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The Effects of Attention-Deficit Hyperactivity Disorder and Depression Symptomatalogy on Reward and Punishment Sensitivity in Adults

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THE EFFECTS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND DEPRESSION
SYMPTOMATALOGY ON REWARD AND PUNISHMENT SENSITIVITY IN ADULTS

by

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A thesis submitted in partial fulfillment of the requirements
for graduation with Honors in the Psychology

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Spring 2018

All requirements for graduation with Honors in the
Psychology have been completed.

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Toby Mordkoff
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ABSTRACT

Reward and punishment sensitivity play important roles in eliciting, inhibiting, and guiding behavior. Previous research has indicated aberrant levels of reward and punishment sensitivity in those with depression or ADHD. However, few studies have explored the synergistic effects of both depression and ADHD on reward/punishment sensitivity, particularly in adults. Study 1 examined performance on a delay discounting task across diagnostic groups (ADHD, depression, co-morbid ADHD/depression, N=119). Study 2 investigated associations between ADHD/depression symptoms and self-report/behavioral measures of reward and punishment sensitivity among N=152 young adults. MANOVAs in Study 1 indicated that diagnostic groups differed in their average rate of delay discounting compared to the control group; however, diagnostic groups did not differ from each other. In Study 2, hierarchical regression models revealed a modest interaction effect between ADHD and depression symptoms in females when predicting behavioral changes to reward/punishment. Sex also moderated the separate effects of ADHD/depression symptoms on reward/punishment sensitivity. Our results suggested that reward/punishment sensitivity processes are altered among individuals with diagnoses and symptoms of ADHD and depression, but that the impact of psychopathology on these processes may vary by sex. Future work should explore sex differences in reward/punishment processing in the context of psychopathology while also investigating associations between ADHD/depression and subconstructs of reward/punishment sensitivity.

INTRODUCTION

Sensitivity to reward and sensitivity to punishment play an important role in eliciting, inhibiting, and guiding behavior (Kim, Yoon, Kim, & Hamann, 2015; Torrubia, Avila, Moltó, & Caseras, 2001). Reward sensitivity refers to the extent to which an individual reaps the emotional, motivational, and behavioral benefits from anticipating and experiencing reinforcing stimuli, whereas punishment sensitivity refers to the extent to which an individual suffers the emotional, motivational, and behavioral consequences from anticipating and experiencing aversive stimuli. Individual differences in sensitivity to reward and sensitivity to punishment can result in a variety of motivational and behavioral differences (Kim et al. 2015). For example, individuals with low levels of reward sensitivity may be more motivated to frequently engage in reward-seeking behavior in order to compensate for diminished sensitivity to a normal level of stimuli (Scheres, Milham, Knutson, & Castellanos, 2007). At the same time, these same individuals may be less motivated to seek out reward because they do not receive the internal emotional experience typically derived from reinforcing stimuli (Alloy, Olino, Freed, & Nusslock, 2016). Individuals with heightened punishment sensitivity, on the other hand, may find that the prospect of reward does not outweigh the potential for punishment given a situation that could produce both types of stimuli (Poon & Ho, 2016). Consequently, these individuals may be more likely to refrain from a behavior that could result in an aversive stimulus, even if there is high probability for reward.

While reward and punishment sensitivity vary across individuals, many studies have also found an association between deviations in reward and punishment sensitivity and a variety of psychological disorders, including attention-deficit/hyperactivity disorder (ADHD) (Blum et al., 2008; Plichta et al., 2009; Scheres et al., 2007) and depression (Bress, Foti, Kotov, Klein, &

Hajcak, 2013; Forbes et al., 2010; Mccabe, Woffindale, Harmer & Cowen, 2012; McFarland & Klein, 2009). Differences in reward sensitivity and punishment sensitivity among individuals with ADHD, individuals with depression, and individuals without either disorder can be understood on both neural and behavioral levels. Currently, studies have implicated several brain systems in the processing of reward and punishment including the behavioral activation system (BAS) and the behavioral inhibition system (BIS) (Gray, 1981; Kim et al., 2015; Torrubia et al., 2001). The BAS is linked to the regulation of reward sensitivity while the BIS is linked to the regulation of punishment sensitivity. Despite the fact that both systems are involved in stimulus processing, it appears that these systems are largely independent of each other (Torrubia et al, 2001). Indeed, different neural structures underlie each of these systems. For example, the BAS includes connections between the medial prefrontal cortex and the ventral striatum. Deficient activity within these networks appears to be associated with hyposensitivity to reward, which, in turn, may result from inadequate dopaminergic activity in these regions (Blum et al. 2008). In contrast, the neural structures that make up the BIS include the insula and lateral orbitofrontal cortex. Because the experience of aversive stimuli leads to activation in the insula and lateral orbitofrontal cortex, unusually elevated activity in these regions indicates hypersensitivity to punishment (McCabe et al., 2012).

Individuals with ADHD and individuals with depression both demonstrate atypical activity in these neural pathways and structures. For example, Scheres et al. (2007) found that children with ADHD demonstrated reduced ventral striatum activation during reward *anticipation* compared to children without ADHD, suggesting potentially diminished reward sensitivity among those with ADHD. In line with this, ADHD has been posited to be a subtype of Reward Deficiency Syndrome (RDS), based on evidence that ADHD and RDS both involve

variants in the genes that affect dopaminergic activity in reward pathways (Blum et al., 2008). Depressed individuals also demonstrate diminished activity in the reward center of the brain during reward anticipation and reception (Forbes et al., 2010; McFarland & Klein, 2009). This is consistent with evidence indicating that anhedonia, or the inability to derive pleasure from everyday activities, is a common symptom of depression (Alloy et al., 2016). Indeed, researchers have hypothesized that impaired dopaminergic pathways in reward-processing structures of the brain is one of the main contributors to anhedonia in depressed individuals (Martin-Soelch, 2009).

While both ADHD and depression appear to share some commonalities in terms of problems with sensitivity to reward, differences arise when it comes to problems with punishment sensitivity. Individuals with depression have shown increased activity in the insula and orbitofrontal cortex when faced with aversive stimuli, which suggests that these individuals also experience high punishment sensitivity (Mccabe et al., 2012). However, the role of punishment sensitivity in ADHD remains unclear, as prior investigations of neural punishment processing in ADHD have yielded inconsistent results. For instance, Stoy et al. (2011) did not find any significant differences in brain activity between adults with childhood ADHD and adults without childhood ADHD during loss anticipation. That is, adults both with and without childhood ADHD had a similar neural response when faced with the prospect of losing money in a monetary incentive delay task. On the contrary, Wilbertz et al. (2015) found that adults with ADHD display increased activity in the amygdala and left interior insula in a similar experimental design involving loss anticipation, which suggests that those with ADHD may actually experience higher levels of punishment sensitivity.

On a behavioral level, various degrees of reward and punishment sensitivity appear to manifest differently between individuals with depression and individuals with ADHD, although the behavior of both clinical groups differs markedly from individuals without these disorders. For example, one study found that children with ADHD tend to focus on immediate rewards rather than future consequences (Drechsler, Rizzo, & Steinhausen, 2008). As a result, these children took more risks and suffered more losses in the Game of Dice task compared to children without ADHD. Another study found that children with ADHD directed more attentional resources to the prospect of reward than the risk of loss (Masunami, Okazaki, & Maekawa, 2009). Indeed, children with ADHD tended to choose "bad decks" (decks with large rewards but even larger losses) over "good decks" (decks with smaller rewards but even smaller losses) in this task (a decision-making paradigm that assesses the extent to which reward and punishment sensitivity impact choices).

Because studies with behavioral measures have found increased reward seeking and risk-taking behavior in individuals with ADHD compared to their non-ADHD counterparts, it may appear as though individuals with ADHD are motivated by a strong internal experience of reward. This conclusion, however, is inconsistent with the findings of the previously discussed neural studies, which reported reduced activation in brain reward systems for those with ADHD. Given these findings, a more accurate model is that reduced sensitivity to reward, an internal experience, produces a need to obtain stronger and more frequent rewards in order to feel reinforced, leading ADHD individuals with diminished reward sensitivity to engage in more reward seeking behavior than individuals with typical reward sensitivity (Beauchaine & McNulty, 2013; Scheres et al. 2007). Furthermore, the reward seeking behavior of those with ADHD is uninhibited by the potential for aversive stimuli, which results in more risk-taking

(Poon & Ho, 2016). In contrast to the reward seeking/punishment avoidance behavior of those with ADHD, individuals with depression are often less likely to seek out rewards (Alloy et al., 2016) and are more likely to refrain from a behavior that could result in punishment (Pinto-Meza et al., 2006); this is likely due to a strong internal experience of punishment.

While there is a large body of literature distinguishing levels of reward/punishment sensitivity and reward/punishment behavior in those with ADHD or depression from those without either of these disorders, few studies have yet to demonstrate the combined impact of both ADHD and depressive symptoms on reward and punishment sensitivity. One study by Garon, Moore, & Waschbusch (2006) examined differences in reward and punishment sensitivity by having three groups of children- children ADHD, children with ADHD and anxious/depressive symptoms, and children without ADHD or anxious/depressive symptoms- participate in the children's version of the Iowa Gambling Task (IGT). Garon et al. (2006) found that children in the ADHD-only group performed significantly worse on the gambling task than those without ADHD. Specifically, they repeatedly chose high-risk desks and suffered many losses. On the other hand, children with both ADHD and anxious/depressive symptoms performed nearly as well as the control group. The differences in ADHD subgroups may be attributed to a hyperactive BIS in those children with depressive/anxious symptoms, which would work to decrease temptation for choosing high-risk, high-loss desks. As a result, it appears that punishment sensitivity distinguishes the decision-making performance of those with depression symptoms from those without these symptoms, even in the presence of ADHD symptoms.

To our knowledge, there are no studies which investigate effects of both ADHD and depression symptoms in adults. As a result, we undertook analyses across two samples to

examine how ADHD and depression symptoms map onto indices of reward and punishment sensitivity among adults, while also considering the role of reward-seeking and punishment-avoidant behavior. Study 1 investigated the effects of ADHD and depression diagnoses on delay discounting of rewards in a clinical sample of adults with ADHD, adults with depression, and adults with co-morbid ADHD and depression. In Study 2, we adopted a dimensional approach, exploring the associations between ADHD/depression symptomatology and delay discounting, behavioral responses to reward/punishment, and BIS/BAS activity in a sample of college students.

Based on a large body of research findings indicating that those with ADHD and those with depression experience hyposensitivity to reward, we expected that measures of reward sensitivity and related constructs would be inversely related with both ADHD and depressive symptoms. Furthermore, we predicted that individuals who have high levels of both ADHD and depressive symptoms would exhibit greater insensitivity to reward compared to individuals with ADHD or depressive symptoms only. Additionally, it was expected that punishment sensitivity and constructs related to punishment sensitivity would be positively related to depressive symptoms but would be unrelated to ADHD symptoms. Consistent with the findings of Garon et al. (2006), we predicted that reward-seeking behavior such as risk-taking would be most present in those with ADHD symptoms and no depressive symptoms. As depressive symptoms increased, we expected individuals with and without ADHD symptoms to engage in less reward-seeking behavior and more punishment-avoidant behavior.

METHOD

Participants

Study 1. Participants for study 1 formed our clinical sample, including 119 adults aged 18-39 years (*M*=24.5 years, *SD*=6.3, 57.1% Female). Participants were recruited from the community through email listservs and outreach to local mental health and psychiatry clinics. Targets for recruitment included those with a previous diagnosis of ADHD, those with a previous diagnosis of depression, and those with no previous diagnosis of any psychiatric disorder (see below). A multi-stage process was used to identify cases and non-cases among those who volunteered. Interested participants first completed an eligibility screening process at stage 1 to evaluate inclusion and exclusion criteria. Participants were excluded if they (1) were not fluent in English, (2) had any physical illness or neurological conditions, including head injuries, which might compromise central nervous system and cognitive functioning, (3) had a history of major psychiatric disorder other than depression or anxiety disorders, (4) had ever been diagnosed with a learning disability, (5) had a history of pre-term birth (birth prior to 33 weeks gestation), or (6) had significant alcohol, illicit drug, or prescription drug abuse (based on the frequency, number of years of use, and total amount used per week), that were considered capable of causing impaired cognitive testing performance. Additionally, participants were excluded if they were taking long-acting stimulant medications (n=77) or were not willing to complete a wash-out of stimulant medication prior to testing (n=12).   A total of 882 participants completed the initial screening process, of which 282 were excluded.

Following the initial screening process, the remaining 600 eligible participants completed the stage 2 screening to determine diagnostic grouping. To be included in the ADHD group, participants had to endorse having a prior diagnosis based upon a comprehensive clinical interview and standardized assessment of psychiatric status (i.e., behavioral rating scales) as well as onset of symptoms and impairment prior to age 16. To be included in the Depressed group,

participants had to endorse receiving a diagnosis of a unipolar mood disorder from a mental health professional based upon a comprehensive clinical interview and standardized assessment of psychiatric status. Additionally, participants had to endorse having at least one mood episode during the past year that required either medication or behavioral treatment. 85 community volunteers presenting with no history of either ADHD or unipolar mood disorder were enrolled in the study as Controls. While a formal matching process was not implemented, Control participants were enrolled to approximately correspond to the clinical groups based on age and sex. Screening procedures resulted in a total sample of 246 participants (109 ADHD, 52 Depressed, and 85 Controls).

Because the current analyses focused on comparisons among individuals with ADHD, depression, and those with a comorbid ADHD and Depression profile, we elected to focus on a subsample from this larger clinical sample. First, because of our interest in reward sensitivity measures, we included only those with relevant data on these indices (n=161). Next, we constructed four groups of participants that included: those with depression only (DEP), those with ADHD only (ADHD), those with both ADHD and depression (ADHD+DEP), and a Control group. The ADHD group consisted of participants with ADHD who also scored below mild clinical thresholds on the Beck's Depression Index (BDI, BDI score <10) and the depressive symptoms subscale of the Adult Self Report (ASR, T Score <65). Similarly, the DEP group included participants with depression with below clinical cut-offs on all ADHD diagnostic measures. The ADHD+DEP comorbid group consisted of participants with ADHD who scored above clinical threshold on both the BDI and ASR (BDI score >10 and ASR score >65). All included Control participants were below clinical thresholds on all measures. The final

subsample consisted of 29 DEP individuals, 30 ADHD individuals, 28 ADHD+DEP individuals, and 32 Controls. All individuals received compensation for their participation.

Study 2. Participants included 152 adults aged 18-25 (M=19.1 years, SD=1.0, 69.7% female, 75.7% Caucasian). Participants were undergraduates at the University of Iowa enrolled in psychology courses (i.e., an introductory course and a research methods course). Inclusion criteria for participants in this study included fluency in English, normal or corrected to normal vision and hearing and the physical ability to complete computer tasks and questionnaires. All individuals received course credit for their participation.

Procedures

Study 1. Each participant in Study 1 completed a comprehensive neuropsychological evaluation, consistent with recommendations for a multimethod assessment of adult ADHD (Frazier, Damaree, & Youngstrom, 2004; Weyandt et al., 2013). The testing procedures included multiple cognitive tests, behavioral observations, self and informant ADHD behavior rating scales, ratings of depression and anxiety symptoms, performance validity tests, and a symptom validity test (see Nikolas, Marshall, & Hoezle, in review). The key measure in this study used to index reward sensitivity was the Monetary Choice Questionnaire. All participants taking stimulant medication completed a 24 or 48-hour wash-out procedure, depending on whether the medicine was short or long acting (M wash-out time =37.4 hours, SD=14.6). Following the completion of the testing battery, participants completed several normed behavior rating scales to assess ADHD, depression, and anxiety symptomatology as well as to measure delay discounting.

Study 2. Each participant completed a 2.5-hour lab visit, which consisted of a short neurocognitive testing battery and administration of several questionnaires (see below).

Measures

Both studies included in this report were focused on identifying patterns of association between ADHD and depression (conceptualized as both categorical diagnoses and symptom dimensions) and indicators of sensitivity to reward and punishment. Below, we describe how sets of predictor and outcome variables were measured in each study. Table 1 summarizes predictor/outcome sets by study.

Study 1 – Predictors. In this study, diagnostic groupings (ADHD, DEP, ADHD+DEP, or Control) served as a predictor for reward sensitivity.

Study 1 – Outcomes. Indices of reward sensitivity were measured via a delay discounting task. The Monetary Choice Questionnaire (MCQ; Kirby, Petry, & Bickel, 1999) measures the degree to which a delay in reward delivery diminishes an individual's preference for a larger reward. For this measure, participants were given 27 choices between immediate monetary rewards and larger delayed monetary rewards. Choices varied in monetary amounts and delay intervals and were framed as follows: "Would you prefer $34 today or $50 in 30 days?" Two measures were used to index reward preferences: the percentage of larger delayed rewards selected (LDR) and the rate parameter (k) of a hyperbolic discounting function. Here, k values represent the indifference point in which a participant shifts from preference of smaller, immediate rewards to preference of larger, later rewards. A small LDR value and a large k value have both indicated more discounting of delayed outcomes (and preference for smaller but more immediate rewards). Discounting of delayed rewards is linked with impulsivity and has been associated with a variety of maladaptive conditions, including obesity (Weller, Cook, Avsar, & Cox, 2008) and substance use disorders (Kirby, Petry, & Bickel, 1999; Vuchinich & Simpson, 1998).

Study 2 – Predictors. In this study, dimensions of ADHD and depressive symptoms were examined as predictors of reward and punishment sensitivity and assessed with the following measures.

ADHD symptoms: BAARS-IV. ADHD symptoms were evaluated using the Barkley's Adult ADHD Rating Scale-IV (BAARS-IV; Barkley, 2011). Participants rated 18 symptoms of ADHD (including symptoms of inattention, impulsivity, and hyperactivity) on a 1-4 Likert scale (*never, sometimes, often, very often).* Sum scores reflected the total extent of ADHD symptoms, with higher scores indicating greater levels of ADHD symptoms. In addition to measuring severity of symptoms, the BAARS-IV identified age of onset and domains of impairment.

Depression symptoms: BDI-II. Depression symptoms were measured using the Beck's Depression Index-II (BDI-II; Beck, Steer, & Brown, 1996), which is based on DSM-IV criteria for depressive orders. Participants reported their experience of 21 different symptoms based on the most recent period of two weeks, including the present day. Responses to each question were assigned a score of 0 to 4, depending on symptom severity. Sum scores reflected the overall extent of depression symptoms present. Higher sum scores indicated a higher level of depressive symptoms.

Study 2 – Outcomes. As in Study 1, we measured Delay Discounting, an index of reward preference, using LDR and *k* values from the MCQ. We also examined several other indices of reward and punishment sensitivity using the following measures.

Behavioral Response to Reward/Punishment: IGT. The Iowa Gambling Task-modified (IGT; Cauffman et al., 2010), a computerized task for measuring affective decision-making in a gambling situation, was used to evaluate behavioral response to reward (gains) and punishment (losses). For this task, individuals were instructed to maximize their winnings by making

decisions between playing and passing cards from four different decks. On each trial,

participants had the choice to play or pass a card from a randomly selected deck. If participants

chose to play a card, they could win or lose a certain amount of money or neither win nor lose

any money at all. Participants immediately learned the outcome of playing a card- that is, they

were informed of whether they won/lost money (if at all) and the amount of money they won/lost

(if applicable). Meanwhile, passing a deck ensured that participants neither won nor lost any

money on that trial, though the outcome that would have occurred had they played the card was

left unknown to the participants. The payoff schedules for each deck reflected the net outcomes

of the original IGT: two of the desks are advantageous and result in gains over repeated play.

The other two decks are disadvantageous and reflect a net loss over repeated play. In addition,

within each type of deck (advantageous vs. disadvantageous), there is one deck in which losses

were experienced infrequently but were relatively large and one in which losses are more

frequent but relatively small. The task was administered over six blocks of 20 trials each.

Three primary indices were calculated for each of the 6 blocks of the task: percentage of

good decks selected (good plays), percentage of bad decks selected (bad plays), and net score.

Percentage of good plays (and bad plays) was calculated by dividing the number of plays from

an advantageous deck (or in the case of bad plays, from a disadvantageous deck) by the number

of times an advantageous (or disadvantageous) deck was presented during a given block.

Overall performance on the IGT was then evaluated based on change over time in both the

percentage of advantageous and disadvantageous decks played, as in Cauffman et al (2010).

Regression slopes were calculated to capture the change in the relative percentage of good and

bad decks played as the task proceeded. The change in the percentage of good decks played is

conceptualized as a measure of approach behavior or reward sensitivity, with more steeply

positive slopes indicating an affinity for decks that result in gains with repeated play. Similarly, the rate of change in negative decks played was conceptualized as avoidance behavior, with steeper negative slopes reflecting greater sensitivity to net losses (or sensitivity to punishment) resulting from playing disadvantageous decks. It is important to note that the percentage of bad decks played is independent of the percentage of good decks played because each trial gives the participant a chance to make a play or pass decision on one random deck.

Activity of BIS/BAS: SPSRQ. The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ; Torrubia et al., 2001) was used to measure the reactivity/responsivity of the BIS and the BAS. The SPSRQ consists of two independent subscales: Sensitivity to Punishment (SP) and Sensitivity to Reward (SR). Based on Gray's model of personality, the SP and SR scales measure activity in the BIS and BAS, respectively. Participants made yes/no responses to a total of 48 questions. BIS/BAS activity was determined based on separate sum scores for each subscale; high SP scores reflected high levels of BIS activity while high SR scores reflected high levels of BAS activity.

Data Analytic Plan

Study 1

Descriptive statistics by diagnostic groupings were computed for both demographic variables (sex, age, ethnicity, and education level) and outcome variables (*k* and LDR values). To examine differences in discounting across diagnostic groupings, we conducted a Multivariate Analysis of Covariance (MANCOVA), with diagnostic grouping as the fixed factor and the discounting indices (e.g., *k*- value and LDR) as the outcomes. Demographic characteristics were included as covariates. Post-hoc tests were then used to identify differences in responding between the comorbid group (ADHD+DEP) and the ADHD and DEP groups.

Study 2

Bivariate correlations were calculated to assess the strength of associations among key variables (ADHD/depression symptom dimensions and outcome variables). A series of hierarchical linear regression analyses was conducted to address our key questions, with indices of delay discounting and reward and punishment sensitivity, assessed via self-report and on the IGT, as the continuous dependent variables. Here, we focused on examining ADHD and depression symptoms as well as sex as key predictors of indices of sensitivity to reward and punishment. Given past work suggesting sex differences in these associations, a series of hierarchical linear regression models were conducted to examine the main effects of ADHD symptoms, depression symptoms, and sex on these indices as well as their synergistic effects (i.e., captured in the two-way and three-way interactions). Here, covariates and main effects (ADHD, depression, sex) were added in the first step, two-way interactions were entered in the second step, and the three-way interaction was added in the final step.

RESULTS

Study 1

Demographic and descriptive statistics. Demographic and descriptive statistics by diagnostic group are presented in Table 2. A one-way ANOVA, along with a series of Chi-squared tests of independence, confirmed that all four diagnostic groups were demographically similar in age, sex, ethnicity, and education level.

Multivariate analyses. The results of our Omnibus MANCOVA test [$F(6,226)=2.41$, $p=.028$, $\eta_P=.060$], excluding covariates, indicated that the diagnostic groups significantly differed in regard to their k and LDR values. Tests for between-group effects for individual discounting indices revealed significant differences in LDR by diagnostic group ($F= 4.928$, $p=.003$, $\eta_P=.115$), but only marginally significant differences in k ($F= 2.274$, $p=.084$, $\eta_P=.056$), The

overall MANOVA remained significant when including age and gender as covariates [$F(6,226)=2.301$, $p=.032$, $\eta_p=.060$].

Post-hoc Tukey tests were then used to examine pair-wise differences between the diagnostic groups. Findings indicated that all three clinical groups differed from controls in regard to their LDR values (ADHD vs. Control, $p=0.05$; DEP vs. Control, $p=0.006$; and ADHD+DEP vs. Control, $p=0.014$), but that the clinical groups did not significantly differ from each other (all $ps>.05$). Thus, findings indicated that all three clinical groups selected a smaller proportion of longer, later rewards than controls, suggesting that both ADHD and depression symptoms were associated with changes in discounting of delayed rewards. Average LDR and *k* values for each group are shown in Figure 1.

Study 2

Bivariate correlations. Bivariate correlations among predictor and outcome variables are presented in Table 3. ADHD symptoms were associated with BIS/BAS activity as indexed by the SP and SR scales from the SPSRQ (SP $r = .362$, $p < .001$; SR $r = .344$, $p < .001$); on the other hand, ADHD symptoms were only marginally related to LDR value from the MCQ ($r = -.157$, $p = .053$) and were not related to behavioral responses to reward and punishment on the IGT. Similarly, depression symptoms were linked to BIS/BAS activity (SP $r = .380$, $p < .001$; SR $r = .251$, $p = .002$) and marginally linked with LDR value ($r = -.136$, $p = .100$) but not associated with IGT outcomes. ADHD symptoms and depression symptoms were also significantly correlated ($r = .496$, $p < .001$).

Hierarchical regression analyses. Hierarchical linear regression models were used to examine the main effects of ADHD symptoms, depression symptoms, and sex and their interactions in predicting indices of delay discounting and sensitivity to reward and punishment.

Covariates, including age and ethnicity along with main effects, were entered at step 1 followed by all three two-way interactions in step 2 and the three-way interaction in step 3. Outcomes included indices of delay-discounting, behavioral response to punishment/reward, and BIS/BAS activity.

Delay-Discounting. There was a marginally significant main effect of ADHD symptoms in predicting the delay discounting *k* value (β= .699, p = .056), such that increased ADHD symptoms predicted larger *k* values (larger *k* values indicating a more precipitous devaluation of a larger, delayed reward). No two- or three-way interactions were significant predictors of delay discounting *k* values. Additionally, neither ADHD symptoms, depression symptoms, sex, nor any of their interactions significantly predicted the proportion of larger, delayed rewards selected.

Behavioral Reaction to Reward/Punishment. In regard to predicting change in the percentage of good plays on the IGT (thought to reflect behavioral reactions to reward), marginally significant main effects for sex and depression symptoms emerged. However, the two-way interaction between ADHD symptoms and depression symptoms also significantly predicted the change in percentage good plays (β=1.176, *p*=.019) as did the three-way interaction between ADHD symptoms, depression symptoms, and sex (β=-1.124, *p*=.027). Examination of simple slopes revealed marginally significant synergistic effects of ADHD and depression symptoms for males, but not females. Specifically, higher ADHD scores were associated with decreased sensitivity to reward for males with low depression symptoms (β=-.22, *p*=.056). However, for males with high depression symptoms, there was a marginally significant positive association between ADHD symptoms and sensitivity to reward (β=.25 *p*=.09). For females,

there was no evidence of synergistic effects between ADHD and depression symptoms when predicting sensitivity to reward.

In predicting change in the percentage of disadvantageous decks played, significant main effects of ADHD symptoms were observed (β=-.733, p=.047) but was qualified by a significant ADHD x sex interaction x (β=.885, p=.017). Examination of simple slopes indicated that ADHD symptoms marginally predicted change in the percentage of disadvantageous decks played in females (β=.175, p=.081), but not in males, such that ADHD symptoms predicted a steeper increase in the percentage of disadvantageous decks selected over time, indicating increased motivation for selecting high-risk desks after learning of their potential for larger rewards.

Finally, significant main effects of depression symptoms (β=-1.088, p=.013) and interactions between ADHD symptoms and sex (β=-.792, p=.037), and between depression symptoms and sex (β=1.021, p=.020) served as significant predictors of change in the net percentage of play. Examination of simple slopes revealed that ADHD symptoms was associated with negative change in net gains for females (β=-.52, p=.022), but not for males (β=-.03, p=.46). This indicated that, for females, increased ADHD symptoms was associated with a decrease in net gains in the task, but that ADHD did not impact changes in gains for males. Conversely, depression symptoms were inversely related to change in net gains for males (β=.39, p=.019), but not for females (β=-.01, p=.77). Again, this indicated that depression symptoms were associated with a decline in net profit on the task for males, but that no impact of depression symptoms on net gains was apparent in females.

BIS/BAS Activity. A significant interaction between ADHD symptoms and sex (β=.476, p=.048) emerged when examining predictors of scores from the Sensitivity to Punishment subscale (thought to reflect *BIS* activity). Examination of simple slopes indicated that increased

ADHD symptoms predicted increased sensitivity to punishment in females (β=.381, $p < .001$) but not males (β=.128, p =.406). The depression x sex interaction was also marginally significant (β=.692, p=.065), and again, suggested a significant relationship between depression and increased SP scores in females (β=.487, $p < .001$) but not males (β=-.035, p =.815). Figure 2 shows average SP scores for high and low levels of ADHD and depression symptoms for both sexes.

Scores from Sensitivity to Reward subscale (thought to reflect *BAS* activity) were significantly predicted by sex (β=-.207, p=.020), such that males reported significantly higher sensitivity to reward than females. The interaction between depression and sex (β=.642, p=.095) was also marginally significant in predicting sensitivity to reward was also marginally predicted by. Again, simple slopes revealed that depression symptoms were predictive of higher sensitivity to reward scores in females (β=.386, $p < .001$) but not males (β=-.034, p=.836). In sum, it appears that ADHD and depression symptomatology predicted increased reward *and* punishment sensitivity, but only in females. Figure 3 shows average SR scores for high/low levels of depression across sex.

DISCUSSION

Although previous research has identified deficits in reward and punishment sensitivity in individuals with depression and individuals with ADHD, few studies have examined the multiplicative effects of ADHD and depression symptoms on these dimensions. Moreover, there are currently no studies to our knowledge which examine this combined effect of ADHD and depression in adults. Our studies add to the current literature by investigating how both depression and ADHD may synergistically contribute to problems in reward and punishment processing in two adult samples across several indices of reward/punishment sensitivity. Study 1,

which examined differences in reward sensitivity among three *diagnostic groups* (ADHD only, depression only, and comorbid ADHD/depression) as well as a control group, found that both ADHD and depression appeared to impact reward sensitivity. However, we did not find evidence for our hypothesis regarding a synergistic effect of ADHD and depression on reward sensitivity. In Study 2, we analyzed reward and punishment sensitivity in a transdiagnostic sample of undergraduates, exploring how dimensional ADHD and depression *symptoms* may be related to outcomes of reward/punishment sensitivity. In this study, we uncovered some evidence of a synergistic effect of ADHD and depression symptoms in predicting reward sensitivity in females. Sex also moderated many of the separate effects of ADHD and depression symptoms on the various reward/punishment sensitivity outcomes included in Study 2.

The results of Study 1 revealed an effect of diagnostic group on reward processing in a delay discounting task, in that all diagnostic groups, compared to the control group, selected smaller, immediate rewards over larger, delayed rewards at a higher rate. This is consistent with our hypothesis, as we expected the impulsive nature of reward-seeking behavior to favor the immediate reward and those with ADHD to demonstrate heightened reward-seeking tendencies. On the other hand, we did not expect individuals with depression to differ significantly from controls. However, our findings regarding the effect of ADHD and depression are in line with past work, indicating that the presence of either an ADHD or depression diagnosis is associated with impaired performance on delay discounting tasks. For example, Scheidal (2013) found slightly steeper discounting of delayed outcomes in adults with an ADHD diagnosis compared to matched controls, attributing this effect to impulsivity in those with ADHD. In a study by Pulcu et al. (2014), individuals diagnosed with major depressive disorder also demonstrated impaired performance on a delay discounting task, discounting very large but delayed rewards at a higher

rate than healthy controls and remitted individuals. Pulcu et al. (2014) posited that hopelessness towards the future (rather than impulsivity) may underlie the preference for immediate reward in individuals with depression. While untested, this could explain why our findings also showed steeper discounting of delayed rewards among individuals with depression.

In contrast to Study 1, Study 2 employed a dimensional approach to investigating the effects of ADHD and depression, focusing on the effects of ADHD and depression *symptoms* rather the absence/presence of a diagnosis. Our second study also included additional measures to more fully explore the links between ADHD/depression symptoms and reward/punishment sensitivity. Results from the IGT revealed moderate evidence for an interaction effect of ADHD and depression for males. Specifically, ADHD symptoms were associated with an *increase* in selecting advantageous decks over time when depression symptoms were also high. Conversely, ADHD symptoms were linked to a *decrease* in advantageous deck selection when depression symptoms were low. While increased selection of advantageous decks is indicative of reward sensitivity and subsequent approach behavior to overall profitable decks, a decrease in selection of these decks could be reflective of decreased motivation to choose decks that yield small rewards (even if these decks come with minimal risk). Such results are consistent with the findings of Garon et al. (2006), in which children with both depression and ADHD symptoms performed as well as controls on a gambling task whereas children with ADHD symptoms alone performed markedly worse.

It is unclear why this interaction effect of ADHD and depression was found in males but not females. Nonetheless, sex continued to moderate effects of ADHD and depression symptoms on other indicators of the IGT as well. For instance, ADHD symptoms were linked to increased selection of disadvantageous decks over time in females, but not males. That is, females with

ADHD symptoms continued to select from disadvantageous decks even as they learned of their risk, suggesting reduced sensitivity to punishment. Regarding net play between advantageous and disadvantageous decks over time, ADHD symptoms predicted net loss over time for females while depression symptoms predicted net loss over time for males. Again, this suggests differences in reward processing between males and females as a function of psychopathology.

On subscales of the SPSRQ, the separate effects of ADHD and depression symptoms were again moderated by sex, as all effects were observed in females only. Based on SP scores, punishment sensitivity and punishment-avoidant behavior was greater in females with higher levels of ADHD or depression symptoms. While an association between depression symptoms and punishment sensitivity coincides with our hypotheses, we did not expect to find a correlation between ADHD symptoms and punishment sensitivity. Nonetheless, findings regarding this relationship have been inconsistent, with several studies reporting heightened levels of punishment sensitivity in those presenting with ADHD symptoms, especially on a neural level. Of particular interest is a study conducted by Gomez and Corr (2010), which found that inattention was positively associated with the SP subscale of the SPSRQ. Because inattention is most predominant symptom of ADHD in adults, it may be the case that inattention symptoms are responsible for the association between ADHD symptoms and sensitivity to punishment in our adult sample.

ADHD symptoms were also associated with higher SR scores in females. While this finding appears to contradict our prediction that those with depression and/or ADHD symptoms would experience reduced levels of reward sensitivity, it is important to note the nature of the items on the SR scale. Rather than focusing on an internal experience of reward, many items of this scale measures reward-seeking behavior, including items like "I prefer activities that lead to

immediate gain" and "The possibility of social advancement moves me to action, even if this does not involve playing fair". Although typical levels of reward sensitivity are associated with reward-approach behavior, those with reduced reward sensitivity can engage in *excessive* reward-seeking behaviors to compensate for their diminished internal experience of typically rewarding stimuli (Beauchaine & McNulty, 2013). Given that a large proportion of questions on the SR scale measure reward-seeking behavior, a positive association between ADHD symptoms and SR score is consistent with our hypothesis.

In addition to ADHD symptoms, depression symptoms were also positively linked to SR score in females. This result is surprising, as much of past research has indicated a blunted capacity for reward-seeking in depressed individuals (see Alloy et al., 2016). On the other hand, our finding suggests that depressed individuals, especially depressed females, may still engage in high levels of reward-seeking behavior.

Study 2 also examined performance on the same delay discounting task employed in Study 1. In contrast to Study 1, very little evidence was found for influence of ADHD/depression on delay discounting. ADHD symptoms were marginally associated with steeper discounting of delayed outcomes; however, depression symptoms were not related to either indicator of delay discounting. Another study conducted by Mies, De Water, and Scheres (2016) also investigated the effects of both ADHD and depression *symptoms* on several delay discounting tasks. They found that depression symptoms, but not ADHD symptoms, were associated with more precipitous discounting of delay outcomes but otherwise found minimal evidence for the influence of ADHD and depression on delay discounting task performance. The slight discrepancy between our results and their results might be explained by differences in indicators used to measure delay discounting; while we calculated k value and percentage of LDR selected,

Mies et al. (2013) determined a subjective value – the amount of money at which an individual becomes indifferent between the two choices – based on the evaluations of two independent raters. It is possible that choice of indicators used for delay discounting tasks may reveal very different information.

Overall, Study 2 found that effects of ADHD and depression on reward/punishment sensitivity as well as reward/punishment related behavior were frequently moderated by sex. Particularly, effects were more often observed in females than males. There are currently no studies which have found gender differences in reward/punishment sensitivity in the context of depression or ADHD symptoms and reward processing. However, many neural studies suggest that reward processing and reward-related decision-making differ by sex given a wide range of conditions. For example, Lighthall et al. (2012) found that under stress, males showed higher levels of activity in brain regions involved in reward processing while women, under the same stress conditions, showed diminished activity in these regions. Another study, which examined sex differences in reward/punishment anticipation and reward/punishment delivery on in adolescents, found that males showed reduced neural activation to prospect of social punishment (Greimel et al., 2018). The same study also reported that males showed more responsivity during the reception of monetary reward than monetary loss while females responded at similar levels for both reward and loss. All in all, these studies (along with our results) reveal the need for further investigation of neural and behavioral sex differences in reward/punishment processing, especially in the context of ADHD/depression symptoms.

Limitations

There are several limitations to note of the current studies. For one, Study 2 relied on self-report measures for gauging levels of symptomatology. It is possible that use of other measures

(i.e., informant ratings, observer ratings) would strengthen effects or yield further evidence of synergistic effects of ADHD/depression symptoms. In both studies, self-report and behavioral measures were used to determine levels of reward and punishment sensitivity. However, such measures may not fully capture the internal experience of reward/punishment reception. More sensitive measures, such as use of functional MRIs during reward and punishment delivery, could demonstrate stronger associations between ADHD/depression and reward/punishment sensitivity.

It also important to clarify that reward and punishment sensitivity can refer to a wide range of distinct but related subconstructs, including reward/punishment anticipation, reward/punishment reception, impact of prior reward/punishment on behavior, and general reward-seeking/harm-avoidance patterns. Delay discounting tasks involve a reward/punishment anticipation component, in that individuals are not actually receiving rewards, but rather, deciding on the conditions of an anticipated reward (smaller, now or larger, later); however, delay discounting tasks also measure constructs which are only indirectly related to reward processing, such as delay aversion (Mies, De Water, and Scheres, 2016). On the other hand, the SPSRQ captures several subconstructs, such as reward-seeking/harm-avoidance and internal experience of reward/punishment reception. Because it may be the case that psychopathological symptoms relate uniquely to different subconstructs of reward/punishment sensitivity (e.g., ADHD symptoms are related to increased reward-seeking but an attenuated experience of reward reception), future work should aim to assess the effects of ADHD/depression on each subconstruct separately and while using multimethod indicators of each. Such research would more clearly characterize relationships between ADHD/depression and components of reward/punishment sensitivity.

Conclusion

       The current study demonstrated effects of ADHD and depression symptoms and diagnosis on reward and punishment sensitivity, suggesting that reward/punishment sensitivity in individuals with symptoms of these disorders deviate from typical levels. However, only modest evidence was found for a synergistic effect from ADHD and depression. Our study also indicates that there may be sex differences which moderate associations between ADHD/depression symptomatology and reward/punishment processing. Future work should further explore how these effects differ by sex while also examining the separate links between ADHD/depression and different subconstructs of reward/punishment sensitivity.

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Table 1. Summary of predictors and outcomes by study.

	Predictors	**Key Outcomes**
Study 1	Diagnostic groupings (ADHD, DEP, ADHD+DEP, Control)	k value (MCQ) LDR (MCQ)
Study 2	Dimensional symptom scores (ADHD and depression)	k value (MCQ) LDR (MCQ) Change in % Good Deck Play (IGT) Change in % Bad Deck Play (IGT) SP/SR sum scores (SPSRQ)

Table 2. Demographic and descriptive statistics for diagnostic groups – Study 1

	ADHD	DEP	ADHD+DEP	Control	*p*
N	30	29	28	32	
% Male	50	34.5	50	37.5	.491
Age	24.23(5.66)	24.07(6.65)	25.68(6.97)	23.91(6.17)	.500
% Caucasian	86.7	86.2	85.7	75.0	.799
% At least some college	96.7	89.7	85.7	96.9	.623
k	0.0221(0.315)	0.0275(0.0350)	0.0221(0.0328)	0.0087 (0.0181)	.084
LDR	46.79(15.46)	43.55(14.87)	48.37(17.17)	57.52(17.94)	.003

Table 3. *Bivariate correlations among predictor and outcome variables in Study 2.*

Variables	1	2	3	4	5	6	7	8		9
1. ADHD	-									
2. Depression	.496***	-								
3. *k*	.153+	.071	-							
4. LDR	-.157+	-.136+	-.753***	-						
5. Change in Advantageous Plays	.003	.058	-.044	-.026	-					
6. Change in Disadvantageous Plays	.107	.133	.051	-.035	.096	-				
7. Change in Net Plays	-.063	-.064	-.100	.044	.654***	-.579***	-			
8. SP	.362***	.380***	.112	-.182*	-.085	.062	-.076	-		
9. SR	.344***	.251**	.073	-.121	.076	-.126	.175*	.451***		-

$^+p \leq .10$; $^*p \leq .05$; $^{**}p \leq .01$; $^{***}p \leq .001$

Figure 1. (A) Average percentage of larger, later rewards selected (LDR value) and (B) average k value across diagnostic groups in the delay discounting task in Study 1.
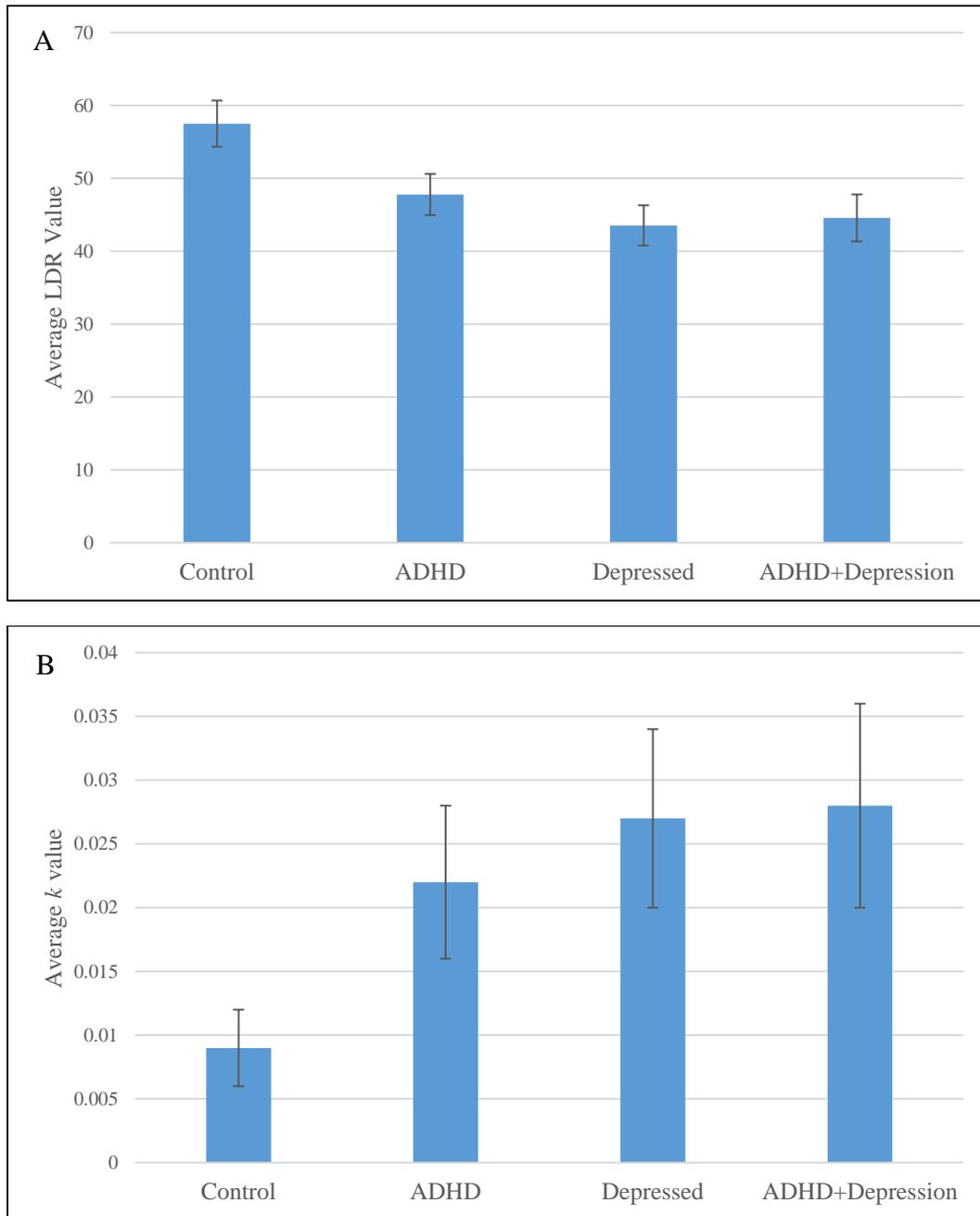
Figure 2. (A) Average sensitivity to punishment subscale (SP) scores for low and high levels of ADHD and (B) low and high levels of depression across sex on the SPSRQ in Study 2.
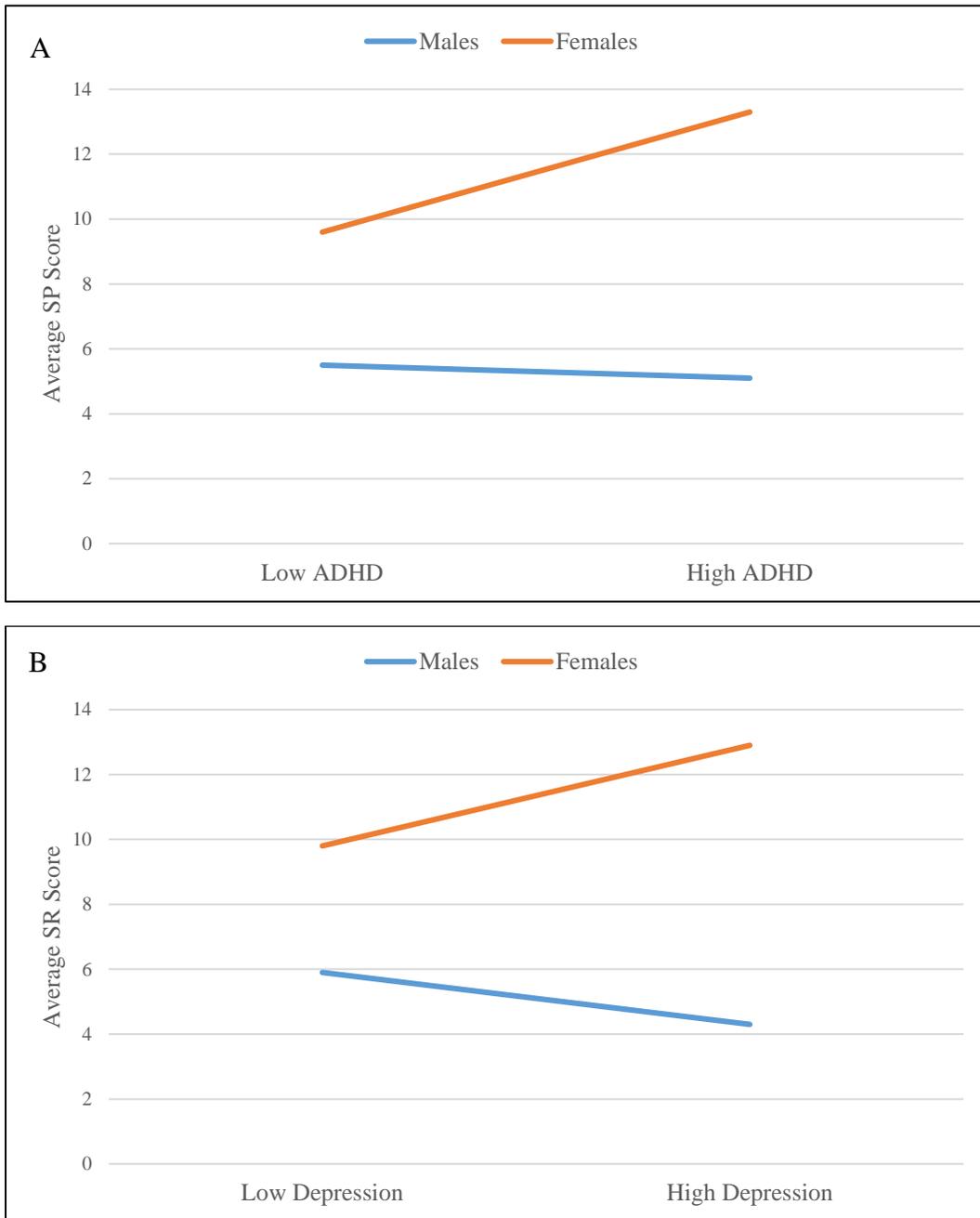
Figure 3. Average sensitivity to reward subscale (SR) scores for low and high levels of depression across sex on the SPSRQ in Study 2.