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MONETARY INCENTIVE DELAY TASK RESPONSE IN A DIVERSE SAMPLE OF ADOLESCENTS: ADVANCING HEALTH PROMOTION IN THIS AGE GROUP

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MONETARY INCENTIVE DELAY TASK RESPONSE IN A DIVERSE SAMPLE OF ADOLESCENTS: ADVANCING HEALTH PROMOTION IN THIS AGE GROUP

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ABSTRACT

The adolescent brain is becoming increasingly recognized as an important and distinct developmental period [1-3]. Adolescence is also a period that has seen a recent increase in sexually transmitted infection (STI) [4]; those between ages 15-24 account for roughly 25% of the United States' population but account for about 50% of annual STI incidents [5]. Current behavioral-only intervention approaches have been limited in their capacity to help advance adolescent health behavior; translational approaches that utilize information about the neurological underpinnings of sexual health decision making offer the opportunity to obtain novel information about young people. The functional magnetic resonance imaging (fMRI)-based monetary incentive delay (MID) task is one method of elucidating the decision-making process of health-behavior. This study aimed to examine neurological activation during the MID task with STI/HIV risk behavior. Participants were 149 adolescents (M_{age}= 16.03 [SD=1.28], 66% male), recruited as part of a larger randomized control trial, with a highly diverse sample of justice-involved youth. Sexual risk behavior was assessed using two variables, *Condom Use* and *Risky Sex*, which were compiled into one 'Risky Sex Index' (RSI). Significant activation was seen in key networks involved in adolescent brain development (i.e., social processing network, mentalizing network, and salience network). Specifically, we observed significant changes to activation for the Low RSI group in the left superior temporal gyrus, right precentral gyrus, and bilateral precuneus. We also found significant changes to activation for the High RSI group in the left thalamus and the right precentral gyrus. Results from this study suggest that areas of the brain that are activated when a loss is perceived differ among the two groups. This difference is important when considering the creation and

implementation of adolescent focused STI/HIV intervention and prevention techniques.

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PREFACE

The Manuscript Format is in use, all other mandatory sections are included, and all pages have been formatted in the accepted font and margin alignment.

TABLE OF CONTENTS

LIST OF FIGURES

FIGURE **PAGE**

LIST OF TABLES

TABLE **PAGE**

The following manuscript is prepared for submission to Frontiers in Developmental Psychology.

CHAPTER 1

INTRODUCTION

Adolescent Sexual Behavior

Recent reports show that HIV and STI rates have been climbing for youth aged 13-25 [6, 7]. Although adolescents account for 25% of the population, they accounted for nearly 50% of new STI and HIV diagnoses in 2020 [8]. According to the CDC Youth Risk Behavior Survey (YRBS) 2021, only 52% of sexually active youth had used a condom the last time they had sex, which was a decrease from the 60.2% reported in 2011. Not only has the rate of condom use declined, but the emphasis of barrier methods, such as condoms, has also declined in American health and sexual education classes [6]. Relatedly, rates for HIV and STI testing have dropped drastically for youth from 2011 to 2021 [8]. These declining rates are quite worrying, because testing positive for STIs represents one of the highest risk factors for the acquisition of HIV/AIDS. As the rates for STI prevention techniques (e.g., condom use, STI/HIV testing) has declined, the overall number of STI cases in adolescents has continued to climb.

The number of cases of chlamydia reported to the CDC remained stagnant from 2016 to 2020, but this is believed to be due to a decrease in STI screening and diagnosis, rather than a decrease in infection [9]. The 2020 total of 1.6 million cases of chlamydia continues to make it the most common notifiable condition in the United States, with 62% of new cases being reported in adolescents[10]. Neisseria gonorrhoeae and primary and secondary (P&S) syphilis rates both rose 45% and 52%,

respectively, from 2016 to 2020 [9]. The greatest rise of both gonorrhoeae and P&S syphilis was reported in females aged 15-24 years old. As rates of syphilis have continued to rise in women of childbearing age, so have the rates of congenital syphilis, which has seen a 235% spike in cases from 2016 to 2020 [10], with early data indicating that this trend did not slow in 2021 [9]. Rate increases have been tied to a lack of education, awareness, and preventative measures (e.g., condom use). A decrease in both STI/HIV testing and condom use poses a huge risk in the transmission of STIs; individuals who acquire any non-HIV STI become more susceptible to HIV infection [7]. HIV is a life-long condition that comes with its own health sequelae; ignoring the recent rise of non-HIV STIs, will reverse the gains that have been made in HIV prevention in recent decades [6]. In adolescent populations, condom use is particularly important to track as it is a meaningful indicator of potential risk for contracting STI[11]. Adolescent sexual activity patterns are distinct from those of adults such that the likelihood of monogamy is low enough that condom use is used as an important predictor of risky sexual behavior [12, 13].Current approaches for creating targeted behavioral interventions for youth have been limited in their capacity to help advance adolescent health behavior interventions for STI risk reduction [5]. Mainly, studies in this area have been focused on adult approaches; largely overlooking the important role of developmental factors relevant for youth in these equations [14, 15]. Adolescents are undergoing both brain and behavior development, which appears to aid in natural plasticity and resilience, making this a favorable time to introduce positive health behaviors [15]. In order to better inform

future intervention strategies, we must consider the unique features of adolescent neurodevelopment in order to improve health promotion programming.

Unique Features of the Adolescent Brain

Adolescents are situated in a unique neurobiological period, which includes substantive biological, neurodevelopmental, and sociodevelopmental changes [3]. In regard to sociodevelopment, adolescence is a transitional period in which young people start to obtain information about their surroundings from their peers, on the developmental journey toward more independent decision making [16-18]. As part of this developmental journey, adolescents become more attuned to the behaviors and decisions of their peers and of their social environment; the value of social information increases, as does their social motivation. As such, in order to create more effective interventions for adolescents, we must aim to better understand how social attunement mechanisms act as protective factors in adolescent sexual decision making. There are three different networks of the brain that are important in adolescent development and thus are likely to be very important in the context of sexual decision making and specifically STI risk reduction [19].

The first area is social processing (see Figure 1); this is a neural network is engaged in recognizing, understanding, and interpreting social cues [15, 20]. During adolescence, these networks are still being developed, leading youth to learn about how to interact with peers in social ways, - including both friend-based interactions and also the beginning of romantic-based social interactions [21]. The field is becoming more aware that youth have the natural propensity for positive/prosocial peer behavior [22, 23]. In fact, in this developmental window, adolescents are more

receptive to positive peer influences compared to adults [22]. The regions that make up the social processing network work together to gather information about the social environment that in turn helps adolescents navigate different social settings [24]; these regions include: the temporoparietal junction (TPJ), posterior anterior cingulate cortex (pACC), superior temporal sulcus (STS), and temporal pole (TP) (Figure 1) [15, 24, 25]. As adolescent brains develop, changes to network strength and connectivity are fortified, in turn refining important social cognitions, such as those that may affect youth decision making around sexual behavior [25].

While metacognition represents the capacity to think about one how thinks about things [26], a second area is mentalizing; this is akin to the process of metacognition for others, and essentially represents the ability to anticipate and cognitively imagine the thoughts of others [27]. This is highly important when thinking about how youth may process decision making of their sexual partners prior to engaging in any sexual decisions. Areas of the brain that are involved in mentalizing include the TPJ, posterior superior temporal sulcus (pSTS), anterior temporal lobe (ATL), and precuneus (Figure 1) [28]. In adolescents, the TPJ plays a role in understanding the beliefs and point of view of others [29], while the pSTS and precuneus both activate during the acquisition of person-specific knowledge [29]. Broadly, each area plays a specialized role in allowing adolescents to engage with and interact with their peers [30]. Further, these brain regions undergo developmental changes during adolescence, in which connectivity between individual areas in the mentalizing network strengthens, allowing for further integration of social information into the network [28]. These network integration changes directly impact the

development of cognitive capacities (e.g., understanding others' mindsets and decision-making processes) during adolescence [31].

A third network that is important in this age group, and in sexual decision making in particular, is the salience network. The salience network is involved in how different situations may feel and how important they are in terms of emotional weight [32], which is particularly relevant for adolescents during sexual health decision making. The regions in this network are hubs for the understanding and integration of valence [15], and they include: anterior cingulate cortex, amygdala, dorsal striatum, and insula (see Figure 1) [15, 32]. Each area within the broader salience network plays a specific role, which becomes more finely tuned throughout adolescence [33-35]. The striatum allows adolescents to integrate emotional value of a situation into their perception of friendships and peer relations [36, 37]. The insula encodes salient environmental information [38], while the connection between the amygdala and anterior cingulate cortex processes the emotional weight of a situation [39]. The integration of outside information into the salience network, through each of these neural regions, helps to guide individual behavior in order to help with decision making [40-42].As adolescents begin to navigate making decisions about sexual behavior, it is important to understand the unique underlying neurological networks and processes that are at play. Prior studies have illustrated significant potential in harnessing the resilient and adaptive nature of the adolescent brain in the context of prosocial peer interactions [3, 6, 15]. Here, we aim to further examine these neural networks as a means enhance our insight into which regions are particularly important in adolescent health risk reduction response.

Utilizing a Translational Framework

Translational studies integrate information from neuroimaging and behavioral studies in order to create targeted intervention techniques and treatments [43]. Translational approaches help highlight when and why different neurodevelopmental areas are available for adolescents, which is critical for informing more impactful interventions. The developmental field is rich with knowledge about the neurobiological mechanisms that lead to health decision making [44], but Crone and Dahl [45] found that the interventions popularized in the behavior literature do not take into consideration the results that have been uncovered in developmental neuroimaging studies.

The adolescent brain has many strengths. Among them is a propensity for resilience [46-48], and a particular social attunement to the decisions of their peers [16]. Both of these strengths stem from underlying neurological changes that help to form the developing adolescent brain into an adult brain. As the adolescent brain matures, the functional connectivity in the social networks strengthen, leading to more successful planning for and engaging in safer sexual decision making [49]. Youth who are positioned to be able to make more thoughtful decisions about their sexual encounters are more likely to practice safe sex behaviors (e.g., frequent condom use, regular STI/HIV testing). For example, positive sexual and/or romantic partner influences could be utilized in intervention strategies in order to create programs that rely on the adolescent's propensity for prosocial decision making. Additionally, the mentalizing and salience networks are undergoing change during adolescence, and therefore could help to inform interventions by demonstrating that young people are

wired to be very empathetic and in tune with their sexual and/or romantic partners [32, 37]. As for resilience, this feature is also crucial to incorporate. There are several neurological features that promote resilience in adolescence [15, 50], which would be critically important to consider when constructing targeted health prevention programs. In order to create appropriate interventions for adolescents, the relationship between these distinctive neurological features and behavioral decision-making abilities must be further examined.

The Monetary Incentive Delay Task

The Monetary Incentive Delay (MID) task was originally developed by Knutson et al., (2000) in order to examine the neural networks that are involved in incentive responses. Knutson et al., (2000) performed this task using fMRI because at the time of development, there were few human imaging studies that examined incentive cues. Specifically, fMRI was chosen as the desired modality due to its comparably high visual resolution, which allowed for close examination of activation in specific brain circuitry during reward and punishment outcomes[51]. In addition to better resolution through an fMRI, brain imaging in general has the advantage, compared to non-imaging tasks, to track neural responses in highly accurate temporal and spatial locations[52]; the MID task allows for researchers to see how neural networks activate and work together during the task [53]. The MID task is a particularly good translational tool for measuring social, mentalizing, and salience relevance [54-56].

The MID task has also been used to examine how the activated areas of the brain can shift depending on different health behaviors (i.e., substance use, risky

sexual behavior, etc.). Relevant to this study, a foundational paper by Karoly et al., (2015) examined how young people engaged in polysubstance use rather than single substance use influenced activation during the MID task. This team found that incentive anticipation trials, regardless of reward or loss, activated a large network of brain areas. REWARD trails, as compared to NEUTRAL trials, activated a network that included the bilateral caudate, thalamus, cingulate, and left insula. Comparatively, the LOSS trials produced activation in the bilateral insula, caudate, thalamus, and anterior cingulate. Karoly's team also found that, when examining neural response for youth engaged in single substance vs. polysubstance use, differences were observed for activation in the nucleus accumbens, which plays a role in incentive processing, only during all three levels of REWARD trials (i.e., $0.20, $1.00, $5.00) [55].

One avenue in which the MID task has been less frequently used is to elucidate underlying neural mechanisms of adaptive health. In this current study, we have decided to take this approach because the adolescent brain is becoming increasingly recognized as its own important health promotive phase of neurodevelopment [2]. This new focus will give us a better understanding of how to create targeted behavior tools and interventions for youth. Current behavior-only approaches are limited in their capacity to help advance adolescent behavior interventions for HIV risk reduction, as many of the current empirically supported behavior interventions were informed by adults and thus did not incorporate adolescent neurodevelopment [45]. Thus, in order to better inform health promotion programs, to help prepare youth for optimal risk reduction, a translational framework should be utilized. Neuroimaging offers an essential lens to "look under the hood" and better understand these strengths

in order to inform more beneficial intervention strategies for HIV risk reduction. It is crucial to understand the neurological underpinnings of the decision-making processes in order to create more impactful interventions.

Current Study

As adolescent HIV/STI rates continue to rise, it is becoming increasingly important to understand how this unique developmental period can help elucidate potential areas to target when creating behavioral interventions for this age group. To inform more impactful health prevention programming, the current study investigated which areas of the brain activate during the MID task, and how brain activation is associated with our key outcome: the risky sex index. We hypothesized that: (1) we would find activation in our key target neural areas (social cognition; mentalizing; salience networks; see Figure 1), [55]and (2) aligning with findings from Karoly, Bryan [55] and [57]we would see differing activation patterns between our two contrasts of interest (i.e., REWARD-NEUTRAL and LOSS-NEUTRAL), and that these differences would also be present in our two sexual risk behavior groups (i.e., high sexual risk behavior and low sexual risk behavior). Specifically, in line with findings from prior studies, we expected to see those engaging in higher risk sexual behavior to exhibit greater neural activation in key target neural areas during incentive reward trials as compared to those with lower sexual risk behaviors [57].

CHAPTER 2

METHODOLOGY

Participants and Procedures

All study procedures were performed with approval of the participating institutional review board. We also obtained a federal Certificate of Confidentiality as an additional level of protection for the youth participants. For this study we performed a secondary data analysis of the data from 149 high-risk youth (M_{age}= 16.03 [SD=1.28], 66% male) who were originally recruited as part of a larger randomized control trial (1R01NR013332-01, MPIs: Feldstein Ewing & Bryan) with a highly diverse sample of justice-involved youth [19, 55, 58]. Participant recruitment was conducted by trained research staff who introduced the project at local community diversion and alternative-to-incarceration programs; they informed youth about the voluntary nature of participation. Informed assent (written) and parental/guardian consent (audio recorded) was required and taken prior to participation.

Eligibility criteria included being between ages of 14 and 18, being a participant within one of the community partner programs, were proficient in English, agreed to get recontacted 3- and 6-months post intervention. Exclusion criteria were kept purposefully broad in order to increase generalizability and included: any youth who were taking antipsychotic medication, endorsed MRI contraindications (e.g., non-removable metal in the body), and loss of consciousness in the last 6 months.

Measures

Demographics. This measure queried about general demographic information, including age, gender, and racial/ethnic background.

Sexual Risk Behavior. Sexual risk behavior was assessed using two variables (*Condom Use* and *Risky Sex*) that have been used widely in prior studies of adolescents [11, 59]**.** Participants were first asked whether they had ever had sexual intercourse, which here is defined as vaginal or anal intercourse, as these methods are the most likely to transmit STIs. Those who answered 'yes' then answered the rest of the sexual risk questions. Participants who did not have intercourse in the 3-month window were removed from analyses as they were not involved in recent sexual decision-making contexts. The Risky Sex Index (RSI) was created by multiplying condom use (reverse scored) by frequency of intercourse [11, 58]. These two variables were chosen in order to encapsulate sexual behavior over a 3-month timeframe; both also provide information about the degree to which this behavior was sexually risky [11]. Using these two variables to create the risky sex index helps to account for the sporadic nature of adolescent sexual encounters; relatedly, number of sexual partners is not included in the index due to the infrequency of monogamy in adolescents as well as the infrequency of safe sex practices (e.g., regular STI testing) such that condom use is an important predictor of risky sexual behavior.

Condom use was asked with the question "In the past three months, how much of the time did you use condoms when you had sexual intercourse?" (1 = never; 2 = almost never; 3 = sometimes; 4 = almost always, 5=Always). Here, a higher number indicates *less* sexual risk. *Risky Sex* was defined as the number of times the youth engaged in sexual intercourse without a condom in the past 3 months. Frequency of

sexual intercourse was asked with, “On average, in the past 3 months only, how often have you had sexual intercourse?” (1 = never; 2 = Once a month; 3 = Once a week; 4 = 2-3 times a week, 5= 4-5 times a week, 6= Almost every day). Additionally, by focusing on only the last 3-months, this helps to mitigate memory errors and response bias to the best of our ability [58].

Functional magnetic resonance imaging task. Past studies utilizing the monetary incentive delay (MID) task have used a variety of different versions. For the current study, we used a version that has gained empirical support through research in adolescents [54, 55]. This task is well suited for adolescents because the monetary incentives are given in increments that are familiar to the participants (i.e., $0.20, $1.00, $5.00), and participants receive their actual earnings at the end of the task [56]. Consistent with prior administration procedures for adolescents, immediately prior to entering the scanner, all participants were informed that they would receive their winnings as soon as they exited the scanner. Participants were also told their current cumulative earnings throughout the task. As youth exited the scanner, they received their earnings in cash.

Study staff informed participants that they must respond by pressing a button when they saw a target square appear on the screen. They explained that during REWARD trials, correct response (hitting the button) would result in earning money, and during LOSS trials, responding would prevent losing money, and during NEUTRAL trials, responding would not impact earnings. Prior to entering the scanner, participants completed a 7-minute practice round in order to teach the participants the rules and to ensure proper understanding of the task. Each task began

with a 250ms cue screen that informed the youth of the trial type (REWARD, LOSS, or NEUTRAL). All cue screens also informed youth of the magnitude of reward or loss ($0.20, $1.00, or $5.00). The task consisted of 2 runs of 72 x 6-second trials, for a total trial time of 7:12 minutes; the task was broken into a total of 54 reward trials, 54 loss trials, and 36 neutral trials (see **Figure 2**). The magnitude was divided evenly across trial-type. A single trial was composed of a cue, which told the participant what type of trial it would be (i.e., reward, loss, or neutral trial), followed by the amount of money they could win or lose (i.e., $0.20, $1.00, $5.00). A delay period of 1165-1934ms followed participant response to the target, and then a feedback screen (1650 ms) told the participant whether they had successfully responded (see **Fig. 1**). The task was programmed using an adaptive algorithm that ensured a 66% correct response rate for all participants. The algorithm adjusted the buffer period between the cue and the target until the 66% accuracy rate is reached. If the participant achieved more than 66% correct, this buffer was shortened to try to decrease their hit rate; if the participant achieved less than 66% correct, the buffer was increased to increase the hit rate. For the present analysis, we focused on the anticipation period of the task in order to better compare with existing literature [54, 55, 60].

fMRI Image Acquisition

MRI images were acquired using a 3T Siemens Trio whole-body MRI scanner (Erlangen, Germany) with a 12-channel head coil at the Mind Research Network (Albuquerque, New Mexico). A high resolution T1-weighted anatomical volume was acquired with a multi-echo magnetization-prepared rapid gradient-echo (MP-RAGE) sequence with the following parameters: (TE = 1.64, 3.50, 5.36, 7.22, and 9.08 ms, TR

(repetition time)= 2.53, TI=1.20 s, flip angle= 7°, NEX = 1, slice thickness= 1mm, 33 slices, FOV [field of view] = 256mm, and in-plane resolution =256x256). Structural images were acquired oblique to the anterior-posterior commissure (AC)-posterior commissure (PC) line+5° to 10,° to diminish susceptibility artifacts. Functional images (BOLD) during the monetary incentive delay task were acquired using a single-shot, gradient-echo echo-planar pulse sequence (TR=2000ms; TE=29ms; flip angle= 75°; FOV =240 mm; matrix size = 64 x 64).

Image Processing and Statistical Analyses.

Analysis of functional images was conducted using AFNI [61].The first three frames of each run were removed to ensure that steady state has been achieved during the acquisition, resulting in a total of 524 images for the final analyses Anomalous timeseries values were first identified using a despiking algorithm in AFNI [61], in order to reduce abnormal signal spikes, and replaced based on temporally neighboring values. All time-series data were then spatially registered in two-and three-dimensional space to the second EPI image of the first run to reduce the effects of head motion and were temporally interpolated to the first slice to account for differences in slice acquisition. Framewise displacement (FD) was calculated on the first derivatives of the head motion data after the transformation of rotations to a 100mm diameter sphere [62]. Data were spatially blurred using an 8 mm Gaussian full-width half-maximum filter and then were converted to standard stereotaxic coordinate space (ICBM 152 Nonlinear Atlases, 2009). As part of preprocessing, a voxel-wise general linear model analysis was used to estimate the data fit by convolving a double-gamma variate function with the study design matrix. These

components were used to build the predicitive model through which we tested our hypotheses. Consistent with prior work [54, 55], a total of 14 regressors was used to model the anticipation phase (3 regressors for the different magnitudes of REWARD trials, 3 for the different magnitudes of LOSS trials, and 1 for the NEUTRAL trials) for both HIT and MISS conditions. Additionally, 12 nuisance motion regressors were included in the model (6 motion parameters and their derivatives). Each explanatory variable (EV) is a condition placed on the subject, and their conditional response has a measurable output of increased blood oxygenation (BOLD) of the particular region.

Main Effects. The main effects of the task were performed via single sample t-test across the entire sample (n= 149) to identify brain regions with significant changes in BOLD signal for REWARD and LOSS trials across the whole brain. In line with previous publications on this task [55], we collapsed across all 3 incentive levels of REWARD and all 3 incentive levels of LOSS to form 3 contrasts of interest: $\text{REWARD}_{\text{Combined}} - \text{NEUTRAL}$, $\text{LOSS}_{\text{Combined}} - \text{NEUTRAL}$, and $\text{REWARD}_{\text{Combined}} - \text{LOSS}_{\text{Combined}}$. All voxel-wise whole brain results were corrected for false positives a $p<.05$ based on 10,000 Monte-Carlo simulations implemented in AFNI (statistical threshold of $p<.005$ and a minimum cluster size = 2432 μL). Whole brain results were analyzed at a threshold of $p<.05$ to identify areas of activation. In order to weed out any spurious correlations that may have emerged, we ran the Monte-Carlo simulations at a threshold of $p<.005$. This smaller threshold broke up large clusters of brain activation, aiding in the identification of areas of increased importance in our analyses. In order to focus specifically on the brain areas and networks most directly related to our hypotheses, we tested whole brain differences during anticipation of REWARD

and LOSS trials. To examine group differences, we conducted a series of independent-sample t-tests with AFNI with incentive condition (collapsed across all three incentive levels), split into high and low RSI group, as the independent variable (IV), and BOLD brain activation as the dependent variable (DV).

Anticipatory activation during the NEUTRAL trials was subtracted from activation during the collapsed REWARD ($0.20, $1.00, $5.00) trials and LOSS ($0.20, $1.00, $5.00) trials to create 3 different contrasts of interest. A total of 6 independent-sample t-tests were performed to examine group differences of LOW vs. HIGH RSI across the 3 contrasts of interest. These 6 independent-sample t-tests consisted of: $\text{REWARD}_{\text{Combined}} - \text{NEUTRAL}$ (LOW RSI), $\text{REWARD}_{\text{Combined}} -$ NEUTRAL (HIGH RSI), $\text{LOSS}_{\text{Combined}} - \text{NEUTRAL}$ (LOW RSI), $\text{LOSS}_{\text{Combined}} -$ NEUTRAL (HIGH RSI). $\text{REWARD}_{\text{Combined}} - \text{LOSS}_{\text{Combined}}$ (LOW RSI), and $\text{REWARD}_{\text{Combined}} - \text{LOSS}_{\text{Combined}}$ (HIGH RSI).

CHAPTER 3

FINDINGS

Main Effects Results

We ran two independent-samples t-tests across the entire sample (*N*=149), from which we observed significant activation in both the REWARD-NEUTRAL and LOSS-NEUTRAL contrasts. The REWARD – NEUTRAL trials activated a large network that included the left posterior cingulate, right superior temporal gyrus, left superior temporal gyrus, and left medial frontal gyrus (see *Figure* 3). The LOSS-NEUTRAL trials also activated a large network that included the left posterior cingulate, right precentral gyrus, and left medial frontal gyrus (see *Figure* 3). While the activation of a large network is consistent with task effects of prior adolescent studies (e.g., [55]), the specific activated areas varied between our results and the results of other studies'.

Group Differences in REWARD and LOSS Responding

The results of the independent sample t-tests for whole brain activation demonstrated significant effect of group (i.e., low RSI, high RSI) on neural network activation (See *Table 1*). The following results were cluster corrected $p<.005$. For the $LOSS_{Combined}$-NEUTRAL contrast in the Low RSI group (see *Figure 4*), demonstrated activation in the left posterior cingulate (z=5.70, cluster size= 3966 voxels), right lingual gyrus (z=3.50, cluster size= 2343 voxels), right precentral gyrus (z = -5.63, cluster size= 751 voxels), left superior temporal gyrus (z=-4.17, cluster size=581 voxels), and left precuneus (z= -4.61, cluster size=276 voxels). The $LOSS_{Combined}$-

NEUTRAL, High RSI group (see *Figure 4)* indicated increased activation in the left lingual gyrus (z=4.44, cluster size= 2985 voxels), left posterior cingulate (z=-3.48, cluster size=1198 voxels), right inferior frontal gyrus (z=4.23, cluster size= 771), left thalamus (z=4.74, cluster size= 609 voxels), left inferior frontal gyrus (z=4.02, cluster size= 586 voxels), right precentral gyrus(z=-3.88, cluster size= 455 voxels), right medial frontal gyrus (z= 5.99, cluster size= 375 voxels), and left postcentral gyrus (z=-3.37, cluster size= 257 voxels). We found increased activation in the left posterior cingulate (z= 7.90, cluster size=18548 voxels) in the $REWARD_{Combined}$-NEUTRAL condition for the Low RSI group. In the $REWARD_{Combined}$-NEUTRAL contrast for the High RSI group, we found activation in the Right Lingual Gyrus (z= 4.39, cluster size= 10640 voxels) and the Right Inferior Parietal Lobule (z=-3.28, cluster size= 400 voxels). The $REWARD_{Combined}$- LOSS contrast for the Low RSI group had increased activation in the left posterior cingulate (z= 5.50, cluster size= 20116 voxels). Lastly, the $REWARD_{Combined}$-$LOSS_{Combined}$ in the High RSI group had increased activation in the left posterior cingulate (z= 4.43, cluster size= 7075 voxels).

Evaluation of Key Networks

Results of the t-tests for activation of the key networks (i.e., social processing network, mentalizing network, and salience network) demonstrated significant activation in certain nodes of these networks (*see table 1*). In the social processing network, we saw significant decreased activation in the left superior temporal gyrus in the Low RSI group for the LOSS-NEUTRAL contrast (z=-4.17, cluster size=581 voxels). In the mentalizing network, we observed significant changes in the left precuneus in the LOSS-NEUTRAL contrast for the Low RSI group (z= -4.61, cluster

size=276 voxels). Lastly, as part of the salience network, we found significant activation in the right precentral gyrus in both the LOSS-NEUTRAL, Low RSI group (z=-5.63, cluster size=751 voxels) and in the High RSI group (z=-3.88, cluster size= 455 voxels). As part of the salience network, we also found activation in the left thalamus (z=4.74, cluster size= 609 voxels) for the LOSS-NEUTRAL contrast in the High RSI group.

CHAPTER 4

DISCUSSION

This study aimed to examine neural activation during incentive anticipation among adolescents across two HIV/STI risk behavior groups. We hypothesized that we would observe neural activation in key target neural areas (i.e., social cognition; mentalizing; salience networks; see Figure 1) [55]. As we were interested in examining the activation of neural networks, we conducted a whole brain analysis in order to elucidate these network activations. We saw activations that aligned with this hypothesis, as well as areas that aligned with previously published studies [55, 58]. Areas involved in the social processing (e.g., posterior cingulate cortex), mentalizing (e.g., precuneus), and the salience networks (e.g., anterior cingulate cortex (ACC)) were shown to have increased activation during the MID task. We also found increased brain response in the inferior frontal gyrus, which prior studies have found to be associated with adolescent risky sex behaviors [58, 63]. Thus, we anticipated that our results would replicate and expand on this work.

The social processing network is engaged in recognizing, understanding, and interpreting social cues [15, 20]. This network is of specific importance during adolescence, as it continues to develop, and leads youth to being to learn how to interact with peers in social ways. We found increased activation of the posterior cingulate cortex, which has been shown to be involved in social processing [15, 24, 25], in almost all conditions (exception: $REWARD_{Combined}$-NEUTRAL, (High RSI)), which is consistent with previous findings suggesting that this area is implicated in a perceived loss and reward receipt [64, 65]. The superior temporal gyrus and superior

temporal sulcus are anatomically close areas of the brain that both have been shown to be involved in social processing [15, 24, 66]. In the current study we found a decreased activation in the superior temporal sulcus in the Low RSI group in the $LOSS_{Combined}$-NEUTRAL contrast, suggesting that social processing may play a role in the anticipation of a perceived loss.

The second key network we aimed to examine was the mentalizing network. This network helps to represent the ability to anticipate and cognitively imagine the thoughts of others [27], and it is highly important when examining how youth may weigh their decisions during important decision making processes. The precuneus plays a key role in mentalizing by allowing the integration of person-specific knowledge into the system [29]. Additionally, the precuneus has shown to play a vital role in successful behavior change in adolescents [67], which may explain why we saw significant changes in precuneus activation in the $LOSS_{Combined}$-NEUTRAL contrast for the Low RSI group. The precuneus's activation in the Low RSI group may indicate that this lower risk group is already attuned to social health promotive factors. Prior studies of adolescents engaged in intervention programs that take a health promotion approach have demonstrated that utilizing social support and community networks have been shown to reduce risk behaviors [3].

The last key network is the salience network. The salience network is involved in how different situations may feel and how important they are in terms of emotional weight [32]. Each node of the salience network help the individual to understand and integrate valence of a situation [15],. Although we did not see increased activation in the key nodes of the salience network (i.e., ACC, amygdala, striatum, insula), we did

see activation in the precentral gyrus and thalamus, which have been shown to activate along with the anterior insula, striatum, thalamus, and supplementary motor area during anticipation of wins and losses [68]. Consistent with our findings, Karoly, Bryan [55] found that the $REWARD_{Combined}$- NEUTRAL trials activated a network that included the bilateral caudate, thalamus, cingulate and insula, and the $LOSS_{Combined}$ - NEUTRAL condition also illuminated a distinct neural network which included the bilateral insula, thalamus, and anterior cingulate. This is consistent with what we found among the RSI groups in the current study and what has been observed in other studies (e.g. Karoly, Bryan [55], Thayer, Ewing [58], Filbey, Dunlop [54], Knutson, Adams [69]).

Our second hypothesis aimed to evaluate the association of neural activation during the MID task and the risky sex index; we anticipated seeing associations between key target neural areas (i.e., neural networks listed above) and higher scores on the risky sex index. Specifically, we were expecting to see associations in increased activation in the social processing, mentalizing, and salience networks. While we did not find activation in all of the main nodes from each network (see Figure 1), we did see differences between the Low and High RSI groups in which areas activated under each contrast condition. In particular, we found that areas of the brain that are activated when a loss is perceived differed among the two groups. When the Low RSI group was presented with a loss, we saw decreased activity in nodes of all three key neural networks (i.e., left superior temporal gyrus, as part of the social processing network; precentral gyrus, often activates along with the salience network; left precuneus as part of the mentalizing network). And we saw increased activity in the

posterior cingulate cortex and lingual gyrus, both of which have been implicated in the social processing network [70, 71].

The High RSI group had an overall increased activation in areas implicated in anticipation of reward receipt. Specifically, the thalamus showed significant activation in the $LOSS_{Combined}$-NEUTRAL contrast in the high group. This area has been shown to activate in response to reward anticipation and receipt [68, 72, 73]. We also found increased activation in motor areas that have been shown to be associated with monitoring performance and integrating feedback about motor performance in order to improve [74]. In particular, the inferior parietal lobe had significant activation for the $LOSS_{Combined}$-NEUTRAL and $REWARD_{Combined}$-NEUTRAL contrasts in the High RSI group.

Future Directions

The results from the present study support the concept of underlying neural differences between individuals engaging in sexual risk behaviors and those not engaging in such. This difference will be important in the creation of adolescent focused HIV/STI intervention and prevention techniques.

Appendix:

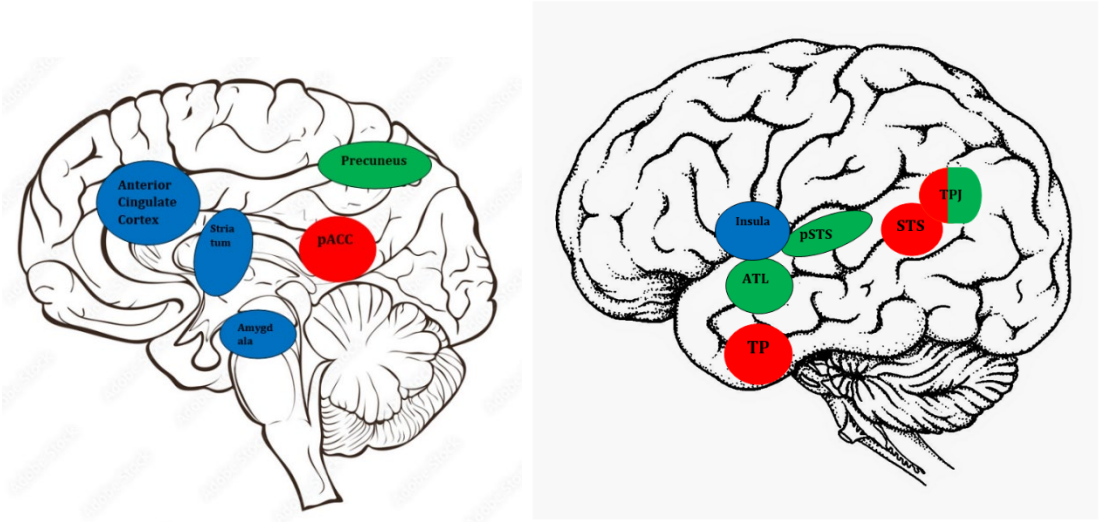


Figure 1: **Brain networks important to adolescent development.** In adolescents, the social processing network (in red) includes the temporoparietal junction (TPJ), posterior anterior cingulate cortex (pACC), superior temporal sulcus (STS), and temporal pole (TP). The mentalizing network (in green) includes TPJ, posterior superior temporal sulcus (pSTS), anterior temporal lobe (ATL), and precuneus. The salience network (in blue) includes the anterior cingulate cortex (ACC), amygdala, striatum, and insula.

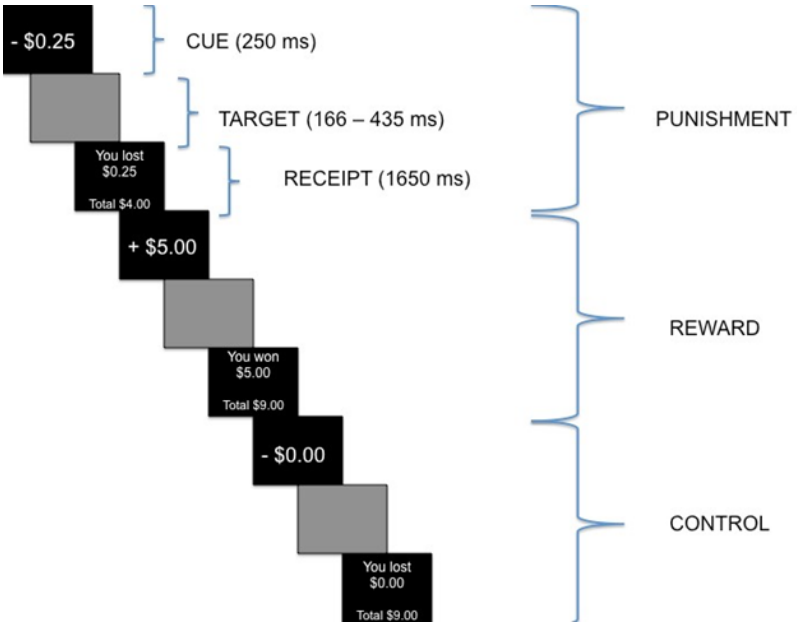
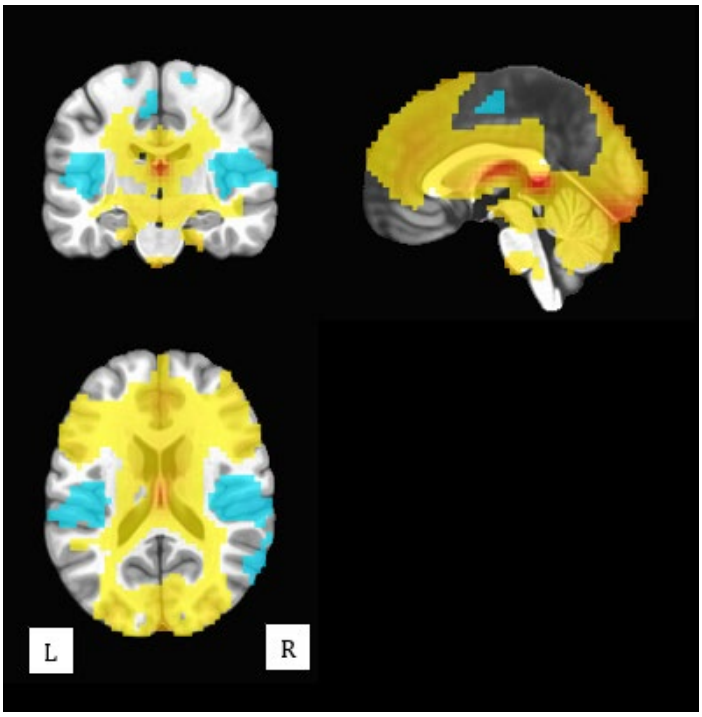


Figure 2: Monetary Incentive Delay Task Design. Illustration of task conditions and regressors. Anticipation block consists of cue+target time periods.

Table 1: Group Effects of Monetary Incentive Delay Task.

Region	Voxels	Peak Intensity	Z	X	Y	Z
LOSS-NEU, LOW RSI						
Left Posterior Cingulate	3966	0.3114	5.698819	0	35.5	4
Right Lingual Gyrus	2343	0.2135	3.469534	-10.5	98.5	-13.5
Right Precentral Gyrus	751	-0.1117	-5.63491	-59.5	0.5	7.5
Left Superior Temporal Gyrus	581	-0.0907	-4.17054	63	4	4
Left Precuneus	276	-0.1265	-4.61027	45.5	77.5	42.5
LOSS-NEU, High RSI						
Left Lingual Gyrus	2985	0.3095	4.4426	0	88	-17
Left Posterior Cingulate	1187	-0.2101	-3.4827	0	53	21.5
Right Inferior Frontal Gyrus	771	0.2486	4.232339	-49	-24	-6.5
Left Thalamus	609	0.2644	4.748365	0	14.5	14.5
Left Inferior Frontal Gyrus	586	0.2364	4.01946	52.5	-20.5	-3
Right Precentral Gyrus	455	-0.1193	-3.88067	-56	11	11
Right Medial Frontal Gyrus	375	0.1655	5.986162	-3.5	-34.5	42.5
Left Postcentral Gyrus	257	-0.0993	-3.37514	56	25	14.5
REW-NEU, LOW RSI						
Left Posterior Cingulate	18548	0.5473	7.86219	0	39	4
REW-NEU, HIGH RSI						
Right Lingual Gyrus	10640	0.6129	4.383874	-7	91.5	-13.5
Right Inferior Parietal Lobule	400	-0.1116	-3.28066	-66.5	28.5	25
REW-LOSS, LOW RSI						
Left Posterior Cingulate	20116	0.2519	5.486786	0	39	4
REW-LOSS, High RSI						
Left Posterior Cingulate	7075	0.3862	4.432731	0	39	7.5

A.



B.

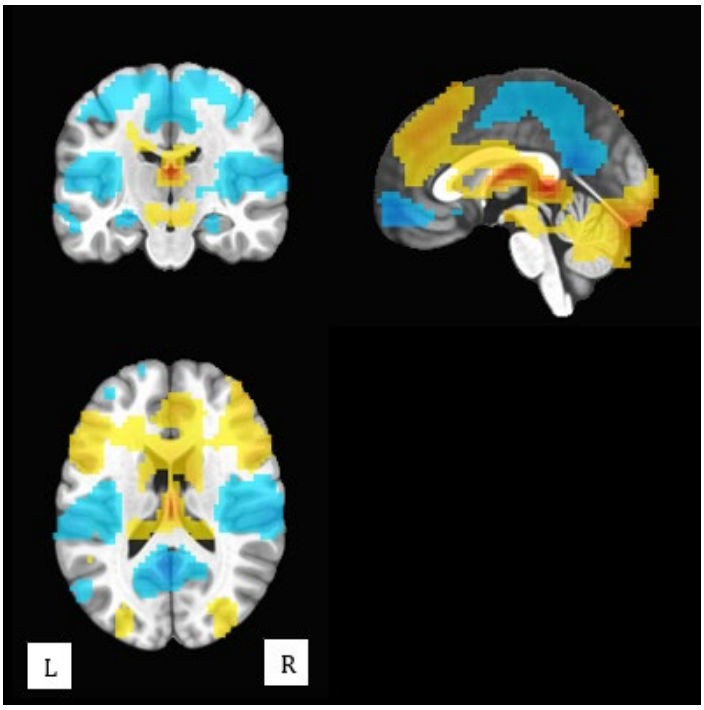


Figure 3. Task main effects across entire sample (N=149). (A) Whole brain activation during REWARD-NEUTRAL anticipation block. (B) Whole brain activation during LOSS-NEUTRAL anticipation block. Each is thresholded at p<.005. The color indicates the t-range. Left (L) and right (R) hemispheres are indicated at the bottom of each figure.

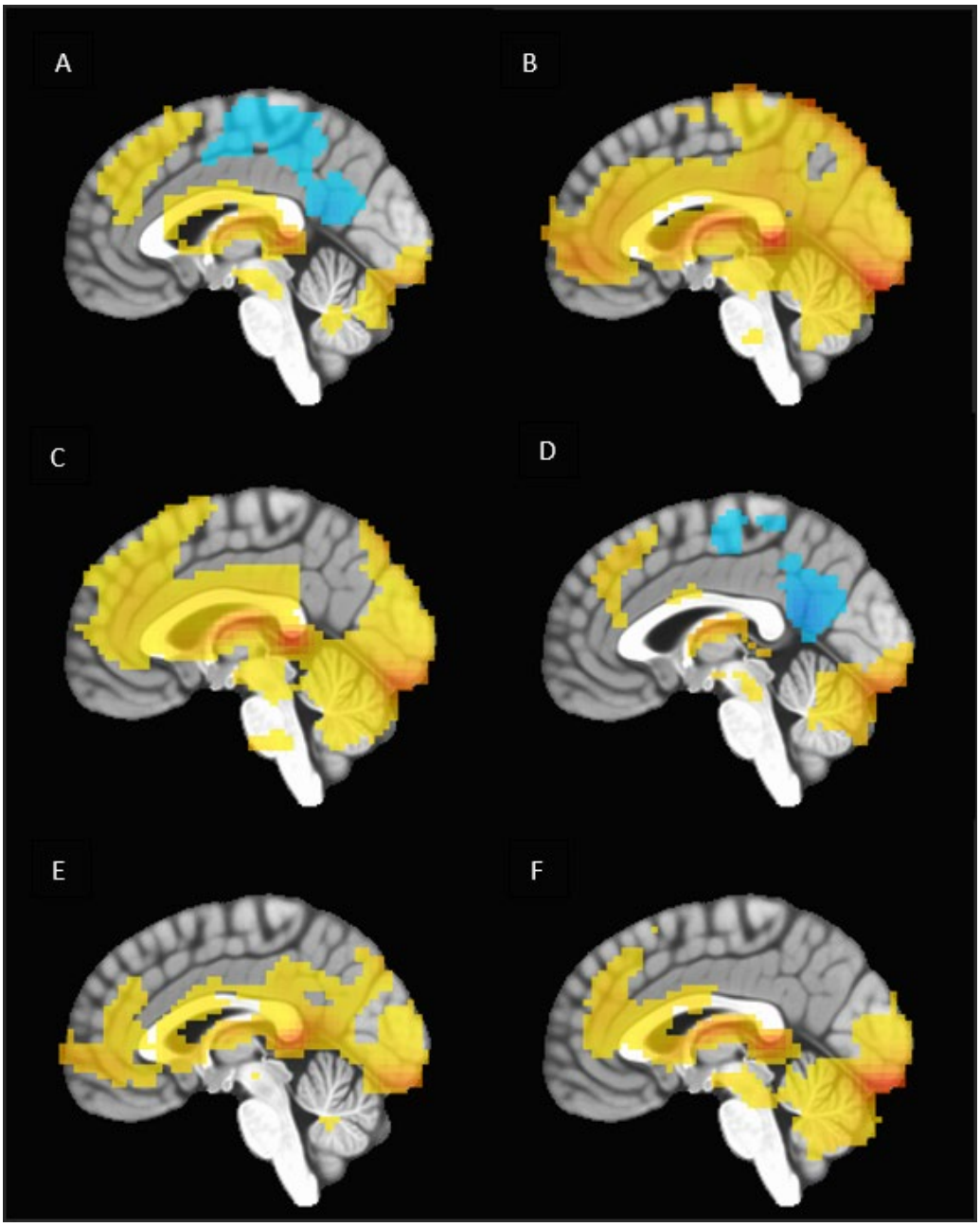


Figure 4: Task group differences. (A). Activation during the Loss-Neutral, Low RSI contrast. (B) Reward-Loss, Low RSI contrast. (C) Reward-Loss, Low RSI contrast. (D) Loss- Neutral, High RSI Contrast. (E) Reward-Loss, High RSI Contrast. (F) Reward-Neutral, High RSI Contrast. Statistical Maps threshold at $p < .005$. The color indicates t range. Blue areas indicate lower activation in the contrast. Yellow areas indicate higher activation in the contrast.

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