endorsement (0 = not at all and 1 = several days of anhedonia) and high endorsement (2 = more than half the days and 3 = nearly every day) on the PHQ-9 item one, and the proportion of hard-task choices on the EEfRT task in participants with PHQ-9 score of 10 or greater. Such a relationship could potentially provide easier identification of impaired approach motivation in depressed participants when the EEfRT is unavailable, as the PHQ-9 is commonly used in clinical settings.

CHAPTER THREE
Results

Total Sample

In total, data from 111 participants were used (see Table 1). Of these, 63% (n=70) had a depression diagnosis and no history of concussion, and 36.9% (n=41) had a depression diagnosis and a self-reported history of concussion. At baseline, the mean age of the entire sample was 47.10 ± 1.6 years, and 71.1% (n=79) were female and 28.8% (n=32) were male. Demographic data including ethnicity and education were missing for two participants. Identified ethnicity was as follows: 1.8% (n=2) were American Indian or Alaska Native, 17.4% (n=19) Black or African American, 2.8% (n=3) were Asian, 74.3% (n=81) were White or Caucasian, 2.8% (n=3) were "more than one race," and .9% (n=1) identified as "other." Almost 15% (n=14) obtained a high school degree or GED, 9.5% (n=9) had a junior college degree or technical school diploma, 27.4% (n=26) some college, 31.6% (n=30) a Bachelor's degree, 12.6% (n=12) a Master's degree, and 4.2% (n=4) held a doctoral degree (J.D., M.D., PhD, D.O., etc.). A majority (83.8%; n=93) of participants had a primary depressive disorder, 14.4% (n=16) had a primary bipolar disorder, .9% (n=1) had a primary trauma-related disorder, and .9% (N=1) had a primary anxiety disorder. In the group of depressed, non-concussed participants, (n=70), 77.1% (n=54) were female, and 22.9% (n=16) were male. In the group of depressed participants with a history of concussion,

60% (n=24) were female and 40% (n=16) were male, with no significant differences on any demographic variables between the concussed/non-concussed MDD groups.

Aim 1a.

The ANCOVA to evaluate the effect of concussion history on willingness to expend effort (n=110) was not significant F (1,108) =.963, p=.329 (see Table 2).

Aim 1b.

Prolonged concussion symptom subjects (n=14) vs depression with no prolonged symptoms (n=26) did not significantly impact willingness to expend effort on the EEfRT as measured by hard-task choices (F (1,38) =.341, p=.563). One participant was excluded due to missing sex data (See Table 3).

Aim 2.

In order to examine the effects of severe depression, a Pearsons correlation was conducted to evaluate the relationship between PHQ-9 score severity (among those with PHQ-9 scores of 10 or above) (n=111) and its relationship with willingness to expend effort on the EEfRT as measured by the overall proportion of hard-task choice selection. This correlation was nonsignificant (r = .089, n =41, p = .581).

Exploratory Analyses.

The exploratory analyses were designed to understand the anhedonia severity rating effect on effort outcomes in depressed/concussed and depressed/non-concussed groups. This was not significant, Pearson x^2 (34, N = 111) = 31.43, p =.594; as such, anhedonia severity did not influence the number of hard-task choices on the EEfRT.

As an attempt to explore the data for the sole purpose of generating further hypotheses, an ANCOVA was run to examine whether concussion and anhedonia endorsement on the PHQ-9

had an interaction effect on the overall proportion of hard-task choices on the EEfRT. The ANCOVA was not significant, $F(1,104) = .195$, $MSE = .038$, $p < .660$. To better understand the relationship between anhedonia and overall proportion of hard-task choices, a simple correlation between anhedonia severity and hard-task choice proportion on the task was completed and was not significant ($r = -.009$, $n = 111$, $p = .923$).

Posthoc Analyses.

Exploratory post-hoc analyses were completed to generate additional hypotheses and explore alternative variables of interest related to the dataset. Analyses were purely exploratory and were uncorrected for multiple comparisons.

To examine the relationship between concussion history and other aspects of reward behavior measured by the EEfRT task, multiple variables were used to further explore the decision-making process. Univariate ANCOVAS were conducted to evaluate the effect of concussion history on proportion of easy-task choices, proportion of no-choice selection, completion rate, average response time, and different probability structures within the task including: low probability/low reward task options, low probability/high reward task options, overall low probability options, medium probability/low reward, medium probability/high reward, overall medium probability options, high probability/low reward, high probability/high reward, and overall high probability options. No significant differences were observed between groups, and all $f<2.23$; all $p>.05$ (see Table 4).

Analyses were then conducted to explore the potential effect of depression severity on the willingness to expend effort. A larger dataset was used (those with any depression symptom severity, including a score of 9 or below, $n = 176$) as well as concussion status on overall proportion of hard-task choices on the EEfRT. A 2 Group (concussed/non-concussed) X 2

Depression Severity (PHQ-9 9 and below; 10 and above) ANCOVA controlling for age and sex was conducted to determine whether there was a significant difference in willingness to expend effort. The main effects of concussion history were not significant for overall proportion of hard-task choices, $F(1,170) = .150$, $MSE = .006$, $p = .699$, depression severity, $F(1,170) = .154$, $MSE = .006$, $p = .695$, nor was the interaction effect depression and concussion, $F(1,170) = .752$, $MSE = .028$, $p = .387$.

Additionally, univariate ANCOVAS were conducted to further investigate the potential effect concussion history and depression severity could have on other task variables related to motivation-based decision making. The data set included 176 participants with any PHQ-9 score severity. Independent variables included depression status and concussion status on dependent variables of proportion of easy-task choices, proportion of no-choice selection, completion rate, average response time, and probability level and monetary value within the task including: low probability, low reward task options, low probability high reward task options, overall low probability options, medium probability low reward, medium probability high reward, overall medium probability options, high probability low reward, high probability high reward, and overall high probability options. There was a significant difference in the proportion of low probability, high reward choices made, $F(1,170) = 5.517$, $MSE = .233$, $p = .020$ (see Figure 2) as a function of depression severity. Those with a depression score of 9 or less (i.e., those with fewer depressive symptoms or in depression remission during the time of assessment) chose to expend more effort on low probability conditions when the monetary value was high ($M = .166$) than those with greater depression severity ($M = .085$). Thus, depression appeared to be the driving force behind level of effort expended on the task, irrespective of concussion history.

Further, in the low PHQ-9 symptom severity group with no concussion history, participants displayed a higher completion rate $F(1,170) = 4.090$, $MSE = .090$, $p = .045$ and faster average response time $F(1,170) = 5.012$, $MSE = 3907984.044$, $p = .026$ (see Figure 3), whereas the low PHQ-9 symptom severity with a concussion history showed a lower completion rate and a longer average response time. However, the very large standard deviations associated with these variables suggest that the data are skewed, and the results suspect.

CHAPTER FOUR
Discussion

The current study sought to uncover potential deficits in approach motivation as a function of both depression and a history of concussion. If a history of concussion were to be associated with an additional risk or burden beyond the effects of depression, approach motivation could serve as both an indicator of dysfunction as well as an indicator for specific treatment (e.g. treatment that includes a focus on motivation). Although none of the main findings were significant, such that a history of concussion in depressed individuals did not reveal an impairment to one's willingness to expend effort on an approach motivation task, this study contributes to the literature in novel ways.

In contrast to the Treadway et al. (2009) study on effort expended in depressed individuals, the current study did not reveal deficits in approach motivation for those with increased trait anhedonia. Importantly though, the current study utilized a one-item measure of anhedonia from the PHQ-9 which is understandably a limited measure of this construct. The current study did find a similar effect of gender to Treadway et al. (2009), with more men choosing hard-task options than women. We did not further explore interactions between anhedonia, probability, and reward magnitude as Treadway et al. (2009) did, due to the lack of significance related to our single-item anhedonia construct and the other nonsignificant findings.

Posthoc analyses were conducted in order to explore more detailed dimensions of the EEfRT test variables. These analyses revealed largely nonsignificant results, although a few potentially interesting findings were seen; however, it should be noted that these findings may be spurious given the number of variables in the analyses and that they had very high standard deviations and were statistically unadjusted. Observed in the exploratory post-hoc analyses was an interaction effect between concussion history and depression on completion rate and average response time during the EEfRT. In the low PHQ-9 symptom severity group with no concussion history (N=38), subjects had a higher completion rate and faster average response time (how quickly they made a decision), whereas the low PHQ-9 symptom severity *with* a concussion history (N=28) showed a lower completion rate and a slower average response time. While the EEfRT task has not been characterized as a test of executive functioning, the slowed average response time could be an effect of slowed decision making. Further, the lower completion rate may suggest that those with concussion and depression were quicker to give up or less likely to persist with effort throughout the task. Giving up on effort tasks could also highlight the lack of expectation of reward, which could be a symptom of depression or an impairment to the decision-making process. Future research may want to examine how these factors influence EEfRT outcomes, as these findings of lower completion rates and slower response times, if valid, could suggest difficulties in aspects of decision-making speed and/or or maintenance of effort.

More plausible is that the exploratory analysis results were spurious due to the multiple comparison and expected experiment-wise error and the high variability in EEfRT scores, as there is substantial evidence to suggest that concussion does not produce long-term cognitive sequalae for most individuals. Concussion has been a source of debate for many years regarding its potential long-term effect upon the brain. Based on the current results, having both depression

and a history of concussion does not appear to influence approach motivation, however. Therefore, these results are largely representative of mainstream thinking regarding concussion, specifically that mTBI does not have long-term complications (Caccese et al., 2020; Meares et al., 2006).

Furthermore, one's self-report of anhedonic symptoms on the PHQ-9 did not appear to influence outcomes on the effort task. Though we cannot conclude that depression accounts for the effort expended on the EEfRT, it appears that depression remains the driving force behind effort expenditure based on the current results and prior studies using the EEfRT (Treadway et al., 2009). In the exploratory analyses, participants with low PHQ-9 symptom severity were willing to expend more effort for low probability conditions that had high reward (monetary value), suggesting that their lower depression severity may lead to engagement in low probability tasks since the reward was high, whereas their counterparts with high depressive symptom severity did not engage, possibly due to the higher depression severity blunting their motivation or decision making for high reward in a low probability task. The high depression severity group could have an impairment in cost/benefit decision making, including undervaluing the reward, overestimating the work required to receive it, or a failure of the decision-making process which influences motivation to pursue it (Treadway & Zald, 2011). Deficits in motivation for reward are driven mainly by low anticipatory pleasure (Sherdell et al., 2012), which also echoes other studies (Treadway et al., 2012) that have observed less sensitivity to information about the reward magnitude and probability of a win when making their choices on the EEfRT. The high depression severity group may have minimized the reward magnitude in the context of the low probability, especially if their motivation was compromised to begin with. Depressed individuals also tend to make errors in predicting between actual and expected outcomes (Gradin et al.,

2011), which may also be evidenced by these results. Depressed individuals may put more emphasis on the low probability aspect of the task, rather than the high reward valuation. MDD patients tend to focus on avoiding loss, rather than approaching gain (Trew, 2011). Nevertheless, there appeared to be no systematic additional influence of a prior history of depression on the current sample's EEfRT performance, once again suggesting that depression is the driving force behind task performance.

Lastly, this study was unique in exploring the effects of a history of concussion in a sample of already depressed individuals recruited specifically for depression research. Many studies begin with individuals who have sustained concussion and analyze their participants from that perspective. This study may be more representative of the broader population, considering the sizeable prevalence of depression. Understanding how concussion may influence a pre-morbid mood disorder is an important aspect to greater understanding of the impact of concussion.

LIMITATIONS

This study has several limitations which may impact interpretation and generalizability of the results. First, the current dataset was a convenience sample of depressed individuals involved in longitudinal research, so may not be representative of the general population with depression. Second, and one of the primary limitations, was the lack of healthy controls. Without healthy control data, it is difficult to determine whether the scores in either group were within the normal range or reflect "impairment" on the EEfRT task. Additionally, it appears that the EEfRT task does not have population-based norms like most clinical neuropsychological tests, which is a limitation. Within the D2K sample, no additional standard neuropsychological tests were administered, so we were unable to validate it with other measures. In a sister study to D2K

which examines resilience in youth (Texas Resilience Against Depression, T-RAD) (Trivedi et al., 2020), there is a healthy control group aged 18-24, but those subjects would not be similar in age to the current sample. Although both of these options limit sample size, this study may be worth pursuing to provide more confidence in depression related to effort outcomes, as well as aiding in further clinical validation of the EEfRT.

Along these lines, there are limitations to the use of the EEfRT as the main outcome assessment, as it is a relatively new task and has yet to be validated and normed, though multiple studies have been completed using this task (Lawn et al., 2016; Lopez-Gamundi & Wardle, 2018; Mansur et al., 2019). Further, we do not yet know how the EEfRT translates clinically, specifically whether impairments seen on the task translate to behavioral outcomes in a real-world setting. Further use of the EEfRT in neurologic, psychiatric, and healthy samples will allow for validation.

Another limitation is that the single-item self-report assessment on the PHQ-9 likely does not adequately capture the motivational aspect of anhedonia. The item asks whether the person has experienced little interest or pleasure in doing things, and since the enjoyment of the reward does not seem to be as impacted as the motivation for the reward in depression, this question misses the elicitation of global anhedonia. Although this measure was chosen specifically for its generalizability and availability in the sample, measures that correlate with the motivational aspect of anhedonia may be more fruitful when examining EEfRT outcomes, such as the Dimensional Anhedonia Rating Scale (Rizvi et al., 2015), or the Blanchard Motivation and Pleasure Self-Report Scale (Llerena et al., 2013).

The EEfRT examines motivation by using an actual monetary incentive. While this is a reasonable approach to assess motivation, individuals would have varying incentive to earn small

amounts of money, let alone varying levels of interest in the amount of money being offered. A study (Szczepanik et al. 2019) examining the appeal of motivation-assessing tasks sought to understand how activities are individualized, which brings up the question whether monetary reward is incentivizing to all people. Future studies may consider asking participants a few brief questions regarding how incented they are by money, and complete analysis based on those who identify feeling motivated by it to better ensure that what is being captured is motivation for reward. Further, it has implications for treatment providers to consider the unique nature of reward, and work with their patients to determine an individualized plan for rewarding activities. If a provider is working with a patient who is not incented by establishing social connections, planning for social engagements may not be a worthy endeavor.

Last, concussion history was coded in the current dataset as being present or absent, which does not account for the variability in severity or nature of the injury. Further, the number of concussions was not taken into account, which may be an interesting avenue for future studies since at least one study has suggested that a higher concussion count may lead to long-term worse outcomes in some individuals (Yrondi, Brauge, LeMen, Arbus, & Pariente, 2017).

Conclusion

Given the absence of research on depression, concussion, and approach motivation, this study contributes to the literature regarding the lack of an effect of comorbid depression and a history of concussion on approach motivation. Though the main analyses were nonsignificant, the exploratory analyses provide some impetus to suggest that more research on various aspects of depression are needed to better break down and understand its component processes and how these may be affected by additional insults to the central nervous system.

FIGURE 1. CONSORT DIAGRAM

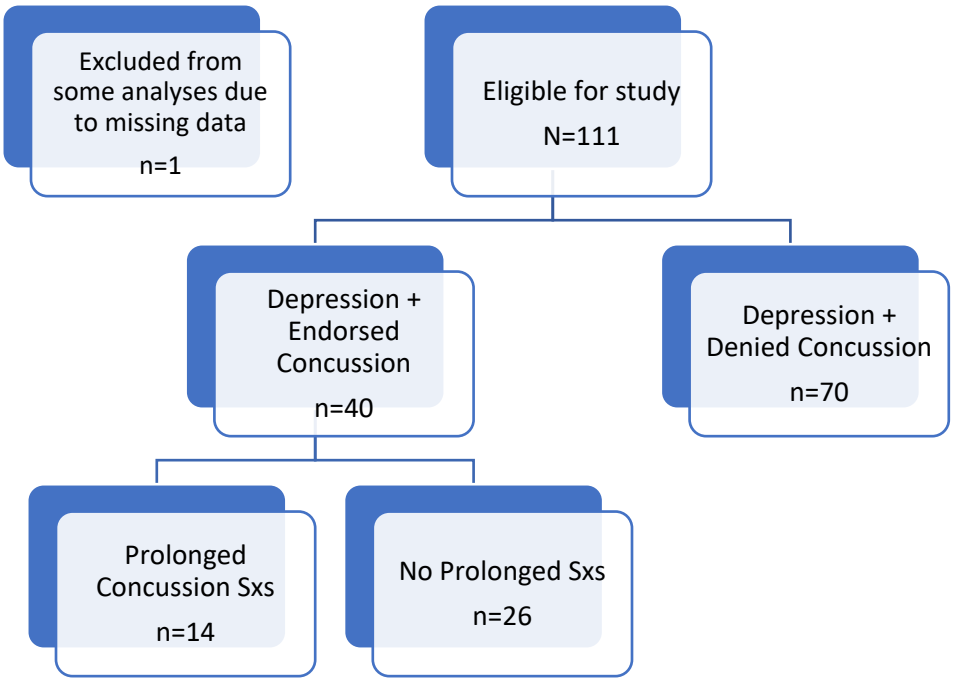


FIGURE 2. EEfRT LOW PROBABILITY/HIGH REWARD CHOICE

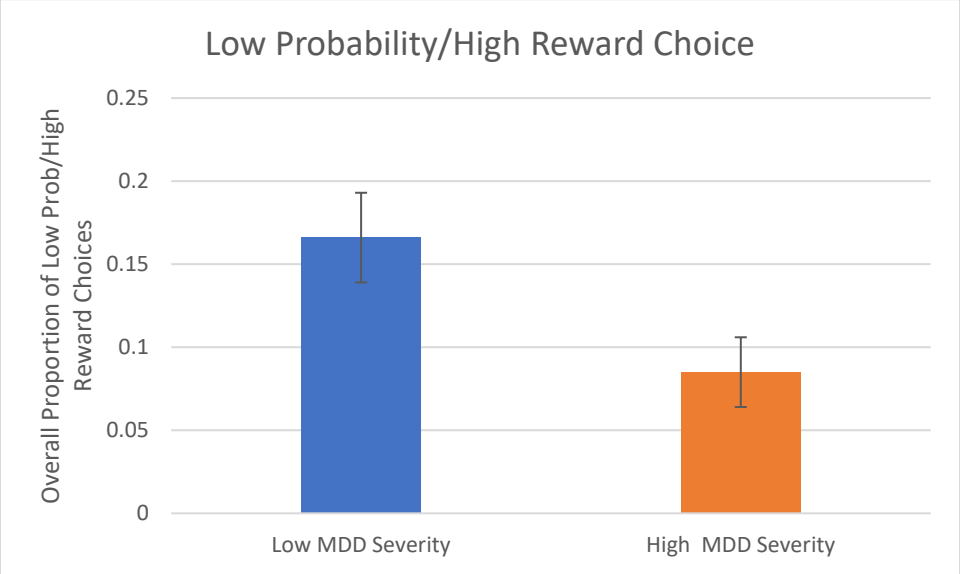
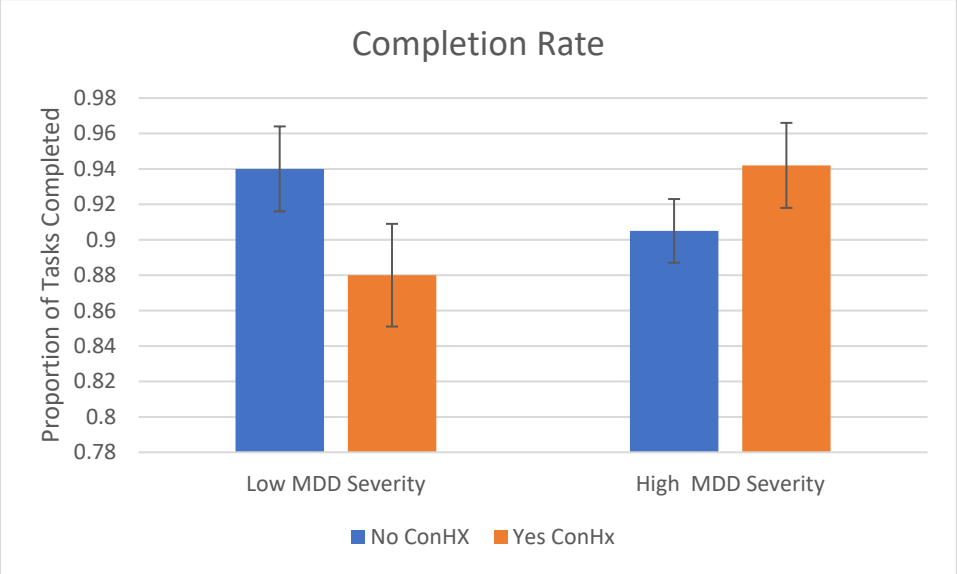


FIGURE 3. EEfRT COMPLETION RATE & AVERAGE RESPONSE TIME



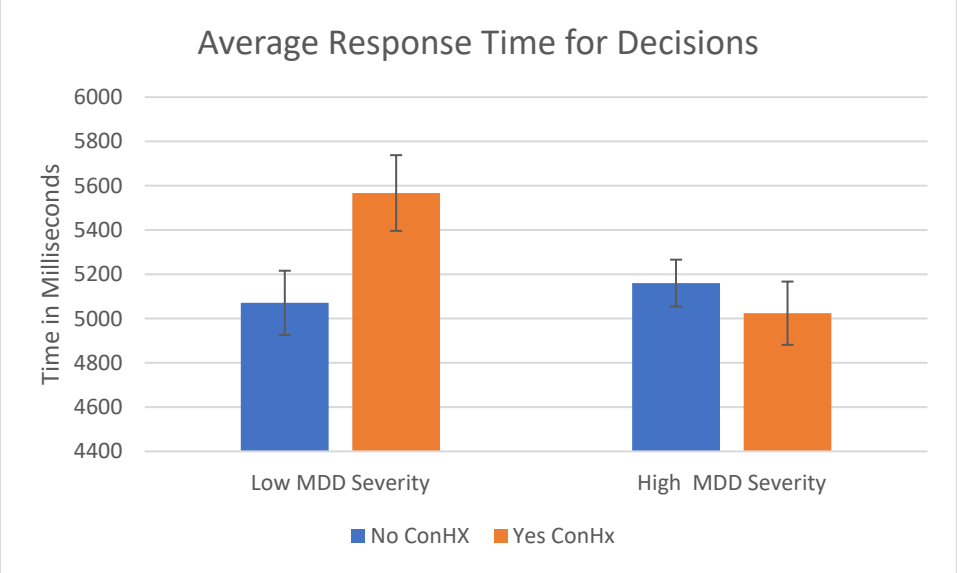


TABLE 1: DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF TOTAL SAMPLE

Demographics	**Total Sample (N=110)**	**Clinical Characteristics**	**Total Sample (N=110)**
Age	47.10 ± 1.6	Primary Diagnoses	
Sex- Female	79 (71.2%)	*Recurrent Major Depressive*	72 (64.9%)
Sex- Male	32 (28.8%)		
Education		*Persistent Depressive*	4 (3.6%)
High School/GED	14 (14.7%)	*Bipolar Disorders*	16 (14.4%)
Junior College/Technical	9 (09.5%)	*Trauma Related Disorders*	1 (0.9%)
Bachelor's Degree	30 (31.6%)	*Generalized Anxiety*	1 (0.9%)
Master's Degree	12 (12.6%)	*Past Major Depressive*	6 (5.4%)
Doctoral/Professional Degree	4 (4.2%)	*Current Major Depressive*	8 (7.2%)
Race		*Lifetime Mood Disorder w/ Psychotic Features*	1 (2.5%)
American Indian/AlaskaNative	2 (1.8%)	PHQ-9 Score	14.32 ± 3.85
Black/African American	19 (17.4%)		
Asian	3 (2.8%)		
White/Caucasian	81 (74.3%)		
More than one race	3 (2.8%)		
Other	1 (0.9%)		

TABLE 2. OVERALL PROPORTION OF EEfRT HARD TASK CHOICES FOR AIM 1A

Concussion History	**N**	**Mean**	**Std. Dev**
Denied	70	.302	.023
Endorsed	40	.340	.031

TABLE 3. OVERALL PROPORTION OF EEfRT HARD TASK CHOICES FOR AIM 1B

Prolonged Symptoms	**N**	**Mean**	**Std. Dev**
Denied	26	.369	.205
Endorsed	14	.299	.233
Total	40	.344	.215

TABLE 4. EFFECT OF CONCUSSION HISTORY ON ADDITIONAL EEfRT VARIABLES OF INTEREST

Variable	***Concussion +/-***	***Mean***	***Std Deviation***
Overall Prop Easy	-	.621	.237
	+	.547	.248
No Choice	-	.072	.231
	+	.108	.260
Completion Rate	-	.900	.172
	+	.926	.146
Average Response Time	-	5184.634	1002.763
	+	5125.802	698.534
Low Probability/Low Reward	-	.141	.213
	+	.119	.165
Low Probability/ High Reward	-	.075	.158
	+	.081	.201
Low Probability Overall	-	.161	.211
	+	.163	.173
Medium Probability/ Low Reward	-	.226	.256
	+	.261	.257
Medium Probability/ High Reward	-	.329	.317
	+	.431	.351
Medium Probability Overall	-	.280	.255
	+	.355	.280
High Probability/Low Reward	-	.373	.322
	+	.413	.306
High Probability/High Reward	-	.559	.381
	+	.625	.382
High Probability Overall	-	.457	.313
	+	.515	.315

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