# Neural Characteristics of Reward in Adolescents: Neural Substrates of Risk-taking, Researcher Degrees of Freedom and a Person-Specific Network Approach.

by

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## DEDICATION

This dissertation is dedicated to the teachers that invest their time and energy into their students' success despite the many barriers, and my parents, Ivan & Olga, who left their family/friends and what little possessions they had in the USSR to allow their kids to have a *chance* at a better future in the United States.

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## ABSTRACT

Adolescence is a key developmental period that is marked by rises in death and disease predominately from behavioral sources. Contemporary neurodevelopment models associate the changes in risk-taking behaviors with the development of socioemotional and cognitive control processes during adolescence. While these neurodevelopmental models have identified adolescent specific change, their generalizability and reliability in prediction of risk-taking have been mixed. The goal of this dissertation is to evaluate how neurodevelopmental models generalize in a sample of high risk and average/low risk-taking adolescents completing a monetary incentive delay (MID) task during functional magnetic resonance imaging (fMRI), and how methodological techniques may influence the underlying interpretations. To evaluate the generalizability of the neurodevelopmental models as it relates to risk-taking behaviors during late adolescence, Study 1 examined whether differences in neural activity of *a priori* regions of interest (ROI) and whole brain analyses during a Big Win versus Neutral reward contrast differed across adolescents with high risk versus average/low risk-taking profiles. In the ROI analyses, there were no significant differences in activation in pre-selected regions during the anticipation of Big Win versus Neutral cues in the task between high risk versus average/low risk-taking profiles. While the whole brain analyses during the same contrast did reveal differences in neural activity between the two risk-taking profiles, the differences were in brain

regions that were outside of regions hypothesized by the neurodevelopmental models. The methodological issue in these findings may in part relate to the selected contrast, Big Win versus Neutral. Some researchers may operationalize the experimental contrast of reward differently. Study 2 evaluated how the ambiguous operationalization of the reward contrasts during the MID task may impact the underlying brain-behavior associations. In mean-level activation maps, there was evidence for greater similarity in the neural activity of reward regions between Big Win and Big Loss cues than is proposed in the reward literature. Moreover, the magnitude and direction of brain-behavior associations were inconsistent across theoretically related behaviors, such as sensation seeking, externalizing and substance use, and regions, such as ventral striatum and insula. The inconsistency in these mean-based approaches may in part be related to the individual differences among adolescents, which may contribute to unique characterization of the underlying neural connectivity that are important to socioemotional and cognitive control processes. Study 3 evaluated group-, subgroup-, and individual-level characteristics of adolescent neural networks of socioemotional and cognitive networks using a data-driven person-specific network connectivity approach. Using this approach, I evaluated how subgroup features in functional connectivity, and connection magnitude and direction were associated with self-reported sensation seeking. Two distinct subgroups were uncovered for each timeseries from the MID runs that tapped a *presumed* state of motivational processing. During the first run, subgroups were significantly related to self-reported sensation seeking. However, this effect was attenuated in the second run and opposite in direction for the combined runs. Some of these differences may relate to habituation or reliability over time and power across methods. These findings highlight the importance that analytic decisions play when mapping brain-behavior associations that are salient to adolescent risk-taking behaviors. This dissertation provides

evidence regarding generalizability and variability in researcher decisions that may be of concern when testing key hypotheses of the neurodevelopmental models and considers steps to bridge the gap between developmental neuroscience and measurement to improve our understanding of adolescent motivational processing.

## Chapter 1 : Importance and Purpose of Adolescence Research

Preventable population health burdens are detrimental to the productivity and longevity of the members of its society (Baltes, 1987; Belsky, 2016). A major focus of life-span research and funding for the National Institutes of Health is to reduce disease burden, early mortality, and control associated costs (Belsky et al., 2015). Adolescence is a key developmental period that is marked by rises in death and disease (Kann et al., 2018), over 70% of which stem from preventable causes such as risk-taking behaviors (Casey et al., 2008). Since adolescents make up over 1.2 billion of the world's population, the influx of preventable death and disease rates observed in this age group is of particular interest to researchers and policy makers alike (Kann et al., 2018; Sheehan et al., 2017; Steinberg & Icenogle, 2019). During the initial decades of the 21st century, theoretical models of neurodevelopment have focused on changes in socioemotional and cognitive control processes that are often linked to changes in risk-taking behaviors (Dahl et al., 2018). While these neurodevelopmental models have identified adolescent-specific change (Casey, 2015), their generalizability and reliability in prediction of risk-taking have been mixed.

The purpose of this dissertation is to consider 1) how the neurodevelopmental models generalize to a sample of risk-taking adolescents and 2) to evaluate the degree to which analytic choice (i.e., contrasts) and models (e.g., mean-based activation versus person-specific connectivity) impacts the interpretation in the brain-behavior findings. First, to evaluate the

generalizability of the models, in Study 1 (Chapter 3), I compare the neural activation of late adolescents that are recruited across two distinct risk-taking profiles: high and average/low. Then, to interpret the degree to which these findings are impacted by analytic choices or a researcher's degrees of freedom in operationalizing variables, in Study 2 (Chapter 4), I consider how the range of contrasts in a reward paradigm alter the associations among different brain regions and behaviors. In Study 3 (Chapter 5), I report the results of a person-specific approach that models the unique *individual patterns* of functional connectivity rather than the group averages that are often used in the field (and are used in Study 1 and Study 2). Given that I have previously evaluated the utility of self-report and neurocognitive measures as they relate to risk-taking behaviors (Demidenko et al., 2019), the emphasis in this dissertation is on the neural measures used in task-based functional magnetic resonance imaging (fMRI). Nevertheless, the self-report, neurocognitive performance and neural measures tapping the constructs of reward are discussed together in this chapter.

Neural constructs provide researchers with the opportunity to draw inferences (Flake et al., 2021), however, assumptions in how risk-taking behaviors and reward constructs are defined may result in findings that are misleading (described in greater detail in Chapter 4). By using the same sample and fMRI task (described in Chapter 2), I can *drill-down* and consider where in a nomological network each pattern of relationships is represented and whether this is consistent with what some contemporary neurodevelopmental models would hypothesize. I provide an expanded definition and description for this nomological network in Chapter 6 but, simply put, the network reflects relationships that constitute a theory which allow researchers to make specific hypotheses about constructs and their measured phenomenon (Cronbach & Meehl, 1955). The

network proposes links among different measures, biological processes, and behaviors that researchers rely on when generating hypotheses.

In the next section, I discuss constructs that are central to the contemporary neurodevelopmental models, how they are often measured and their associated limitations. Specifically, I briefly summarize the phenomena during the early part of the 21st century that have been central in the research literature on adolescent neurodevelopment and risk-taking behaviors.

## Neurodevelopmental Models: Phenomena and Limitations

Over the course of the last two decades, self-report, neurocognitive, and neural measures have played a prominent role in specifying developmental shifts during adolescence that may explain risk-taking behaviors, which has informed both policy and interventions (Steinberg & Icenogle, 2019). These distinct measures have specifically focused on tapping two latent constructs: reward sensitivity and self-regulation. These two constructs are core to the neurodevelopmental models that propose to explain the influx in risk-taking as a function of the increased motivation toward rewards (i.e. socioemotional processing), and decreased goal-oriented decision-making, as a function of not yet mature self-regulation (i.e. cognitive control). Both of which have been observed to significantly change from early to late adolescence (Shulman et al., 2016, Dahl, 2004). Reward sensitivity is subsumed by the socioemotional system that increases an adolescent's motivation toward pleasurable experiences, such as going to a party and drinking or speeding in a car with friends. Self-regulation is subsumed by the cognitive control system and the immature development of self-regulatory processes. This is often exhibited by adolescents being unable (or unwilling) to inhibit risk-taking behaviors, such as not pausing to think through the consequences of an action like texting while driving. The

unobserved nature of these constructs has placed the onus on researchers to approximate them both in and out of the lab setting.

Given the unobservable nature of reward sensitivity and self-regulatory processes, researchers have had to define and designate measures to attain numerical values of this phenomenon (Flake & Fried, 2020). To attain a comprehensive numerical representation of reward sensitivity and self-regulation, researchers have measured the constructs using the three approaches mentioned above: self-report, neurocognitive performance, and neural activation. By measuring at multiple levels, researchers can fill the nomological space of the phenomenon and demonstrate consistent theorized links in the observed relationships among the latent phenomena and the associated behaviors. Moreover, by using more than one type of method to capture reward sensitivity in the network, such as self-report and neurocognitive tasks of reward sensitivity, researchers can also lessen concerns relating to method bias (Shadish et al., 2002). To date, the self-report, neurocognitive, and neural empirical evidence have been incorporated into the neurodevelopmental models and considered important to risk-taking behaviors (Shulman et al., 2016).

Before considering how self-report and neurocognitive measures are related to the neural processes from the perspective of the neurodevelopmental models, it is helpful to consider what hypothesized processes these two types of measures were designed to capture. First, self-report measures of sensation-seeking are postulated to capture an individual's explorative/novelty seeking tendencies. While the construct of reward seeking is difficult to capture objectively, through well-crafted measures, like the brief sensation seeking scale (BSSS), researchers quantify this phenomenon via a set of questions that include: "I would like to explore strange places", "I prefer friends who are excitingly unpredictable", or "I would like to try bungee

jumping" (Hoyle et al., 2002). Measures of sensation seeking, such as the BSSS, are considered to express an underlying construct of reward/approach behaviors (or trait reward sensitivity). BSSS is interchangeably used with other self-report measures, such as the behavioral inhibition system/behavioral approach system scale (i.e., BIS/BAS; Carver & White, 1994). Second, whereas self-report measures may capture a dimension of trait reward sensitivity, neurocognitive tasks tap into a related dimension of reward sensitivity that relates to a state of the self-reported measure(s). For example, the Balloon Analogue Risk Task (BART) measures reward sensitivity and risk propensity under variable levels of uncertainty (Lejuez et al. 2002). Participants pump a balloon to accumulate money, but each pump risks the balloon popping and losing unbanked money. Continued inflation increases the risk of loss and so behavioral parameters (e.g., average adjusted pump counts) from the task are used to estimate a participant's level of reward sensitivity compared to other participants that completed the task. Together, the self-report and neurocognitive measures provide a multi-method measure of the construct of reward sensitivity that may holistically describe an adolescent's decision making strategy when exposed to a salient environment (Chein et al., 2011; Crone & van der Molen, 2004).

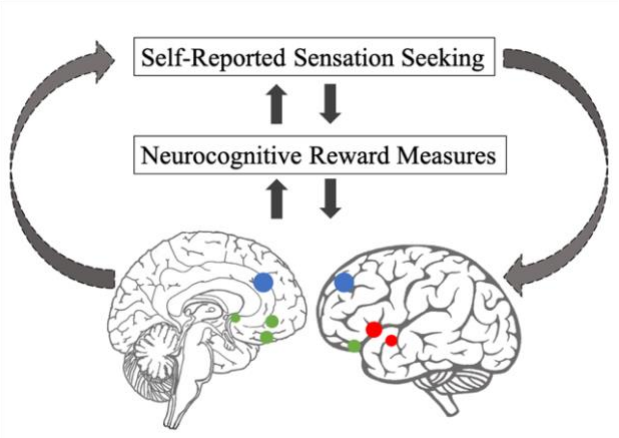


*Figure 1.1.* Bidirectional Associations: Self-report, Neurocognitive, and Neural Measures
Colored Regions - Blue = cognitive control; Green: Approach; Red: Salience. *See Figure 1.2 for specific labels*

With respect to the underlying biological process, self-report and neurocognitive measures are theorized to share a mechanism that reflect the bidirectional association among the reward sensitivity measured using different phenomena in the nomological net. In Figure 1.1, I

express the postulated interrelations between self-report, neurocognitive, and neural regions that are involved in reward-relevant decision making. Reward-relevant decision making is theorized to be characterized by approach-sensitive striatal regions in the brain that are inundated with dopamine (DA) receptors, such as the Ventral Striatum (VS)/Nucleus Accumbens (NAcc) (Ernst & Spear, 2009; M. Zuckerman, 1979). DA is hypothesized to play a major role in motivational processes (Berridge, 2007). Therefore, DA-rich reward regions are considered to underpin trait and state reward processes (Ernst & Spear, 2009). Adolescents that evoke increased activation in VS/NAcc regions to rewarding stimuli, without the optimal activation in cognitive control regions, may be more likely to engage in real-world risk-taking behaviors. This distinction between reward and cognitive control regions results in risk-taking is a central hypothesis of neurodevelopmental models (Casey et al., 2008; Ernst et al., 2006; Luna & Wright, 2016; Steinberg, 2010). However, it is worth noting that the field continues to debate whether the increase or decrease in the response of DA receptors (Samaha et al., 2021) or the activation in DA-rich reward regions contributes to approaching motivational stimuli (Galván, 2010).

Changes in self-report and neurocognitive measures of reward sensitivity and self-regulation are presumed to reflect the etiology of socioemotional and cognitive control regions. Specifically, the neurodevelopmental models (explained in more detail in Chapter 3) highlight the disparate developmental trajectories of

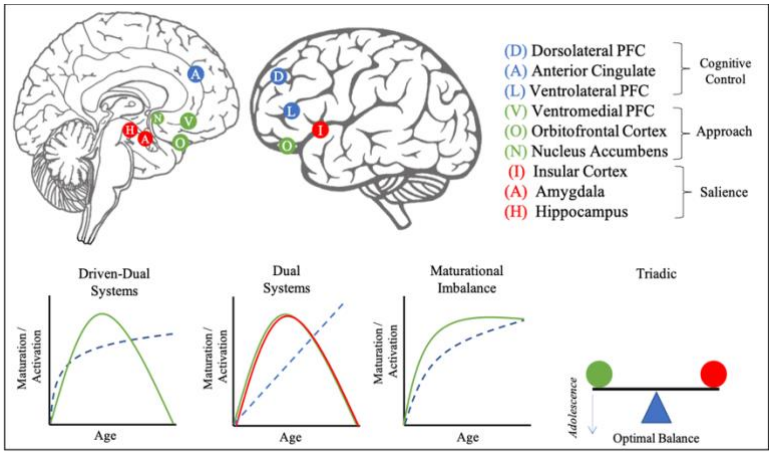


*Figure 1.2*. Examples of Current Neurodevelopmental Heuristics
Note: Amygdala is presented laterally, for representation, but is located closer to the medial wall.
Colored Regions – Blue: cognitive control; Green: Approach; Red: Salience

increased activation in the early developing VS/NAcc and the late maturing prefrontal cortex (PFC). The hypothesis is that the *imbalance* between the overactive NAcc and immature PFC has consequential impact on decision making during adolescence. Over the course of the last 15 years, four neurodevelopment models have been proposed that have several overlapping features but differ in important features (Figure 1.2). These neurodevelopment models have led to an expansive portfolio of adolescent studies focused on the neurodevelopment of risk-taking behaviors (Casey et al., 2008; Ernst et al., 2006; Luna & Wright, 2016; Steinberg, 2008).

To date, this portfolio of research has provided evidence that relates the measured phenomena of reward sensitivity and self-regulation to risk-taking tendencies (Shulman et al, 2016). However, studies have not yielded generalizable results in the prediction of real-world risk-taking behaviors (Demidenko et al., 2019; Sherman et al., 2018). This has made it challenging to define the relationships of measured phenomena and adolescent behavior in a nomological network and to make inferences about real-world risk-taking behaviors.

In some cases, variability in the literature may be attributed to the lack of exploration of the hidden or unexpressed assumptions about constructs central to the neurodevelopmental models (Fried, 2020). For example, neurocognitive measures of reward often serve as proxy measures of risk-taking behaviors (Qu et al., 2015), which are then interpreted as interchangeable with real-word risk-taking behavior in brain-behavior studies from which broad conclusions are derived. Same can be said regarding the methodology used to ascribe phenomena to neural activation in fMRI. In fMRI, not only can the techniques for mathematical preprocessing differ among research labs, but how "reward" is defined may also impact interpretations on the behalf of researchers (Botvinik-Nezer et al., 2020b). In some ways, the flexibility in how constructs are defined and what measures are used by researchers may tangentially relate to what the late

Walter Mischel referred to as the "Toothbrush Problem" (Mischel, 2008): researchers treat others' and their own preferred self-report, neurocognitive, and fMRI task contrasts differently, often preferring their own. While there is often merit in these decisions, without understanding how these decisions fit into a specified nomological network, drawing generalizable inferences across studies becomes quite challenging.

In other cases, support for some of the neurodevelopmental models may fail to appreciate the degree of implicit bias towards the models. Despite the widespread use and acceptance of the neurodevelopmental models (as of January 2022, combined citations exceeding 8000; see Casey et al., 2008; Ernst, 2014; Ernst et al., 2006; Luna & Wright, 2016; Steinberg, 2008, 2010), it is increasingly apparent that convergence among similarly measured constructs, that are central to these models, is often weak, or one may argue even non-existent, such as between self-report and neurocognitive performance (Demidenko et al., 2019; Eisenberg et al., 2019). Similarly, the predictive utility is often variable, or one may argue even non-existent, when it comes to real-world behaviors for neurocognitive and neural measures (Demidenko et al., 2019; Sherman et al., 2018). In some literature, the lack of similarity among measures is briefly mentioned but the overarching utility of the constructs is preserved to justify the importance of the heuristic in developmental research. For example, in a large cross-cultural analysis, researchers stated, "*We recognize that […], it is common to find weak correlations between self-report and behavioral measures of putatively similar constructs […] but we believe that the overarching categories provide helpful heuristics*." (Steinberg et al., 2018, p. 2). After this statement, the authors reported <1% variance explained in neurocognitive constructs of reward/self-regulation by domain-similar self-report measures. While evaluating the importance of effect sizes that occur over time is a complex and delicate issue (Funder & Ozer, 2019), combining these measures and

making developmental inferences relies on trust in the conceptual aspect of the theory rather than the empirical evidence for the postulate.

It was recently pointed out that psychologists have altered labels of constructs (or theories) to conceal their genesis and increase the seeming novelty of findings (Proulx & Morey, 2021). This is not to say that the evidence for the neurodevelopmental models is not representative of the data. Rather, there are scenarios where some phenomena are not distinct from those generated in the past. To appreciate the preference for the modern-day neurodevelopment models, it is worthwhile to consider a brief history of adolescent research. In the next section, I consider some historically retained perspectives of adolescence that will be relevant to the discussion of theoretical gaps in the section thereafter.

## Historical Overview of Adolescence

To put the modern-day postulates of adolescent risk-taking behaviors and certain underlying ideologies into perspective, it is important to consider a brief history of research on adolescence. In the review in this section, I maintain the focal point of this dissertation which relates to neurodevelopmental models that emphasize adolescents' increased propensity to engage in risk-taking behaviors (expanded on in the next section). Hence, the context of this historical review will prioritize topics pertaining to the reward sensitivity/novelty seeking during adolescence.

Before plunging into the historical overview of the adolescent literature, it is worthwhile to consider the difficulty in defining this developmental period. At the start of the 20$^{th}$ century, adolescence was broadly characterized as the age between 14 to 24 years (Sawyer et al., 2018). Later, it was defined by some as approximately 11 to 16 years using the Tanner Stages of pubertal development, which varies between males and females. Subsequently, the World

Health Organization (WHO) defined adolescence as 10 to 20 years. Since then, expanded definitions of adolescence have included ages 10 to 25 years (Ledford, 2018). Nevertheless, this expand range may be debated by adolescent researchers given that the latter years, 19 to 25, are considered as emerging adulthood, which is characterized as neither adolescence nor adulthood given the social differences (Arnett, 2000). In fact, the difficulty in defining adolescence has posed issues when researchers have used discrete age cut-offs, such as early-, mid-, and late-adolescents, for group comparisons in neurodevelopmental research (Galván, 2010). Taking all these perspectives into account, I will retain the expanded 10 to 25 year definition of adolescence, which is approximately characterized by the onset of puberty and the offset of cortical development (Bethlehem et al., 2021).

Within the last decade, a large proportion of research considered the adolescent period to be in an imbalance, or susceptible to social and rewarding stimuli (Baker et al., 2020; Casey et al., 2008; Courtney et al., 2020; Shulman et al., 2016; Steinberg, 2008). In some instances, youth were characterized as 'all gas and no brakes' (Bell & McBride, 2010; Payne, 2011, p. 8) – unable to quell their motivation towards rewarding stimuli. Although considered a poor stereotype (Payne, 2011), this contemporary perspective is not far removed from the *storm and stress* hypothesis from the early 20$^{th}$ century (Hall, 1904a), and the role of the self-fulfilling prophecy providing credence to theories about adolescent behavior in the mid-20$^{th}$ century (Bandura, 1964).

Several perspectives were formative in what we now know and think of adolescence, but none more so than the early pioneering work by G. Stanley Hall. A fair proportion of the two volumes written in 1904 (Hall, 1904a, 1904b) cover the physical changes of the body, such as height, weight, and muscle development. The rich cross-cultural tabulated data, after accounting

for secular trends, is consistent with today's reviews of the physical changes that occur during adolescence (Dahl et al., 2018). Then, relating to the marked increase of the sensitivity towards rewards during adolescence, Hall referred to the plasticity of the mind, the influx of sensitivity to rewarding experiences, or "strong emotions" (Hall, 1891), increasing importance of peer and social influences (Hall, 1904b), and the heightened engagement in criminal behavior (Hall, 1904a). Citing data from Italy, Germany, Russia, England, Austria, and the United States, Hall presented a drastic rise in criminal behavior during adolescence. He attributed these changes to multiple factors including heredity, the environment, and the nature of criminals to act *impulsively*, which he indicated was a trait of adolescents (Hall, 1904b). Despite Hall's technological limitations, he associated some of these adolescent behaviors with the neural changes that occurred during this developmental period, noting the connections of the fibers in the brain (Arnett, 2006).

When Hall brought adolescent research to the forefront, he made references to emotional and neural features that are still being studied today. For example, Hall stated that the "… *cerebral elements may connect different brain areas, and thereby to establish psychic unity among discrete factors of our personality…"*. He described adolescence as being a *"nascent period"* which is *"…without government and regulative function…"* (Hall, 1904a, pp. 323–324). Hall reiterated that this perspective of youth dated back to Aristotle, who proclaimed that "*…for the young are heated by nature as drunken men by wine... For the same reason they are easily deceived, as being quick to hope."* (cited in Hall, 1904, p. 522). In these writings, there are striking similarities between the work presented by Hall (1904a, 1904b) and contemporary neurodevelopmental models (Shulman et al., 2016). For instance, contemporary models describe

the important changes in the connectivity between cortical and subcortical brain regions that coincide with emotional development during adolescence (Casey et al., 2019).

Nonetheless, there is evidence that work by Hall retained ideologies and prejudices that stemmed from perspectives of the late 19th and early 20th century (Arnett, 2006; Hall, 1882, 1891). For example, it is understood that Hall's work is rooted in Lamarckism (Arnett, 2006), which is a theme exhibited by publications on evolution in the 19th century. Not yet familiar with the nascent field of genetic heritability, Hall grounded aspects of animal's history in man through '*mental heredity*', whereby individual differences occurred through the interaction with the environment and instinctual feelings (such as pleasure) that comprised the '*comprehensive of the whole human race'* (Hall, 1904b, p. 61). This formulated the ancestral (automatic) systems, which can be modified via the adaptive (plastic) systems that are influenced by others. According to Hall, and perhaps comparable to the bottom-up systems today, adolescence was a physiological second birth when *'morbid ancestral traits and features appear"* which excites behaviors that are rich in emotion (Hall, 1891, p. 205). Hall's work also embraced his early religious convictions. He emphasized the normal and universal (non-religious) process of conversion that should occur during adolescence for *'…moral, existential, and psychological*' reasons (Arnett, 2006, p. 194), arguing that religious beliefs and morality strengthened the character but science during early adolescent development may make the mind dry (Hall, 1891). A review of Hall's early work exhibits the ideologies of its time, a distinction that is based on transitory knowledge (Arnett, 2006).

Hall paved many paths, establishing psychology in the US, which helped promote fields of thought throughout the 20th century on the topic of adolescence (Bringmann et al., 1992). His evolutionary and genetic perspectives influenced the literature on education, child rearing, labor,

religious training, and vocational guidance (Rogers, 1969). Then, by virtue of Hall's invitation of Sigmund Freud to the US in the early 20th century, two major schools of thought of adolescent behaviors eventually emerged: Psychodynamic and Psychosocial Theories (Miller, 2009). Since Erik Erikson trained under Freud, by the 1960's both Psychodynamic and Psychosocial theories were used by psychologists and psychiatrists to explain adolescent behaviors (Erikson, 1968; Group for the Advancement of Psychiatry Committee on Adolescence, 1968). Like Hall, who discussed the *disease of the mind* and the instinctual drives that contributed to behavioral problems during adolescence, Freud and Erikson contributed their own ideas on instinctual behaviors.

Psychodynamics emphasized the importance of intrapsychic processes like instinctual, sexual, aggressive, intellectual, and intrinsic valuations (Group for the Advancement of Psychiatry Committee on Adolescence, 1968). Psychodynamics postulates that the intrapsychic processes are characterized by the onset of adolescence, whereby adolescents use different methods to cope with puberty, and the offset of adolescence, whereby the '*intrapsychic forces stabilize*', reducing poor behaviors (Group for the Advancement of Psychiatry Committee on Adolescence, 1968, p. 63). The intrapsychic processes lead the adolescent through the experience of individuation which is independent judgement that strikes a balance between not disagreeing or agreeing with parents (Steinberg & Cauffman, 1996). Not far removed from Freud's intrapsychic dynamics, Erikson's Psychosocial theory highlighted that the *crisis* during adolescence was related to the identity that the adolescent developed or that the adolescent was in the process of developing (Erikson, 1968; Steinberg & Cauffman, 1996). By navigating the identity crisis appropriately, an adolescent would emerge without the influx of behavioral problems that they may have been at risk to develop.

Psychodynamic and Psychosocial theories were not accepted universally in the 1960's as it was argued that the portrayal of a *crisis* during adolescence was a remnant of Freudian thought (Rogers, 1969). Behaviorists, social cognitive psychologists, and theorists emphasized that the environment provides information that is important to developing behavioral or social expectations that can be incorporated into a working model of the environment (Ferster & Skinner, 1957; Rogers, 1969). Rather than overemphasizing biological factors, as seen in behaviorism, social cognitive theories emphasized the variability in adolescent behavior as a function of cross-cultural and mass-media sensationalism. Their position was that the deviant adolescent excites more attention than the average adolescent, serving as a self-fulfilling prophecy which promotes ideological biases that all adolescents are "deviant" or "impulsive" (Rogers, 1969). Despite best efforts to move away from Freudian constraints, Freudian thought continued to influence the nomenclatures of measures until the end of the 20th century, as seen in reference to impulsivity as "ego-undercontrolling" (White et al., 1994, p. 194).

Over the course of the 20th century, the field slowly divorced itself from the school of thought that adolescents were 'maladjusted' or 'second-rate students' (Rogers, 1969, p. 27). By the late 20th century, developmental psychologists began to consider the dynamic interplay of biological and environmental factors (Bronfenbrenner & Morris, 2007; Lynch & Cicchetti, 1998; Sameroff, 2010). New perspectives considered the mechanisms that may underly delinquent behaviors and whether some adolescents had early predispositions or adolescent-limited behaviors (Casey, 2015; Moffitt, 1993). Researchers considered the psychosocial issues of adolescent behaviors (Cromer & Stager, 2000), contending that development does not occur in a vacuum and therefore the interplay of different factors may cause some adolescents to be either at-risk or resilient to behavioral problems (Burt, 2002). This perspective helped influence

strategies to intervene on adolescents who were at highest risk. To characterize the mechanism for individuals who are more (or less) susceptible during adolescence to behavioral problems, Dahl (2004) pressed for multidisciplinary efforts to explain the paradox of cognitively capable youth engaging in maladaptive behaviors.

From the late 19th to early 21st century, there was a clear change in the subject content of adolescent research, whereby behavior and neural measures increased in the field. In part, this ideological shift towards the end of the 20th century and early part of the 21st century can be explained by the American Psychological Association's (APA) promotion of the "Decade of the Brain" in the 1990's (McGaugh, 1990) and subsequent "Decade of Behavior" in the 2000's (Higgins & Bickel, 2000; Science, 1998). These shifts motivated the use of self-report, neurocognitive performance, and neural measures of adolescent development (described earlier). Consequently, this expanded research on the brain, and behavior that was used to characterize adolescent development, is outlined in contemporary neurodevelopmental models (Casey et al., 2008, 2019; Ernst et al., 2006; Steinberg, 2008, 2010).

The consensus, across a century of perspectives on adolescent development, has been that adolescence is an important developmental period with unique changes in affective and behavioral processes. In fact, evidence over a century of research consistently demonstrates that adolescents exhibit increased rates in internalizing problems (Cyranowski et al., 2000; Hall, 1904b; Solmi et al., 2021), risk-taking and externalizing behaviors (Hall, 1904a; Johnston et al., 2020; Kann et al., 2018), and criminal behavior (Hall, 1904a; Puzzanchera, 2021). These distinct shifts in affect and behavior have motivated the pursuit of empirical evidence to help inform interventions and policy decisions. To date, findings have already had a major impact on the United Nations' decisions to enact policies to protect individuals under 18 years old from

violence, exploitation (Ruck et al., 2016), as well as several decisions by the U.S. Supreme Court regarding life sentences without parole (Steinberg, 2013, 2017).

Yet, the seemingly time-locked theories of adolescent behavior and development represent several ideological shifts. In research, ideological issues are believed to permeate most areas in psychology (Cowles, 1989; Shadish et al., 2002) and, in some cases, reflect explanations that stem from contemporary social or political undertones (Smith & Pollak, 2020). As mentioned earlier, to fit the modern narrative, psychologists may conceal the labels in their work to appear more novel (Proulx & Morey, 2021). The social and political ideologies are evident in the description of adolescents used across time: Youth are heated by nature in the ancient Greek philosophy; youth have no regulative governance to control impulses or "storm and stress" at the beginning of the 20th century (Hall, 1904a); youth's impulsive outbursts result from primitive behaviors and desires per the psychodynamic perspective (Group for the Advancement of Psychiatry Committee on Adolescence, 1968); youth navigate the identity crisis or role confusion per the psychosocial perspective (Erikson, 1968); youth's deviance explains behaviors and political activism (Rogers, 1969); the rise in crime is due to youth who are labeled as "superpredators" (Blumstein, 2002); youth are 'all gas and no brakes' (Bell & McBride, 2010; Payne, 2011, p. 8); or in the present day, youth are sensitive to reward and are 'imbalanced' until they reach neurodevelopmental maturity (Casey et al., 2008, 2019).

Hall's time-locked ideologies are of notable significance. For example, Hall painted adolescents, especially female adolescents, in a dismissive light with statements such as "*An ideal or typical male is hard to define, but there is a standard ideal woman. Because her mind is, more than that of man, essentially an organ of heredity…*" (1904b, p. 567). Furthermore, some of Hall's views were biased by views about eugenics that were widespread during the 19th and 20th

centuries (Briggs, 2021). For example, in the Scientific Monthly Hall wrote, "*Some are born to be hewers of wood and drawers of water, and are fortunate if they can be made self-supporting; practical slavery under one name or another must always be their lot*", when discussing democratic issues at the time (1924, p. 466).

Most ironic of the political ideologies that indirectly gave rise to the research on adolescence is rooted in G. Stanley Hall's work. Hall's research on adolescence branched out of the field of child-rearing and moral problems. These two fields were, in part, driven by broad nationalism in the 1820's when Americans decided that British books were no longer suitable for teaching (Demos & Demos, 1969). Given the examples of time-specific ideologies that may be social and political, it is imperative to unearth hidden assumptions and any lingering ideologies in modern theories to appropriately characterize both adolescent development and behaviors. When examined under a microscope, researchers may discover that old concepts may have been repackaged as new, something that Keating and colleagues elaborated on elsewhere (Keating et al., in press).

Given the hidden assumptions and layers of ideologies in the history of adolescent research, I leverage the limitations discussed in the previous section and the history from this section to identify the theoretical gaps in the next section. These theoretical gaps are central to the empirical investigations that are the focus of Chapters 3, 4 and 5.

## Theoretical Gaps

As described in the last section, a theme that may be conveyed across adolescent literature from the 19th through to the 21st century is that adolescents are increasingly sensitive to rewards and often lack the ability to make goal-oriented decisions when environmental cues are especially salient (Dahl, 2004; Hall, 1904a; Rogers, 1969; Shulman et al., 2016). This theme has informed neurodevelopmental frameworks, such as the Dual Systems Model (Steinberg, 2010), Driven Dual System Model (Luna & Wright, 2016), Imbalance Model (Casey et al., 2008), and Triadic Model (Ernst et al., 2006), that rely on both inductive and deductive properties. In the context of induction, observations rely on measuring a proposed phenomenon, such as reward sensitivity via self-reported sensation seeking, which relate to an overarching construct within the theory (Figure 1.3). The measures serve as a numerical representation of an attribute or phenomenon that a researcher is interested in quantifying (Briggs, 2021). In the case of reward sensitivity, the inductive reasoning is that adolescent *should* exhibit greater reward sensitivity (especially those that engage in the highest risk-taking behaviors) than children or adults. For example, if measuring the construct of reward using neurocognitive performance from the BART, greater sensitivity to rewards would be reflected in higher adjusted pump counts on the measure. By collecting this neurocognitive performance data from a sample of 8- to 30-year-old adolescents, a researcher may find that between 16-20 there is peak in reward sensitivity on the BART task. From this, the researcher may conclude that there is empirical evidence for the

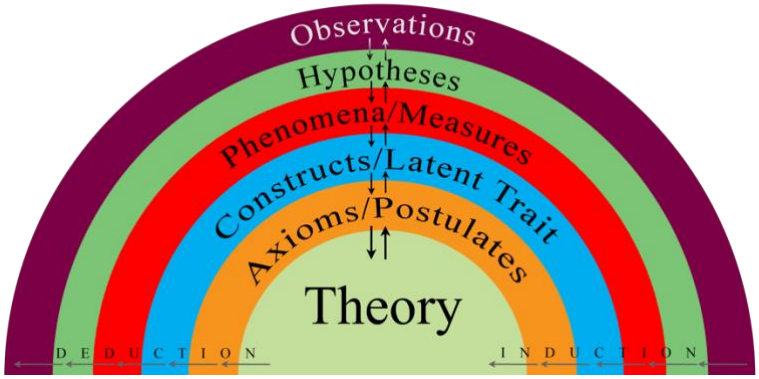


*Figure 1.3*. Flowchart from Postulated Theory to Observations

theory that mid-to-late adolescence coincides with increased reward sensitivity. The reverse is true, too, in deductive reasoning. The theory can inform constructs that inform measured phenomena, which then inform a set of hypotheses and represent observations in the lab or real-world. In this scenario, the theory is that adolescents are more motivated by rewards. Therefore, a researcher may identify a set of measures to tap the construct of reward and capture a participant's reward sensitivity, like self-reported sensation seeking (e.g., BSSS) or neural activation of reward regions during fMRI task motivational processes (e.g., Monetary Incentive Delay (MID) task). Within constraints of sampling and measurement error, this would allow the researcher to attempt to generalize the broader neurodevelopmental models in their respective sample(s) and determine whether there are development differences within these measures of the reward constructs. Hence, the theory helps structure the *hypothesized* observation: an adolescent will show *greater* activity in reward regions in response to salient stimuli than an adult or child during an fMRI task (Muthukrishna & Henrich, 2019).

While the broader theory serves as a useful heuristic to explain neurodevelopmental changes of reward systems, an inability to interpret results may arise when there is discordance between the sub-theories relating to the constructs and measured phenomena (or auxiliary theories; Meehl (1990)). For example, the neurodevelopmental models may have merit but relationships among the measures of the constructs, such as neurocognitive performance on the BART and neural substrates of reward during the MID task within the hypothesized nomological network, may be unverified. When testing hypotheses, the disagreement can materialize at the level of: a) the proposed construct, when the construct doesn't measure the domain we intended to measure, b) the theory or postulate, for instance the deduction that all adolescents (or select adolescents) are more sensitive to rewards than other age groups, may be an overly broad

mischaracterization, or c) the design of the study, such as considering only a single operationalization of reward or a static process of reward that may, in fact, be dynamic (Cronbach & Meehl, 1955). Often, there is widespread acceptance of reasoned assumptions that are templated as 'self-evident truths' (Hull, 1952, p. 14) and generalizations of theories that are beyond the measured phenomena (Lerner, 2006).

Not knowing whether failure occurs at the theory, construct, measured phenomena, or design level presents a paradox for researchers that can neither confirm nor deny the theory or its constructs (Cronbach & Meehl, 1955). This has been especially true of neurodevelopmental models since the perspectives have received criticism with respect to inconsistencies in findings (Crone & Dahl, 2012; Meisel et al., 2019; Pfeifer & Allen, 2012; Romer et al., 2017), a lack of convergence across key components of the models and precisions in the test (Pfeifer & Allen, 2016; Sherman et al., 2018), and overgeneralizations of findings that may not be true for the typical adolescent (Bjork & Pardini, 2015; Romer et al., 2017; Willoughby et al., 2013). An example of this can be found in Steinberg and colleagues (2018) that was highlighted in a prior section. The authors took non-zero positive correlations between measured phenomena of reward sensitivity and self-regulatory constructs as evidence for the benefits of the theoretical constructs, an approach that is at odds with construct validation (Flake et al., 2017) and a major limitation of theory building in psychology (Grahek et al., 2021). This level of ambiguity and lack of precision raises several issues for the postulates of the neurodevelopmental models. Moreover, the level of ambiguity and complexity is concerning to the theoretical framework because a theory should be testable, falsifiable, parsimonious, and make few assumptions (Oberauer & Lewandowsky, 2019).

The central premise that developmental change in reward sensitivity coincides with an influx in risk-taking behaviors has not generalized well in studies on adolescent neurodevelopment. Several national studies demonstrate that risk-taking behaviors, such as substance use, increase significantly from mid-to-late adolescence (Centers for Disease Control and Prevention, 2020; Johnston et al., 2020; Kann et al., 2018; Substance Abuse and Mental Health Services Administration., 2020). However, a review of the neurodevelopmental findings on reward activity and reward sensitivity reported that there is minimal evidence for a link between the neural activation and risk-taking behaviors during adolescence (Sherman et al., 2018). One reason for the lack of association may stem from the fact that many studies often focus on samples before the 18-23-year peak in risk-taking, which precedes the peak in mortality rates from unintentional injuries and substance use behaviors (Bjork & Pardini, 2015; Johnston et al., 2020; Willoughby et al., 2013). This is relevant to neurodevelopmental frameworks, given that earlier work highlights, in part, deaths resulting from unintentional injuries, substance use and drinking and driving behaviors during adolescence (Casey et al., 2008). Sherman and colleagues (2018) examined 22 studies in which only 41% of the studies included adolescents that are older than 17 years. When older adolescents were included in the studies, this was often within a sample that included a broad age range, such as 10 to 26 years (Braams et al., 2016) or 8 to 26 years (Van Leijenhorst, Gunther Moor, et al., 2010). While these younger samples and broad age ranges answer valuable developmental questions about early onset behaviors or broad developmental changes, they lack the precision to evaluate hypotheses about the neural differences that exist between adolescents who do and don't engage in risk-taking when these behaviors *peak* (Pfeifer & Allen, 2016). Thus, it becomes challenging to pinpoint neural substrates that coincide with peaks in risk-taking.

A second issue that may contribute to the lack of association between neural activation and real-world risk-taking behaviors stems from fMRI studies that heavily rely on neurocognitive tasks as proxies of risk-taking (Chein et al., 2011; Qu et al., 2015). While reward tasks have been reported to elicit robust activation in reward related regions (Bartra et al., 2013), some of the tasks used during fMRI research of adolescents often have limited associations with real-world risk-taking (Demidenko et al., 2019; Duell & Steinberg, 2020; Eisenberg et al., 2019). This suggests that studies of neural substrates of risk-taking should include measures of real-world risk-taking behaviors rather than solely relying on task parameters from risk proxies if researchers intend to make conclusions about real-world risk-taking and/or decision making.

The third and final problem is that discerning evidence for and against neurodevelopment models becomes especially difficult given the large number of tasks that are used in task-based fMRI. Neurodevelopmental research of reward processing employs a wide range of fMRI tasks and contrasts which add to analytic flexibility (Flannery et al., 2020; Richards et al., 2013; Sherman et al., 2018). This is helpful in obtaining a broad characterization of reward processing across different conditions. However, in cases when there is some support for postulates of the neurodevelopmental models, such as the NAcc predicting substance use behaviors, there is often substantial heterogeneity in task designs and contrasts used (Tervo-Clemmens et al., 2020). The flexibility and ambiguous decisions (Simmons et al., 2011) in task-based fMRI contribute to increased numbers of ‘researcher degrees of freedom’ (Gelman & Loken, 2014) and may add to false positives (Hong et al., 2019). Given the hidden assumptions in task-based fMRI contrasts (Caplan, 2007), the underappreciation of construct validity in fMRI (Poldrack & Yarkoni, 2016) may incidentally contribute to the ambiguity in findings pertaining to the neurodevelopmental models. In a biased scenario, researchers will prefer one contrast over others (as discussed earlier

in the context of the "Toothbrush Problem") for the benefit of the theoretical position (Grahek et al., 2021). This limits our ability to see whether different constructs do or do not align with the phenomena that is proposed in the nomological network.

Given the acknowledged issues in neurodevelopmental research, it is critical to understand the neural substrates of real-world risk-taking and to consider how methodological approaches impact findings. If the hypotheses derived from neurodevelopmental models of adolescent risk-taking generalize, we would expect to see higher risk-takers exhibit greater activation in reward regions during reward processing than adolescents that engage in lesser risk-taking. However, if neural substrates are not found to be reliably associated with self-report risk-taking behaviors, which is a central hypothesis, then neurodevelopment research would benefit from considering how analytic decisions (e.g., task contrast type, or selection of parcels to assess for neural activation) may impact brain-behavior associations in task-based fMRI. Spanning the contrast space may provide some patterns in brain-behavior associations that are proposed by the neurodevelopmental models, something a single contrast may fail to reveal. However, if consistent patterns are not evident in the range of contrasts, modeling dynamic relationships of the brain may be an appropriate alternative to traditional univariate techniques since mean-based approaches may simply be inadequate in capturing the interplay of brain regions (Beltz, 2018). Novel methods of time-series fMRI consider the coactivation among brain regions for a given individual (Casey et al., 2019; Lydon-Staley & Bassett, 2018). This may capture the coactivation between socioemotional and cognitive control brain regions that are central to neurodevelopmental models, consider how they interact during a reward paradigm, and whether the person-specific network dynamics differ among levels of other measures which tap a related construct, such as self-reported novelty seeking.

As mentioned at the start of this chapter, the purpose of this dissertation is to evaluate some of the relationships from the nomological network that are proposed by neurodevelopmental models. Specifically, I evaluate the neural substrates of adolescent behavior and the effect of analytic decisions on these results across three investigations. In Chapter 2, I begin by describing the recruitment strategy for the sample that is the basis for these investigations and a description of the fMRI task and acquisition techniques employed. In Chapter 3 (Study 1), I consider whether the neurodevelopmental models postulate that neural activation in socioemotional and/or cognitive control regions differentiate high and low risk-taking late adolescents. Given the decisions that go into the analytic choice in Study 1, in Chapter 4 (Study 2), I examine the similarities and differences of the positive and negative valence contrasts in the MID task during fMRI. I also evaluate whether the contrast definitions alter brain-behavior associations in a direction that a theory of the reward construct would indicate. In Chapter 5 (Study 3), I go beyond traditional mean-based fMRI analyses to consider whether subgroups of adolescents demonstrate variation in their dynamic connections between regions in cognitive control, salience, and approach brain regions (Figure 1.2) during a reward task. Then, I consider how this functional connectivity in brain regions is meaningfully related to self-reported sensation seeking. Finally, in Chapter 6, I cover how the findings from Study 1, Study 2, and Study 3 fit into a nomological network of findings, the implications of these findings, and future directions from the nomological network perspective.

## Chapter 2 : Adolescent Health Risk Behavior Study: Sample Recruitment, Design and Characteristics

All three studies of this dissertation will utilize data from the Adolescent Health Risk Behavior (AHRB) study. The AHRB study was designed to characterize the behavioral, cognitive and neural basis of adolescent health risk behaviors. For this study, $10^{th}$ and $12^{th}$ graders (N = 2,017) from southeastern Michigan were enrolled to participate. The study is comprised of two phases, a longitudinal survey (Phase 1) and longitudinal brain imaging phase (Phase 2). This dissertation leverages both the self-report data from Phase 1 and neuroimaging data from Phase 2.

### Recruitment Phase 1 & Phase 2

During Phase 1, the longitudinal survey, participants completed several self-report measures and a battery of neurocognitive tasks across three waves (Figure 2.1). During Wave 1 (W1), participants completed surveys during high school class periods. These were administered using computer assisted self-interviewing (CASI) and computerized neurocognitive tasks within one-week of survey administration. Surveys assessed engagement in 15-health risk behaviors (described below) and a range of related psychosocial constructs, such as self-reported sensation seeking and impulsivity. The neurocognitive tasks assessed reward processing/sensitivity (via Balloon Analogue Risk Task and Iowa Gambling Task), self-regulation/impulsivity (via Go/No-

go and Delay Discounting Task), and memory (via Digit Span). During W2-W3, participants were re-administered the self-report surveys and neurocognitive tasks using web-based assisted interviews that they completed on their own time. Of the 2,017 W1 enrolled participants, 56% of the participants completed two or more waves of data collection and 45% completed W2 or W3 (Table 2.1), respectively. Recruitment of participants was conducted at the school and/or school district level, using a quota sampling approach. Specifically, schools were recruited to maximize sample diversity on socioeconomic status (SES) and race/ethnicity, with replacements sought for schools that declined participation (almost always for

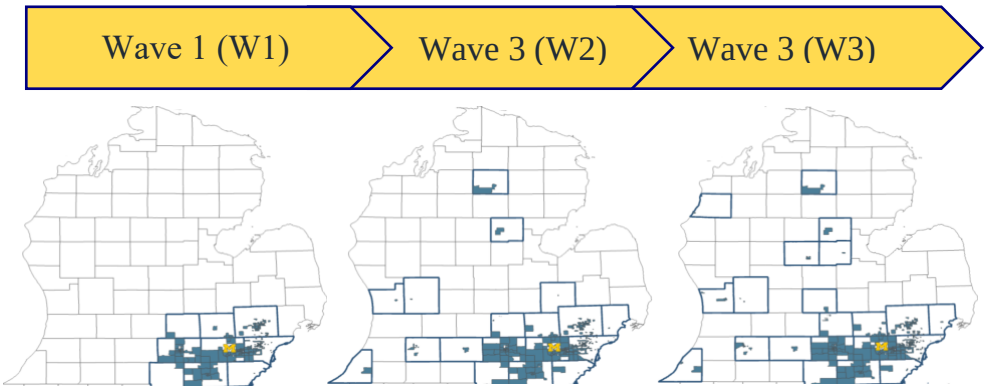


*Figure 2.1*. AHRB Study Wave 1 – Wave 3: participant's Associated Counties/Census Tracts in Southeastern Michigan During Study

*Table 2.1*. Demographic characteristics for Phase 1: Longitudinal Survey

| | **Wave 1** (N=2017) | **Wave 2** (N=913) | **Wave 3** (N=913) |
|---|---|---|---|
| | | *M (SD)* | |
| Age (Years) | 16.7 (1.1) | 18.3 (1.2) | 19.3 (1.2) |
| Grade | 11.0 (1.0) | 12.5 (1.2) | 13.5 (1.3) |
| Sex, Female *n* (%) | 1114 (55.2) | 542 (59.4) | 560 (61.3) |
| Race, *n* (%) | | | |
| White Non-Hispanic | 1100 (54.5) | 556 (60.9) | 548 (60.0) |
| Black or African American, Non-Hispanic | 449 (22.3) | 162 (17.7) | 185 (20.3) |
| Hispanic, All Races | 159 (7.9) | 54 (5.9) | 59 (6.5) |
| Other | 299 (14.8) | 128 (14.0) | 121 (13.3) |
| Parental Education, *n* (%) | | | |
| High School or Less | 487 (24.1) | 183 (20.0) | 171 (18.7) |
| Some College | 567 (28.1) | 227 (24.9) | 234 (25.6) |
| College | 559 (27.7) | 272 (29.8) | 287 (31.4) |
| Beyond College | 327 (16.2) | 194 (21.2) | 198 (21.7) |

internal scheduling reasons). The recruitment strategy was intended to approximate the demographic characteristics of the population in Michigan, whereby 81% identified as White, 15.2% as Black or African American, and 5.1% as Hispanic or Latino (of any race) in the 2019 American Community Survey (U.S. Census Bureau, 2019).

One of the aims of the longitudinal multi-phase design was to characterize neural differences of risk-taking behaviors. Hence for the neuroimaging phase (Phase 2), participants were recruited based on Phase 1 W1 (P1W1) self-reported risk behaviors. During P1W1 participants self-reported on their engagement in 15-risk behaviors that are comparable to those collected in the Monitoring the Future survey (Johnston et al., 2020) and Center for Disease Control and Prevention's Youth Risk Behavior Surveillance Survey (Kann et al., 2018). Specific health risk-taking behaviors include the use of cigarettes, e-cigarettes, alcohol, marijuana, amphetamines, narcotics, sedatives or streets drugs, and texting while driving, drowsy driving, driving while under the influence of alcohol, riding with an alcohol-impaired driver, having unprotected sex, physical fighting, and risking serious injury to self. To characterize an overall engagement in risk-taking behaviors, confirmatory factor analysis was used to create a Behavioral Misadventure Scale (BMS) latent factor of the 15-health risk behaviors.

Phase 2 participants were recruited based on a high ($\geq 75^{th}$) and low/average ($20^{th}$ to $60^{th}$) percentile score on the BMS from the full P1W1 sample. The decision to recruit $\geq 75^{th}$ percentile on the BMS for the "high" risk group was to ensure that there was a sufficiently high-risk engagement as compared to other adolescents in the full sample. Furthermore, the $75^{th}$ percentile was a balance between ensuring that adolescents with high-risk engagement were represented but also allowing a large enough pool of adolescents to obtain diversity across several demographic characteristics. The reason that the average/low risk profile group was based on the $20^{th}$ to $60^{th}$

percentile on the BMS was two-fold: first, the lead investigators wanted to ensure that we recruited enough adolescents, and second, the lead investigators didn't want to recruit adolescents that engaged in an abnormally low number of risk behaviors as this may capture a different, risk-averse adolescent profile. For Phase 2 W1 (P2W1), 115 adolescents were recruited (Table 2.2). As expected, the only demographic characteristics that the P2W1 risk-groups (high versus average/low) differed on were age (Table 2.2). In other words, participants in the high risk-taking group were older (Mean = 19.9) than participants in the average/low risk-taking group (Mean = 19.0) during their scan visit.

*Table 2.2.* Demographic characteristics for Phase 2: Neuroimaging

| | Low/Average (N=73) | High (N=42) | Total (N=115) | Effect Size |
|---|---|---|---|---|
| | | *M (SD)* | | |
| Age (years) | 19.0 (1.2) | 19.9 (1.2) | 19.3 (1.3) Range: 17-21 | *d* = .75*** |
| BMS | -0.27 (0.12) | 0.84 (0.54) | 0.14 (0.64) | *d* = 2.83*** |
| Sex, Female *n* (%) | 45 (61.6) | 22 (52.4) | 67 (59.3) | φ = -.09 |
| Race, *n* (%) | | | | φ = .22 |
| White Non-Hispanic | 46 (63.0) | 34 (81.0) | 80 (69.6) | |
| Black or African American, Non-Hispanic | 16 (21.9) | 4 (9.5) | 20 (17.4) | |
| Hispanic, All Races | 6 (8.2) | 3 (7.1) | 9 (7.8) | |
| Other | 5 (6.8) | 1 (2.4) | 6 (5.2) | |

BMS = Behavioral Misadventure; *d* = Cohen's D.

## Description of fMRI Task, Acquisition and Preprocessing

For P2W1, participants completed the neuroimaging protocol on average 30.9 months (SD = 5.0) after completing the P1W1 survey (see Appendix A, Figure A1). During the P2W1 protocol, participants reviewed study activities with research staff, completed necessary consent documentation, and practiced tasks that were administered during the functional magnetic resonance imaging (fMRI) session. Research staff explicitly notified participants of the possible $30 compensation that would be contingent on their in-scan performance during the Monetary

Incentive Delay (MID) task. After the pre-scan activities were completed, participants completed a one-hour scan protocol that consisted of: structural MRI, one run of the Emotional Faces task and two runs of the MID task, and one run of resting state fMRI and diffusion tensor imaging.

In this dissertation, I use the MID task which is designed to elicit robust activation of reward regions that are central to substance use behaviors and that are a primary component of the BMS (Balodis & Potenza, 2015; Bartra et al., 2013; Diekhof et al., 2012). The MID task is a reward paradigm (Knutson et al., 2000) that has been shown to evoke robust activation of reward regions (discussed more in-depth in Chapter 4). While the task does not tap self-regulatory systems, the MID task is an appropriate task to evaluate key reward mechanisms that are pertinent to adolescent risk behavior models (Shulman et al., 2016) as the task has been repeatedly shown to elicit activation in key reward regions, such as the VS, insular cortex and medial prefrontal cortex (mPFC)(Knutson & Greer, 2008). The ventral striatum (VS) and insular cortex are engaged during the anticipatory phase and the mPFC is engaged during the feedback phase of the task.

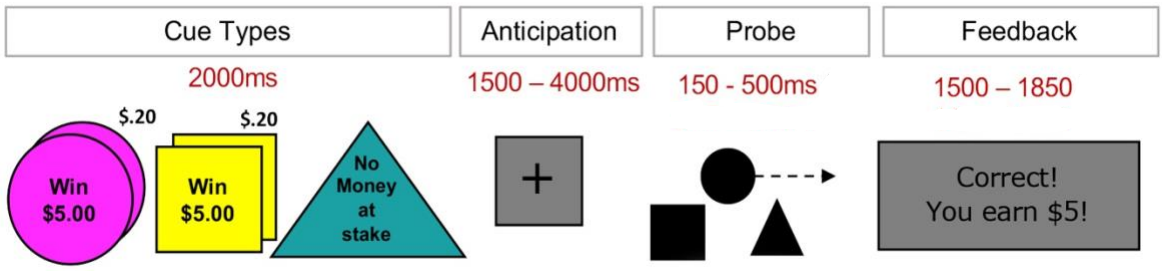


*Figure 2.2.* ABCD Monetary Incentive Delay Task Schematic.

Neurodevelopmental studies (as discussed in Chapter 1) converge on the hypothesis that adolescence is marked by the increased motivation towards rewarding stimuli due to changes in reward circuitry (Galván, 2010). Changes in dopamine receptors within reward regions, such as the VS, and the tonic phase of dopamine (Luciana & Collins, 2012) may be a key vulnerability to

substance use during adolescents (Ernst & Luciana, 2015). These differences in reward circuitry are believed to contributed to the reactivity to novel and rewarding stimuli, which leads to engagement in substance use behaviors. Given the prominent role of role of motivation (or anticipation of reward) in the MID task and the critical role of dopamine in anticipation ("wanting") and not feedback ("liking") (Berridge & Kringelbach, 2015), this task is a reasonable design to model to motivation towards approaching rewarding stimuli. As described in the Adolescent Brain Cognitive Development (ABCD) study® design, the MID is sensitive to developmental and addiction-related effects (Casey et al., 2018)

The MID task design used in the AHRB (Figure 2.2) is comparable to the task design used in the ABCD study (Casey et al., 2018). Each trial of the task starts with the anticipatory phase that consists of five cue types: Win $5, Win $0.20, Lose $5, Lose $0.20 and 'No Money At Stake'. These cues indicate the reward type for the duration of that trial. The cue phase lasts for 2000ms and is then followed by a fixation cross (1500-4000ms). Followed by the fixation cross is the probe phase that requires a participant button press within a predefined window (based on their average mean response time (MRT)). The probe phase is followed by the feedback phase (1500-1800ms) that indicates the outcome of that trial (e.g., "Correct! You earn $5"). The task is a performance contingent reward design (Richards et al., 2013), so if the participant responds *within* the probe window they will receive the reward as indicated by the cue type at the beginning of the trial (e.g., "Win $5" or "Lose $5"). Using the MRT plus two standard deviations on correct trials, the MID task individualizes the difficulty to reach around 60% accuracy rate by adjusting the difficulty, that is, making the probe duration wider or narrower. In this version of the task, for each MID run, the task includes 50 trials (10 for each cue type), for a combined 100 total trials (20 for each cue type) across the two runs. Although the

57% overall accuracy during the task was slightly below the 60% target (see Appendix A, Table A1 and Figure A2), accuracy was highest for the Win $5 and Lose $5 reward cues, 63% and 60%, respectively, as expected. The only distinction between the MID task used in the AHRB and ABCD study is that the AHRB study uses an earlier version which does not register mean response times for *missed* trials.

To model the blood-oxygen-level-dependent (BOLD) signal during MID task, both high resolution and functional data were acquired using a GE Discovery MR750 3.0 Tesla scanner with a standard adult-sized coil (Milwaukee, WI). A full-brain high-resolution T1 SPGR PROMO scan was acquired that is used in preprocessing (TR = 7000ms, TE = 2900ms, flip angle = 8°, FOV = 25.6 cm, slice thickness = 1 mm, 208 sagittal slices; matrix = 256 x 256). Before the MID task, a fieldmap was acquired using spin-echo EPI (TR = 7400ms, TE = 80 ms, FOV = 21.6 cm, 90x90 matrix) with opposite phase encoding polarity (A→P, P→A). Two functional T2*-weighted BOLD MID runs were acquired in the axial plane using a multiband EPI sequence (MB factor=6) of 60 contiguous axial 2.4 mm slices (TR = 800ms, TE = 30 ms, flip angle = 52°, FOV = 21.6 cm, 90x90 matrix, volumes = 407).

FMRI data: (1) were reconstructed; (2) had realignment and field map correction applied in SPM12; and (3) had physiological noise removed using RETROICOR (Glover et al., 2000). Preprocessing was then completed using FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) FEAT (FMRI Expert Analysis Tool) Version 6.00. This included: (4) registration to high resolution structural and standard space MNI 152 image using FLIRT using a Full search 12 DOF (Jenkinson & Smith, 2001; Jenkinson, Bannister, Brady, & Smith, 2002); (5) motion correction using MCFLIRT (Jenkinson et al., 2002); (6) non-brain removal using BET (S. M. Smith, 2002); (7) spatial smoothing using a Gaussian kernel of FWHM 5mm; (8) grand-

mean intensity normalization of the entire 4D dataset by a single multiplicative factor; and (9) highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma=50.0s).

## Preface for Study Chapters 3 to 5

As mentioned earlier, for each study in this dissertation (Study 1 to Study 3) I use the MID task fMRI data. Of the 115 participants eligible for inclusion, 11 participants were excluded for the following reasons: Seven participants were not safe to magnetic resonance imaging (MRI), and four participants completed the scan but were excluded from analyses due to non-recoverable artifacts in the images ($n$ = 3) or failing to respond during the MID task ($n$ = 1). After data were reconstructed and quality control checks were performed, a sample of N = 104 (Table 2.3) had available MID task fMRI data. The final fMRI subsample (N = 104; Age Mean = 19.3, *SD* = 1.3; Female 57%) did not differ from the full sample in age, sex, or time from the original survey. Due to the recruitment strategy described above, this sample consists of two distinct risk profiles based on the BMS, high and low/avg. In Figure 2.3, I plot the distribution, the raw data points, and the boxplot representing the means and standard deviations of the risk-taking profiles from the sample that are based on the BMS. The cluster at the high end of low/avg risk-takers does not overlap with the high-risk profiles that are more variable given different rates and types of risk-taking engagement. The distinction between the low/avg and high risk-takers in Figure 2.3 is central to testing the

*Table 2.3.* Demographics for P2W1 sample with MID Data

| | $n$ = 104 |
|---|---|
| Age | 19.3 (1.3) |
| BSSS | 3.31 (0.4) |
| Sex, Female *n* (%) | 59 (56.7) |
| Race, *n* (%) | |
| Black, non-Hispanic | 15 (14.4) |
| White, non-Hispanic | 74 (71.2) |
| Other | 6 (5.7) |
| Hispanic/Latinx | 9 (8.7) |

BSSS = Brief Sensation Seeking

hypothesis in Chapter 3 (Study 1). To avoid redundancies, the information provided above is not repeated in subsequent chapters. The description of the sample, task design, task administration, fMRI acquisition and preprocessing that is described above is consistent for studies in Chapter 3 to Chapter 5. Therefore, in each chapter the reader is referred to this chapter for this information. When necessary, such as fitting the general linear models for fMRI data, contrast selection, or modeling the timeseries data, this information is expanded and supplemented in the respective chapter.

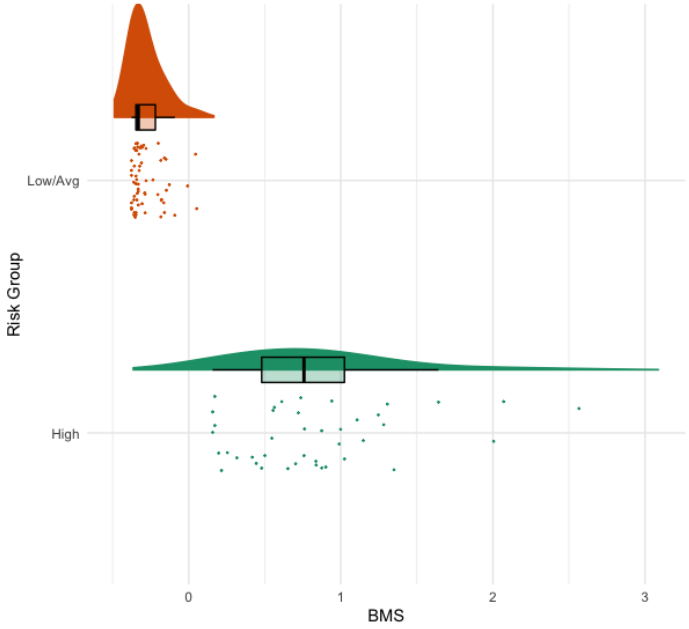


*Figure 2.3*. Separation of Behavioral Misadventure scores of Risk Groups for P2W1
BMS = Behavioral Misadventure Score.

Each chapter will focus on slightly different self-reported behaviors from Phase 1 that'll help address the core question in that study. For example, Study 1 uses the BMS and self-reported risk-taking behaviors to evaluate whether brain activation differs across risk-taking profiles when substance use and mortality from unintentional injuries peak (Centers for Disease Control and Prevention, 2020; Willoughby et al., 2013). Then, Study 2 uses a set of substance use and psychological characteristics (e.g., sensation seeking, externalizing, impulsivity) to identify links between theoretically related self-reported items and constructs of reward as defined by reasonable MID contrasts. Finally, Study 3 uses self-reported sensation seeking to evaluate the association between a trait measure of motivation toward positive experiences and person-specific brain coactivation during a state of motivational processing.

## Chapter 3 : Cortical and Subcortical Response to the Anticipation of Reward in High and Average/Low Risk-taking Adolescents.[1]

As elaborated on in Chapter 1, adolescence is one of the highest health risk-behavior periods in human development, whereby adolescents are characterized as having the highest rates of *preventable* mortality and morbidity stemming from risk-taking (Kann et al., 2018). An overwhelming 70% of adolescent deaths in the United States are related to preventable causes, such as suicide, homicide, risky driving, risky sex, and substance use (Casey et al., 2008; Kann et al., 2018). Although it is recognized that these risk-taking behaviors contribute to increased rates of morbidity and mortality in adolescence, many programs that have been developed to reduce these risky behaviors have been minimally effective (Ferdinand et al., 2015; Hale et al., 2014; Steinberg, 2008). This makes it paramount to understand biological change and developmental variation underlying adolescent risk-taking (Dahl, 2004). In particular, knowledge about adolescent neurodevelopment has the potential to inform both policy-making and interventions for those at highest risk (Dahl et al., 2018). As described in Chapter 1, several neurodevelopmental models (Casey et al., 2008; Ernst et al., 2006; Luna & Wright, 2016; Steinberg, 2008) have ascribed changes in socioemotional and cognitive control systems to the increase in risk-taking during adolescence. However, the generalizability of these findings remains unclear.

[1] Chapter 3 corresponds to Demidenko et al. (2020), published in *Developmental Cognitive Neuroscience*

## Neurodevelopmental Models: Differences and Similarities

Despite broad similarities across current neurodevelopmental models in the function of socioemotional and cognitive systems, there are several key differences (see Figure 1.2 in Chapter 1). The *Triadic model* (Ernst et al., 2006) focuses on the balance between the regulatory, approach and avoidance systems. The regulatory, or cognitive control system, which is critical in monitoring and adaptation, functions as a conductor to facilitate behaviors by balancing information across multiple systems (Ernst et al., 2006; Richards et al., 2013). Then, the approach system, which has positive valence, focuses on rewarding stimuli that drives an organism to engage in novel behaviors. The avoidance system, which has negative valence, focuses on harm to help notify the organism of whether a stimulus should (or should not) be approached. Together, the approach and avoidance systems are conceptually related to the brain regions part of the socioemotional system. However, in the Triadic model each system has its own associated brain regions. Specifically, the regulatory system involves the ventrolateral PFC (vlPFC), dorsolateral prefrontal cortex (dlPFC), and anterior cingulate cortex (ACC; Richards et al., 2013); the approach system involves both the orbital frontal cortex (OFC) and ventral striatum (VS); and the avoidance system involves the amygdala (central nucleus for operant behavior and lateral/basolateral for conditioning stimuli) and insula. Combined, these regions exchange information and perform the goal-oriented decision making.

As opposed to the balance across three systems in the Triadic model, the *Maturational Imbalance* (Casey et al., 2008), *Dual Systems* (Steinberg, 2008), and *Driven Dual Systems* (Luna & Wright, 2016) models emphasize the role of the cognitive control system in suppressing inappropriate (or salient) thoughts and actions associated with the socioemotional system in favor of goal-oriented behaviors, reducing the effect of reward sensitivity. The Maturational Imbalance

model (Casey et al., 2008) explains that the inability to behave in a goal-oriented manner reflects the immature development of the cognitive control system, supported by the vlPFC, which reduces the influence of reward sensitivity, supported by the Nucleus Accumbens (NAcc). In contrast, the *Dual Systems* Model (Steinberg, 2008) contends that decisions are a clash between cognitive control (mPFC/OFC/dlPFC) and social-emotional (Amygdala and VS) regions. The post-pubertal maturation of reward regions leads to increased reward seeking, especially in the context of peers, as a function of rising dopamine-rich receptors in the NAcc and declining dopamine autoreceptors in the PFC, which function as a negative feedback loop reducing the PFC's ability to suppress inappropriate thoughts and actions. Similarly, the *Driven Dual Systems* model (Luna & Wright, 2016) contends that cognitive control is the key system in governing appropriate goal-oriented actions. However, in contrast to the Imbalance and Dual System models, the Driven Dual System model proposes that cognitive control systems are largely developed by late childhood/early adolescence and focused instead on the hyperactivation of the reward regions (VS) due to the proliferation of DA receptors that increase the appetitive/motivation systems and, in turn, drive riskier behaviors.

Each of these neurodevelopmental models emphasizes the importance of early sensitization of dopamine systems in reward regions of the brain following puberty. While changes in the socioemotional system increase sensitivity in reward regions, which heighten the likelihood in engaging in risk-taking behaviors, the alteration in cognitive control contributes to improved cognitive capacity to reduce these risk-taking behaviors. Together, these discrete systems interact as adolescents are exposed to salient stimuli in their environments. Notably, in the three models, there is overlap across the brain regions that underlie socioemotional (approach/avoidance) and cognitive control systems, such that approach processing largely involves areas of the VS and

OFC; avoidance processing is supported by the amygdala and mPFC; and cognitive control is attributed to regions of the dlPFC, ACC, OFC, and/or vlPFC.

In line with the neurodevelopmental models, a review on adolescent neural activation during reward processing has identified a similar set of brain regions (Silverman et al., 2015). On average, adolescents exhibit greater activation in the VS, OFC, amygdala, ACC, insula (region involved ascribing valences), and the posterior parietal cortex (region involved in self-regulation) than adults. These brain regions often play a central role in the literature that assess the associations between risk-taking and neural activation during processing of reward and emotional stimuli. In many instances, the VS is hypothesized to underlie substance use and alcohol related problems during adolescence (Ernst & Luciana, 2015; Galván, 2013; Heitzeg et al., 2014; Tervo-Clemmens et al., 2020). In fact, studies have shown that activation in the VS during the anticipation of rewards is associated with susceptibility to future substance use (Cope et al., 2019; Büchel et al., 2017), effects resulting from substance use (Martz et al., 2016), and a genetic precursor to alcohol problems (Heitzeg et al., 2014).

## Variability in Neural Activation & Risk-taking Studies

Reviews that have examined neural predictors of risk-taking behaviors in adolescents report substantial variability across studies, providing only mixed support for the neurodevelopmental models with respect to risk-taking. Multiple reviews report that comparison groups have varied greatly in categorizing children, adolescents, and adults (Crone & Dahl, 2012; Galván, 2010). Furthermore, tasks have often utilized different analytic strategies, baseline conditions, and magnitudes (or probabilities) of reward. A recent review by Sherman et al. (2018) reported that risk-taking is indexed by different neural substrates across studies, categorized, for example, by lab-based measures of risk in tasks, generalized sensation seeking, or perceptions of

risks. Critical to spurious effects issues in fMRI (Button et al., 2013; Yarkoni, 2009), 70% of the studies that were reviewed were substantially underpowered (N < 50). Oftentimes, researchers solely used region of interest (ROI) approaches, which focused attention where findings were expected, and overlooked alternative brain regions posited by competing neurodevelopmental models.

While much of this early work is poised to ask important questions about developmental differences that contribute to a sparse literature, different age criteria, targeted sampling, and measurements of risk across studies may have contributed to mixed findings (Braams et al., 2015, 2016; Büchel et al., 2017; Cope et al., 2019). As noted in Chapter 1, some studies have used samples with mixed age ranges (Braams et al., 2016) or ages that are outside of a window when risk behaviors peak (Bjork & Pardini, 2015), such as restricting survey data to age 14 and imaging data to age 16 (Büchel et al., 2017). Other studies use recruitment strategies that focus on estimating the effects of puberty (Braams et al., 2016; Peper et al., 2013) or populations in disadvantaged communities (Cope et al., 2019), making it difficult to discern neural substrates of risk-taking behaviors in a normative adolescent population. These studies may be useful in answering questions about broad developmental differences and neural differences preceding risk. However, when risk-taking behaviors are recorded at different ages across studies, this can complicate conclusions related to the neurodevelopmental models. For instance, reward processing is associated with substance use in Cope et al. (2019) but not in Braams et al. (2016) and only under the condition of high sensation seeking in Büchel et al. (2017).

One way to answer the question of whether neural activation during reward processing differentiates risk-taking behaviors is to be more precise about the design and prediction of the model (Pfeifer & Allen, 2016). If the core question is, “What neural activation during reward

processing differentiates risk-takers?", one approach is to use a normative sample during the developmental peak in risk-taking behaviors and reward processing. In which case, the 18-23 age range would be an appropriate developmental peak of risk-taking (Bjork & Pardini, 2015; Steinberg et al., 2018; Willoughby et al., 2013), which renders a more precise inference about risk-taking and reward processing during adolescence.

## Current Study

In the current study, a large and diverse population of typically developing high school adolescents were recruited ($10^{th}$ and $12^{th}$ graders, N = 2017 in the full sample). Adolescents provided self-reports on real-world risk behaviors in multiple categories. To address previous limitations of broad age ranges (Pfeifer & Allen, 2016), sampling, and insufficient proxies of real-world risk (Sherman et al., 2018), as described in Chapter 2, a targeted subsample (N = 104) was recruited from the full sample representing two distinct risk-taking profiles during late adolescence. So that we can appropriately compare risk-taking profiles, the subsample of adolescents were classified as high ($75^{th}$ percentile and above) and average/low risk groups ($20^{th}$ – $60^{th}$ percentile) based on the Behavioral Misadventure Scale (BMS). This subsample completed a neuroimaging protocol to evaluate differences in neural activity that are associated with risk-taking behaviors. We utilized both whole brain and *a priori* brain regions (ROIs) from an empirical consensus based on the research literature in our analyses (Galván, 2010; Sherman et al., 2018). In a subsequent comparison, high and average/low risk groups' neural activation profiles were assessed based on the longitudinal stability of their BMS risk profiles over time, which has not been previously studied. The stable risk-taking profile may capture differences in a consistent pattern of risk-taking behavior that may be more relevant to vulnerability in long-term negative outcomes.

In these analyses, the Monetary Incentive Delay (MID) task (Knutson et al., 2000; described in Chapter 2 and discussed in depth in Chapter 3) was used to model neural activation of reward. Although this task is used to evaluate the prevailing neurodevelopmental hypothesis that greater activation in reward regions is associated with increased risk-taking behaviors, the task is not designed to answer questions about activity in cognitive control regions. Nevertheless, given the prevailing hypothesis that adolescents are motivated to approach rewards, this analysis focused on a Big Win versus Neutral cue anticipation contrasts in the MID task (Galván, 2010). While alternative contrasts have been used to model anticipation of reward in prior studies (Büchel et al., 2017; Cope et al., 2019; Heitzeg et al., 2014), the decision to use this contrast was two fold. First, this contrast was selected given prior research reporting a significant difference in activation in reward systems between adolescents and adults (Bjork et al., 2010). Second, this contrast was selected because it provides an equally weighted comparison of trials in the two conditions (i.e., 20 of Big Win and 20 of Neutral cue trials). Taken together, if the neurodevelopmental hypothesis generalizes to this sample and design, it is hypothesized that adolescents in the high-risk group will demonstrate greater activation in socioemotional regions during the anticipation of reward, especially in the VS, compared to the participants who have a low/average risk profile. Alternatively, adolescents in the low/average risk group should show decreased activation in the VS region and increased activation in the cognitive control regions, especially the dlPFC, compared to the high-risk group.

## Methods

### Participants

Participants in this study are a Phase 2 subsample ($N$ = 104; $M_{Age}$ = 19.3; $SD_{Age}$ = 1.3; 57% Female; 71% White, 14% Black, non-Hispanic, 6% Hispanic/Latinx) of adolescents from the Adolescent Health Risk Behavior (AHRB) study, as described in Chapter 2.

### Risk Group Classification: Behavioral Misadventure

A questionnaire assessed participants' self-reported engagement in 15 risk behaviors in the last 12 months. Risk behaviors included: using substances such as 1) cigarettes, 2) e-cigarettes, 3) alcohol, 4) marijuana, 5) amphetamines, 6) narcotics, 7) sedatives or 8) street drugs (including cocaine, heroin, ecstasy, and LSD); 9) distracted driving (e.g., texting while driving); 10) drowsy driving; 11) driving while under the influence of alcohol; 12) riding with an alcohol-impaired driver; 13) having unprotected sex; 14) physical fighting; and 15) other risks resulting in serious injury to oneself (e.g., riding a bicycle without a helmet). To summarize the overall engagement in risk-taking behavior, and to give adequate weighting for low frequency but high health impact risk behaviors that could be used in identifying health risk profiles, the sample was randomized into two halves to conduct a principal component analysis (PCA) with the first half and a confirmatory factor analysis (CFA) with the remaining half. A behavioral misadventure factor score (BMS), on which all the risk-taking behaviors loaded significantly, was saved for the entire sample and used in subsequent analyses (Cronbach $\alpha$ = .78). Based on this latent factor score, a high risk group was classified based on a 75$^{th}$ percentile cutoff, and an average/low risk group based on falling within the 20$^{th}$ to 60$^{th}$ percentile from the full Wave 1 sample (N = 2,017). As described in Chapter 2, this produced distinct groups that were non-overlapping (see Figure 2.3 in Chapter 2). The BMS variable had a strong association with a factor-derived score of substance

use (self-reported 12-month marijuana, alcohol, e-cigarettes, cigarettes, and illicit drug use; RMSEA: .08; CFI: .97; TLI: .95; SRMR: .03), $r$ = .94, and the number of past 12-month self-reported health risk behaviors, $r$ = .89 during Wave 1.

### fMRI Task

To evaluate the neural activation of reward processing, the MID task (Knutson et al., 2000) was used to model the neural signatures of the anticipation of monetary reward (Bjork et al., 2010). For more information on the design, please refer to Chapter 2. As noted in Chapter 2, participants were explicitly told that their performance on the task during the scan (for example, $5 Win Cue was associated with an opportunity to win $5 and a $5 Lose cue was associated with an opportunity to not lose $5) would be associated with the compensation they can get for their cumulative earnings during the MID (Maximum $30).

In these analyses, we focused on the contrast of the anticipatory Big Win versus Neutral cue. As discussed in Chapter 2, neurodevelopmental frameworks (Shulman et al., 2016) describe the marked increase in motivation towards rewarding stimuli during adolescents. The motivation towards rewarding stimuli may, in part, lead to increased engagement in risk-taking behaviors, such as substance use. The anticipation phase during the MID task (as expanded on in Chapter 4) captures a "wanting" processes that is a key component of dopamine (Berridge & Kringelbach, 2015), making is a reasonable phase to model for capture adolescent reward sensitivity.

### fMRI Data Acquisition

FMRI data was acquired using the protocol described in Chapter 2.

## Analyses

### fMRI Data Analyses

FMRI data was preprocessed using the sequence of steps that are described in Chapter 2.

First-level analyses were performed by using FEAT. To control for the temporal effect of motion of the BOLD signal, we used the command *fsl_motion_outliers* to generate an additional confound list censoring frame displacement (FD) volumes that exceeded FD > .9. To average across the two runs, a second-level model was defined for each participant using fixed-effect analysis in FEAT.

Whole Brain

Group-level analyses were performed using non-parametric permutation tests to create null non-parametric distributions and control type 1 error rates (Eklund et al., 2016), with cluster correction performed using Threshold-Free Cluster Enhancement (TFCE) in order to differentiate both focal and broad level activation that may be lost using standard parametric models (Smith & Nichols, 2009; Winkler et al., 2014). As described in Pfeifer et al. (2019), non-parametric models reduce assumptions about spatial distributions of noise within fMRI and reduce false positive rates.

Regions of Interest

*A priori* regions of interest (ROI) from Neurosynth (www.neurosynth.org) were used to evaluate differences of mean signal intensity for reward anticipation in high versus average/low risk groups (Appendix B, Table B1). These regions were selected based on overlap in original descriptions of the dual systems models (Casey et al., 2008; Ernst, 2014; Steinberg, 2008) and from 18 studies, Appendix B, Table B2 (totaling 70 coordinates, with overlap; see Appendix B, Figure B1) described in two reviews of adolescent neurodevelopment and risk behavior findings (reviewed in Galván, 2010; Sherman et al., 2018).

To control the type 1 error rate and to consider relationships among ROI's that may differentiate risk and age profiles, a Multivariate analysis of variance (MANOVA) was performed. Subsequently, to examine the association between risk profile and mean signal intensity of each

ROI, fourteen multiple regression models were performed, controlling for age. False Discovery Rate (FDR) was used to control for multiple comparisons (14 multiple regression models), and adjusted p-values were reported where significant differences arise (Benjamini & Yekutieli, 2001; Noble, 2009).

### Post-hoc Analyses

To evaluate the effects of stable, multi-wave risk profiles, a combination of self-report measures of risk-taking behaviors across W1-W3 was used to define 'stable high' (that is, 75$^{th}$ percentile or higher on two waves of survey responses) and 'stable average/low' (20$^{th}$-60$^{th}$ percentile on two waves of survey responses) risk profiles. These profiles were used to re-examine the ROI and whole brain analyses to determine whether there were significant differences between the stable high versus stable average/low risk behavior profiles used to predict neural activation.

## Results

### Descriptive and Behavioral

There were no significant group differences between overall performance (accuracy and response times) in the high and average/low risk groups ($p > .05$) during MID trials nor for Big Win or Neutral trials (Table 3.1). The accuracy scores were derived from adaptive testing to ensure an approximate success rate of 60%, which was achieved, indicating that the manipulation worked. The absence of an accuracy difference should not be interpreted as a meaningful finding. Notably, as described in Chapter 2 and Appendix A, response times were collected by E-Prime only for accurate trials. Finally, there were no significant differences in time before Phase 1 Wave 1 and Phase 2 Wave 1 scan 1, sex, or parental education between groups ($p > .05$; Appendix A, Figure A1).

*Table 3.1.* Demographic characteristics and behavioral performance of full sample completing the Monetary Incentive Delay Task by Risk Profile

| | Average/low | High | Total | Effect Size |
|---|---|---|---|---|
| | *n* = 63 | *n* = 41 | *n* = 104 | |
| Sex, Female *n* (%) | 37 (58.7) | 22 (53.7) | 59 (56.7) | Φ = .02 |
| Race, *n* (%) | | | | |
| Black, non-Hispanic | 12 (19.0) | 3 (7.3) | 15 (14.4) | |
| White, non-Hispanic | 40 (63.5) | 34 (82.9) | 74 (71.2) | |
| Other | 5 (8.0) | 1 (2.4) | 6 (5.7) | |
| Hispanic/Latinx | 6 (9.5) | 3 (7.3) | 9 (8.7) | |
| | *M (SD)* | *M (SD)* | *M (SD)* | |
| Age | 19.0 (1.2) | 19.8 (1.3) | 19.3 (1.3) | *d* = .64** |
| Parental Education | 4.4 (1.1) | 4.1 (1.2) | 4.3 (1.2) | *d* = .26 |
| BMS | -0.28 (0.1) | 0.83 (0.8) | 0.16 (0.6) | *d* = 1.95*** |
| Overall Acc. % | 57.4 (3.2) | 56.2 (3.1) | 56.9 (3.2) | *d* = .38 |
| Win Big | 63.7 (9.2) | 61.2 (9.1) | 62.7 (9.2) | *d* = .27 |
| Win Small | 56.8 (9.5) | 59.3 (9.7) | 57.8 (9.6) | *d* = .26 |
| Neutral | 49.8 (14.2) | 44.5 (14.5) | 47.7 (14.5) | *d* = .37 |
| Lose Small | 56.3 (9.5) | 56.5 (7.7) | 56.4 (8.8) | *d* = .02 |
| Lose Big | 60.2 (10.5) | 59.4 (10.4) | 59.9 (10.4) | *d* = .08 |

BMS = Behavioral Misadventure Score; WASI IQ = Wechsler Abbreviated Scale of Intelligence; Parental Education: 1 = grade school or less, 2 = Some High School, 3 = Completed High School, 4 = some college, 5 = completed college, 6 = graduate or professional school. Acc = Accuracy; d = Cohen's d (Small = .2; Medium = .5, large = .8)
*p* < .05*, *p* < .01**, *p* < .001***

As expected, high risk (N = 41) and average/low risk (N = 63) groups varied with respect to age. Specifically, those in the high risk group were significantly older (p < .01, *d* = .64; M = 19.8, SD = 1.3) than those in the average/low risk group (M = 19.0, SD = 1.2; see Table 3.1). Due to the significant age-related difference found in sensitivity to reward processing in previous studies (Bjork et al., 2010; Dhingra et al., 2019), age was covaried out in the subsequent

analyses. Age was significantly related with risk groups ($r$ = .30) and the continuous BMS variable ($r$ = .39).

Region of Interest (ROI) Analyses

To examine the association between reward anticipation and adolescent risk behaviors, we used hypothesis-driven *a priori* ROIs to examine recent theoretical models (Appendix B, Table B1). Among the 14 ROIs, the MANOVA revealed no significant activation difference between risk profiles (average/low versus high), Wilk's lamba = .83 $F(14, 87) = 1.26$, $p$ = .25, nor an interactive effect of risk group (high versus average/low) and age, Wilk's lamba = .93 $F(14, 87) = 0.93$, $p$ = .53. This indicated that there were no adjusted-mean differences in reward anticipation activation among the 14 ROIs that are associated with age or self-reported risk. In the multiple regression models examining the association between risk profile (high versus average/low risk) and activation to the anticipation of Big Win versus Neutral trials among the 14 ROI's, controlling for age, there were no significant associations when correcting for multiple comparisons (Appendix B, Table B3, for corrected and uncorrected values).

Whole Brain Analyses

Consistent with prior work using the MID task, the task used in this study evoked robust activation of the reward regions during reward anticipation as hypothesized (Appendix B, Figure B3). To examine whether Wave 1 high risk (N = 41) and Wave 1 average/low risk (N = 63) groups differed in neural activation during reward anticipation, we conducted a nonparametric whole brain analysis (adjusted for age). Contrary to the hypothesized neurodevelopmental models, and reflecting inconsistencies in recent literature, there were no significant group differences in activation in brain regions specified in the neurodevelopmental models (e.g, aforementioned *a priori* ROI's). Moreover, the high risk group (N = 41) did not exhibit greater

activation in any voxels/clusters when compared to the average/low risk group (N = 63). However, consistent with recent evidence (Sherman et al., 2018), in a direct contrast between groups, the average/low risk group exhibited several significant clusters in the whole brain analysis when compared to the high risk group that were outside of the regions specified in the neurodevelopmental models. Specifically, the average/low risk group had greater activation ($p <$ .05; FWE-Corrected) in the dorsal striatal, precuneus, posterior parietal, primary visual cortex, primary motor cortex, and cerebellar regions (see Table 3.2; Figure 3.1).

*Table 3.2.* Whole Brain Analyses: significant differences in activation for Average/low versus High Risk group adolescents to anticipation of Big Win versus Neutral contrast

| Wave 1 Average/low (N= 63) > High (N = 41) Risk-taking | | | | |
|---|---|---|---|---|
| Cluster Index[a] | Cluster peak x, y, z | # of Voxels | Cluster Label [b] | *p* * |
| 14 | *-15, -3, 16* | 722 | Left-Caudate | .03 |
| 13 | *22, -62, -16* | 208 | Right Cerebellar | .03 |
| 12 | *16, -82, 4* | 129 | Right Primary Visual | .04 |
| 11 | *-22, -72, 2* | 70 | Left Primary Visual | .04 |
| 10 | *-17, 23, 12* | 44 | [c]Left-Caudate Nucleus | .04 |
| 9 | *6, -74, 10* | 36 | Right Primary Visual | .04 |
| 8 | *-10, -60, 50* | 36 | Left Precuneus | .04 |
| 7 | *18, -36, 34* | 25 | [c] Posterior Cingulate | .04 |
| 6 | *-16, -50, -8* | 22 | Left-Secondary Visual | .04 |
| 5 | *34, -30, 28* | 19 | [c] Left-Parahippocampal | < .05 |
| 4 | *4, -40, 42* | 17 | Posterior Cingulate | < .05 |
| 3 | *-4, -32, 62* | 11 | Primary Motor | < .05 |
| 2 | *-4, -72, -2* | 10 | Left Visual | < .05 |
| Longitudinally Stable Average/low (N = 37) > Stable High (N = 33) Risk-Taking | | | | |
| Cluster Index[a] | Cluster peak x, y, z | # of Voxels | Cluster Label [b] | *p* # |
| 4 | *30, 32, 34* | 181 | Right Dorsolateral Prefrontal Cortex | .052 |
| 3 | *-8, -60, 48* | 17 | Left Precuneus | .071 |
| 2 | *4, 20, 40* | 15 | Paracingulate Gyrus | .074 |

**[a]** Cluster index identified using fsl command *cluster* that identified peak clusters in volume, index 1 not reported due to number of voxels = < 3, clusters plotted on MNI brain in Figure 3.1 and Figure 3.2.
**[b]** To identify region for cluster label, we used a combination of reverse inference on neurosynth.org/locations to identify top association with cluster activation and cross-referenced with *FSL Harvard-Oxford Cortical Structural Atlas*
**[c]** Implies regional association, due to peak being in white matter.
* Probability $\alpha < .05$ used to threshold results of TFCE output from randomise
# Lowered $\alpha < .08$ used to threshold results of TFCE output from randomise (< .05, results null)

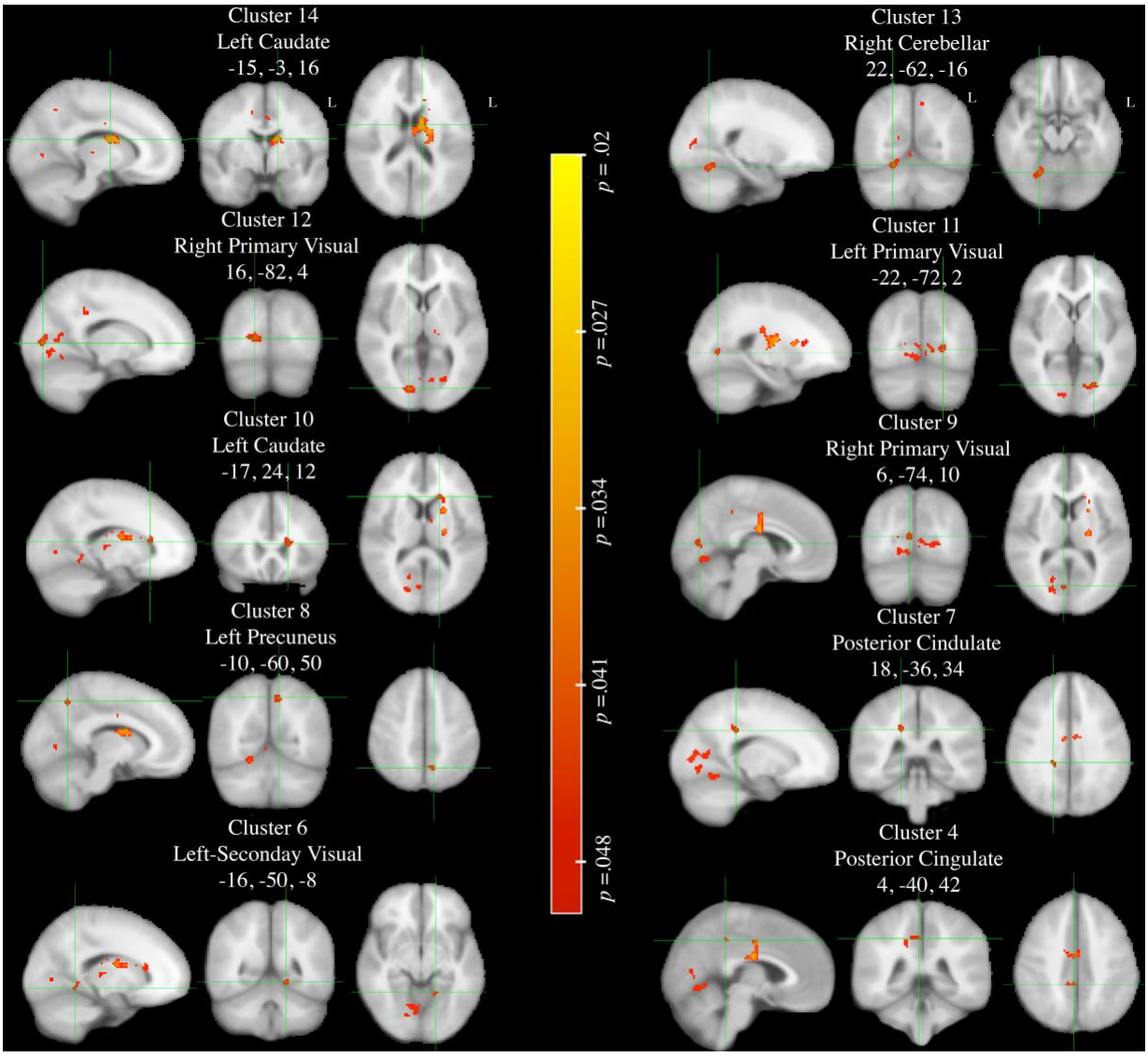


*Figure 3.1.* Whole Brain Permutation Wave 1: Average/low Risk > High Risk Profile during (FWE-corrected) anticipation of Big Win versus Neutral contrast, thresholded $p < .05$
Non-permutation test includes 5000 permutations, using FSL *randomise* with threshold-free cluster enhancement. Statistical maps thresholded at lower value .05 – clusters selected from Table 3.2

Post-hoc Analysis of Adolescents with Stable-Risk Group Membership

For the multi-wave comparison of risk profiles, reward anticipation for stable high and stable average/low were compared. As expected, based on the age effects noted above, there was a significant difference in the number of adolescents that moved to the high risk group versus moved to the average/low risk group ($X^2(3) = 94.6$, $p < .001$, $\Phi = .98$), whereby 23 adolescents (Mean Age = 18.6, SD = 1.1) moved from the average/low risk group to the high risk group and five adolescents (Mean Age = 19.0, SD = 1.4) moved from the high risk group to the average/low risk group. Participants that moved into high risk or average/low risk groups across waves did not significantly differ in age, sex, or parental education ($p > .05$). After excluding adolescents that transitioned to different risk groups (N = 27) and those that did not complete a questionnaire in a subsequent wave (N = 6), 71 adolescents had longitudinally stable risk profiles: 37 stable average/low risk (M Age = 19.0, SD = 1.3) and 34 stable high risk (Mean Age = 19.8, SD = 1.3). Analyses between the stable high risk and average/low risk groups provided a more stringent test of this individual difference.

Post-hoc Region of Interest Analyses

The post-hoc analyses, evaluating ROI differences in stable high risk versus stable average/low risk groups, demonstrated comparable results to the wave 1 risk profile. Specifically, the analysis of variance among the 14 ROIs, MANOVA revealed no significant association between risk profiles (average/low versus high), Wilk's lamba = .67 $F(14, 53) = 1.82$, $p = .06$, and no interactive effect of risk group (high versus avg/low) with age, Wilk's lamba = .85 $F(14, 53) = 0.64$, $p = .81$. Like Wave 1 risk profiles, stability of profiles over time did not reveal a relationship among the 14 ROI's. Moreover, the 14 multiple regression models revealed comparable results to the Wave 1 risk groups. In the multiple regression models, when corrected

for multiple comparisons, there were no significant associations between risk-taking profiles and the mean activation during Big Win versus Neutral contrast (Appendix B, Table B3, for corrected and uncorrected values).

Post-hoc Analyses Whole Brain Analyses

The post-hoc analysis, evaluating the whole brain activation to the anticipation of Big Win versus Neutral condition in stable high risk versus stable average/low risk groups, demonstrated different results from that of the Wave 1 sample-defined risk profiles. Specifically, the nonparametric TFCE analysis revealed no significant clusters that surpassed the $\alpha < .05$. At a lower threshold of $\alpha < .08$, in a direct contrast between groups, significant clusters were revealed (see Table 3.2; Figure 3.2). Specifically, greater activation was shown in the Left Precuneus ($p$ = .07) in average/low risk versus high risk groups. Likewise, at a lower threshold ($p < .08$), average/low risk-takers demonstrated greater activation in the Right dlPFC (p = .05) and the Paracingulate Gyrus (p = .07). These results suggest slight convergence with, in addition to variability between, the single versus multiple wave assessment of risk profiles in whole brain activation that necessitates increased power. Notably, using the Euclidean distance between peak coordinates

$$\sqrt{(x_{whole\ brain} - x_{ROI})^2 + (y_{whole\ brain} - y_{ROI})^2 + (z_{whole\ brain} - z_{ROI})^2} \quad (3.1)$$

used by Hong et al. (2019, pp. 387), when comparing the peak location of dlPFC in the whole brain results to that of the *a priori* dlPFC coordinate, there was a 64.5mm distance between peaks, suggesting difference in the location of peak activation. Furthermore, like the stable profile subsample (N = 71) and the full sample (N = 104), activation in the Right dlPFC was present only at a lower threshold, $p$ = .05 and $p$ = .06, respectively. Statistical maps of tests and

presentations of ROIs from meta-analysis coordinates are available on Neurovault (neurovault.org/collections/6282/).

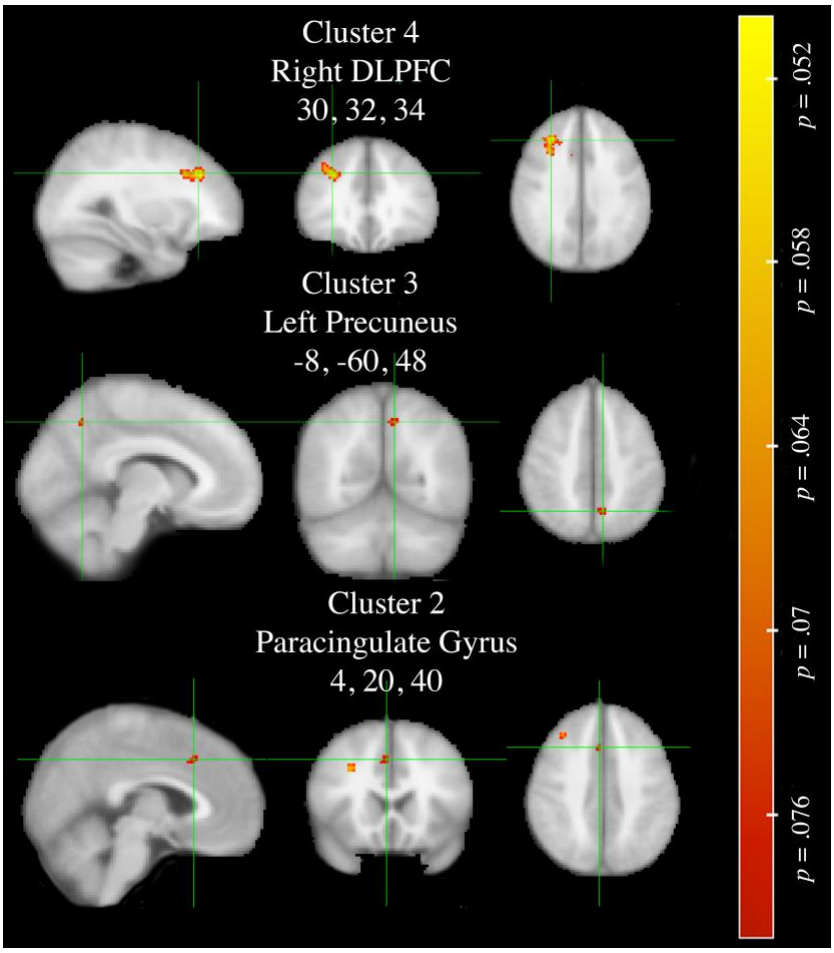


*Figure 3.2.* Whole Brain Permutation Longitudinally Stable Average/low > High Risk groups during anticipation of Big win versus Neutral contrast, thresholded $p < .08$ (FWE-corrected)

DLPFC = Dorsolateral prefrontal cortex.
Non-permutation test includes 5000 permutations, using FSL *randomise*

Sensitivity Analyses

To examine whether there was a continuous effect of BMS and/or from Wave 1 on brain activation during Big Win versus Neutral anticipation phase during the MID task, we created a nonparametric model (FSL *randomise*) to test the continuous variables of BMS, age and brain. The continuous BMS model, covaried for age, demonstrated no significant associations ($p > .05$) between BMS and brain. However, at a lower bound threshold ($p < .08$), comparable clusters were found in the continuous BMS model (Appendix B, Table B4) and the dichotomous comparison of high versus average/low risk groups (Table 3.2). This reduced effect in the

continuous model may be explained by the increased association between BMS and age (*15%*) versus risk group and age (9%). Meanwhile, no significant effect of age (continuous) on brain was present, with or without the covariate of the BMS in the non-parametric model.

## Discussion

Over the last 15 years, several neurodevelopmental models have been proposed to explain, in part, the rise in risk-taking behaviors during mid-to-late adolescence. Despite a strong commitment to exploring the neural differences in socioemotional and cognitive control processing across a broad age-range, inconsistencies in definitions of age and risk-taking have led to mixed interpretations (Crone & Dahl, 2012). Furthermore, proxies of risk-taking behaviors and *a priori* ROI analyses have contributed to heterogeneous results that have not replicated the postulates from theoretical models (Sherman et al., 2018). To our knowledge, this study is the first to use several ecological measures to derive high risk and average/low risk profiles among adolescents, as well as longitudinally stable profiles of high risk versus average/low risk, to explore prospective neurodevelopmental differences using both *a priori* ROI and whole brain analyses. The variability in results and lack of generalizability of neurodevelopmental models in this and prior studies may be related to sample sizes, independent variable and parameter selection, ROI identification, and an assumption of homogeneity in adolescents.

Using prior literature and predefined ROIs based on neurodevelopmental models, there was little evidence for increased recruitment of reward neurocircuitry in high risk versus average/low risk profile adolescents during the anticipation of rewards. Although frequently researched regions, specifically the ‘hot spots’ of reward processing (Woo et al., 2017) like the ventral striatum, produced the predicted robust activation in statistical maps during the anticipation of a big monetary reward compared to a neutral cue, this activation did not

differentiate risk-taking profiles among adolescents. In some ways, the latter finding supports the notion evoked by Sherman et al. (2018), whereby studies have not consistently found differences across risk-taking behaviors that are often cited by neurodevelopmental models.

To avoid constraining interpretations to *a priori* ROIs and behavioral properties of the task, a nonparametric analysis on the whole brain was conducted that revealed both significant and non-significant results. In the initial comparison of high risk versus average/low risk profiles from Wave 1, the comparison revealed increased activation in the high risk group across a broad range of brain regions. These included the dorsal striatal, primary visual, primary motor, precuneus, posterior cingulate, and cerebellar regions. However, when using more than one wave of self-report risk-taking behaviors to quantify stable high risk and average/low risk profiles, the activation differed from the Wave 1 whole brain analysis. Specifically, neither of the clusters of activation based on Wave 1 analysis were represented in the stable high risk and stable average/low risk analysis at a $p < .05$ level. Taken together, the findings indicate differences in independent variable and parameter selection, whereby power and the heterogeneity across subjects alters results.

Recent inconsistencies in findings in the neurodevelopmental literature can be attributed to multiple sources, such as sample sizes (Button et al., 2013; Cremers et al., 2017) and non-independent analyses which can contribute to 'voodoo' correlations (Vul et al., 2009). It has been noted in recent reviews that neuroimaging studies suffer from small sample sizes, where the average sample size in adolescent risk behavior literature is <50 participants (Galván, 2010; Sherman et al., 2018). Cremers et al. (2017) argued that small samples, such as N = 30, are one source of misleading results. A review of early fMRI research demonstrated that a frequent strategy used was to compute separate correlations of voxels/clusters with behavior that

exceeded a threshold in a group-level map. This led to brain and behavior correlations that, on occasion, exceeded even the intraclass correlations of the brain regions of interest (Vul et al., 2009). Some of these correlations are attributable to extremely small samples that systematically inflate correlation between neural activation and behavior (Yarkoni, 2009).

Equally as important, the differences in tasks and contrasts between studies are often overlooked. For example, in the 23 studies of adolescent risk-taking reviewed by Sherman et al. (2018), it is evident that several different tasks are administered in the literature, such as the MID, Stoplight signal, Wheel of Fortune, Iowa Gambling, and Coin-flip task. While attempting to model associations with risk-taking behaviors, these tasks likely vary in the cognitive processes they engage (Richards et al., 2013). These between-study differences of tasks make it difficult to discern the generalizability of neural associations with behavior. Animal models have demonstrated that learning what to approach and what not to approach is variable. While some circuits are related to prediction error, others may be related to goal-oriented models (Eshel & Steinberg, 2018). For instance, the Balloon Analogue Risk Task (BART), MID, or Wheel of Fortune tasks may relate to distinct circuits that play an important part for learning the action and event values through trial and error. Whereas affective and peer paradigms may relate to efferent working models that make decisions regarding future events which may impact goal-directed choice. In the latter decision-based tasks, values are estimated with each action using inferences based on costs, benefits, and some forms of neural signals' ability to generalize to new situations (Rangel & Hare, 2010; Schultz, 2015).

Distinctions in how decisions are made may be critical as there are heterogeneities in animal behaviors, whereby some rely on trial-and-error and others on goal-directed choice (Eshel & Steinberg, 2018). With respect to neural properties, such intricacies may impact the region of

activation. Although the VS/NAcc dominate the core locations of risk/reward processing in the neurodevelopmental models, neural processing may depend on different aspects, such as the type of learning (or encoding paradigm). If this is the case, differences between designs may depend on whether the processing relates to afferent or efferent systems, whether a reward is contingent on action, and/or whether a stimulus is related to a primary or secondary reward (Haber & Behrens, 2014; Padoa-Schioppa & Conen, 2017; Szczepanski & Knight, 2014). These distinctions are critical in assessing whether results do (or do not) converge across studies and have a similar predictive utility.

Studies evaluating the central tenets of the neurodevelopmental models have largely interpreted the task activation of the VS/NAcc to reflect approach (or motivation to act) which may be associated with risky behaviors. Approach systems, however, may also be related to attentional processes and thus be difficult to disentangle using abstract task contrasts. There is growing evidence that the VS (which includes the NAcc) is actively involved in effort and intrinsic motivation (Schouppe et al., 2014), which can be associated with value (Inzlicht et al., 2018). Therefore, activity during task performance in some brain regions, such as the VS/NAcc and dorsal striatum, may reflect an interactive effect of reward and attention (Breckel et al., 2011; Krebs et al., 2012). If this is the case, reward and attention may arise from similar neural mechanisms (Westbrook & Braver, 2016), making it difficult to derive an accurate assessment of reward using abstract methods of subtraction in task-based fMRI (Poldrack & Yarkoni, 2016). This is a core issue that I elaborate on in Chapter 4 as it relates to the MID task and in Chapter 6 as it relates to evaluating the nomological network. To derive improved estimates of *reward* or *risky decision making* in task-based fMRI, increased attention should be given to the construct validity of tasks and their hypothesized estimates of cognitive processes.

Outside the domain of neural estimates, there is substantial heterogeneity in the behavioral definition of risk-taking behaviors. Research on normative samples often utilizes variables that may not be ecologically valid proxies of real-world risk behavior. While some use psychological characteristics such as sensation seeking (Bjork et al., 2008b; Kahn et al., 2015), general measures of risky behaviors (Op de Macks et al., 2016; Saxbe et al., 2015), substance use (Bjork et al., 2011; Chung et al., 2015), or the likelihood of engaging in future risk (Galvan et al., 2007), several studies associate neural activation as a function of a task parameter of risk. For example, studies use parameters from risky driving (Cascio et al., 2015), probability, or gambling tasks (Eshel et al., 2007; Op de Macks et al., 2016; Qu et al., 2015; Telzer et al., 2015). These proxy-based measures of risky behavior may be inappropriate as laboratory tasks since they require larger samples to capture small effects (Sherman et al., 2018), show limited evidence for age-related differences (Defoe et al., 2015), and often serve as weak predictors of real-world risk behaviors in normative adolescent populations (Demidenko et al., 2019).

For neurodevelopmental models to be used as indicators of sensation seeking and risk behaviors, it is important to acknowledge that adolescent behavior is heterogeneous and that this behavior should be modeled as such (Bjork & Pardini, 2015; Sherman et al., 2018). With respect to the dynamic system of the brain, the assumption that individuals are homogenous is often violated (Beltz et al., 2016). Thus, it is important to identify unique and similar patterns in the individuals which, in turn, may be used to more effectively explain behavioral change (Beltz & Gates, 2017). This alternative technique may be more appropriate in identifying networks, which have been proposed in earlier reviews (Pfeifer & Allen, 2012), that may offer some stability of measurement within and between participants, as opposed to the mean-level task effects that often have weak test-retest reliability (Elliott et al., 2019). Since the location of activation in a

particular region may vary between samples (or individuals; see Hong et al., 2019), response-patterns or heterarchical systems may be an alternative method to model differences in location, timing, or interactions of neural activation (Haxby et al., 2011; Pessoa, 2017). Moving forward, a measure that accounts for the brain being a dynamic and plastic system may be more appropriate to speculate about the interaction of neural systems, how these systems change across tasks and time, and what the underlying neural signatures of risk-taking may entail. I address this topic further in Chapter 6.

## Study Considerations

Although this study attempts to quantify risk behaviors in developing adolescents, the limitation of the analyses is that some of the parameters vary from previous studies. Prior work that evaluated risk-taking behaviors and neural activation incorporated cross-sectional and longitudinal analyses differed in the definitions of risk and task parameters. For example, in cross-sectional samples, while Benningfield et al. (2014) examined the association between discounting (as measured by Monetary Choice Questionnaire) and differences in activation to big, small, and neutral rewards, Claus et al. (2018) examined the moderating effect of substance use on the association between brain activation and risk-taking tendencies during the BART. In longitudinal analyses of adolescent risk behaviors, Qu et al. (2015) explored the mediating effect of the VS activation on the association between parent-child relationships and risk-taking during the BART. In a separate longitudinal analyses, Braams, van Duijvenvoorde, Peper, & Crone (2015) examined associations between changes in the NAcc response during a Two Choice task (heads or tails) and risk performance as captured by the BART as well as self-report measure of the Behavior Inhibition System/Behavior Action System. Not surprisingly, due to variability in

definition of risk and parameters, results varied from study to study. In Chapter 3, I will elaborate on this variability as it arises within task contrasts, such as the MID.

Importantly, this study focused on individual differences among adolescents. Thus, the results do not capture age-related change that is represented in the neurodevelopmental models. Instead, this study focused on variation across risk profiles, both cross-sectionally and longitudinally, to determine whether the variability in risk-taking behavior among adolescents, at or near the developmental peak of risk-taking, can be explained by neural activation that has been posited by previous models. Although age-related effects were not present here, the age-related trends may still be evident in the models but the heuristics may not necessarily provide the evidence necessary to explain differences between adolescents who do and do not engage in risk behaviors, as was previously suggested (Spear, 2000).

## Conclusion

This is the first study to our knowledge that examines differences in neural activation across real-world risk profiles (from multiple waves) at a focal-age range when risk behaviors peak during adolescence. The results in this study demonstrate that the previously hypothesized models did not explain the variation in risk profiles and whole brain differences may depend on how risk profiles are defined. Moreover, common hot spots of reward related research, such as the VS, do not differentiate general risk profiles among adolescents, even though the task elicited a robust activation pattern that replicates prior research. The lack of generalizability suggests researchers should reassess how individual differences in risk are measured and modeled in the developing adolescent brain, and how these measurement differences influence reproducibility of results, predictive utility, and interpretation for future interventions.

## Chapter 4 : Methodological and Interindividual Variability: How Monetary Incentive Delay (MID) Task Contrast Maps Vary and Impact Associations with Behavior[2]

Due to the hypothesized role of reward systems in wanting, liking, and learning about rewarding stimuli, neural measurements of reward processing have become a central focus in the study of various psychopathologies and problem behaviors (Berridge & Robinson, 2003; Ernst & Luciana, 2015). The Monetary Incentive Delay (MID) task, which was introduced in Chapter 2 and used in Study 1, specifically, has been frequently used to measure neural substrates of approach and avoidance mechanisms during reward processing (Knutson et al., 2000). Univariate contrasts that index neural activation during different stages of the MID task, have been employed to study dysfunction in reward related processes and various maladaptive behaviors (Balodis & Potenza, 2015; Dugré et al., 2018). More recently, the task has been incorporated into large scale longitudinal studies (Casey et al., 2018; Schumann et al., 2010) to index developmental changes in reward mechanisms and their links with negative behavioral outcomes. Despite frequent use of univariate contrasts from this task, there are relatively few studies that have examined how methodological choices made by investigators (e.g., researcher degrees of freedom), such as contrast choice, may impact their results and interpretations about their findings. Therefore, this study aims to clarify the interaction between methodological and

[2] Chapter 4 corresponds to Demidenko et al. (2021), published in *Brain & Behavior*

interindividual variability in MID task contrast maps, and how these interactions affect their associations with psychological measures including substance use and socioemotional functioning. These analytic choices may in part propose an explanation for the variability in findings between studies as described in Chapter 1 and Chapter 3.

## The MID task and Theories of Reward Processing

As of this publication, the MID task has been used in functional magnetic resonance imaging (fMRI) research for 20 years and is considered a robust measure of incentive motivation (Knutson et al., 2000; Knutson & Greer, 2008). The *instrumental-reward task* delivers rewards that are contingent on performance involving a timed button response (Richards et al., 2013), whereby different neural regions are recruited depending on whether the reward is being anticipated (i.e., wanted) or consumed (i.e., liked) (Haber & Knutson, 2010).The task was designed to localize reward-related brain activation in substance use populations (Knutson & Heinz, 2015) and identify correlates of individual differences in positive and negative arousal (Wu et al., 2014). A central assumption of the task, inspired in part by the literature on Pavlovian conditioning (Pavlov, 1927) and dopamine responses to positive cues (Schultz, 1998), is that there are brain regions responsible for anticipating and responding to salient stimuli that have positive or negative valence. Projections from the dopamine (DA) rich ventral tegmental area (VTA) are thought to enhance activation in striatal regions that respond to reward anticipation (e.g., tones or cues that predict incentives) and in mesial prefrontal regions that respond to reward outcomes (Breiter et al., 1996; Knutson et al., 2000). The task allows a comparison of valence (winning, positive valence, or losing, negative valence, big or small rewards) and temporal phase (anticipation or outcome).

Activation patterns within anticipation and outcome phases would be expected to align with recent theories of reward processing. For instance, the first stage during cue presentation (prior to probe, or response phase), may be modeled as a 'wanting' phase, eliciting motivation (or saliency of the reward/cue). This *anticipation phase* should evoke robust activation in striatal regions as DA has been shown to have robust effects on wanting (or incentive salience) in both animals and humans in the ventral striatum (VS) and ventral pallidum (Berridge, 2007, 2019; Berridge & Kringelbach, 2015). Conversely, when modeling the *outcome phase* (or liking), one would expect less activation of VS (as only ~10% of neurons in NAcc facilitate pleasure) in response to the pleasure of reward. Hedonic 'hot-spots' are more likely to be represented in the insula and OFC (Berridge & Kringelbach, 2015) which are reported to be modulated by opioid receptors (Berridge et al., 2010; Buchel et al., 2018; Korb et al., 2020).

It is notable that the specific univariate contrasts used to index reward-related psychological constructs often vary considerably between studies. In cases of wanting rewards, reward anticipation is operationalized using contrasts such as: All Win versus Neutral (Bourque et al., 2017; Martz et al., 2018; Xu et al., 2017), Big Win versus Neutral (Cao et al., 2019; Cope et al., 2019; Papanastasiou et al., 2018) or Big Win versus Small Win cues (Stevens et al., 2018; van Hulst et al., 2015). Likewise, in the case of reward consumption, reward feedback is operationalized using contrasts such as: Reward Hit versus Neutral Hit (Chan et al., 2016; Mikita et al., 2016; Swartz et al., 2019) or Reward Hit versus Reward Miss cues (Mikita et al., 2016; Navas et al., 2018; Richards et al., 2016). The use of different contrasts to probe the same reward-related constructs is one major source of variability in the MID literature.

The vast majority of fMRI analyses using the MID task focus on specific, unmodulated phases of the task. However, previous work suggests that modulators based on formal models of

reinforcement learning may be important to incorporate into the task to account for individual variability not captured in standard subtraction analysis (Bjork et al., 2010; Oldham et al., 2018). Although reinforcement learning models have been successfully applied to the MID task (Cao et al., 2019), the utility of prediction error is still debated (Berridge & O'Doherty, 2014) and it remains to be seen how expected value and prediction error model parameters (positive or negative) modulate the signal in the anticipation and outcome phases. Such modulators may be critical in accounting for individual level variation that drives performance and learning values that may be represented in subcortical and cortical neural signatures (Balleine & O'Doherty, 2010). As contingencies in the MID are based on performance, and therefore relatively uncertain, the task differs from traditional RL paradigms used to investigate prediction-errors. Nonetheless, previous work has recommended the use of modulators in the MID task (Bjork et al., 2010; Oldham et al., 2018), and recent studies have found that prediction error was positively related to activation in the bilateral VS (Cao et al., 2019) and substance use problems in young adults (Cao et al., 2020).

## Differential use and Researcher Degrees of Freedom in MID Task

Although the MID task has been used extensively to study dysfunctional reward processing in populations with substance use disorders (Balodis & Potenza, 2015), it has also been incorporated into other studies of neurodevelopment and broader psychopathology. In addition to the use of predicting health risk behaviors of adolescents (see Chapter 3), various versions of the MID task have been used to investigate reward related changes as a function of age (Bjork et al., 2010; Dhingra et al., 2019), social vs non-social rewards (Schwartz et al., 2019), psychosocial characteristics of impulsivity and sensation seeking (Büchel et al., 2017; Cao et al., 2019; Joseph et al., 2016), early adversity (Boecker et al., 2014; Gonzalez et al.,

2016), substance use (Aloi et al., 2019; Cope et al., 2019; Karoly et al., 2015; Nestor et al., 2019; Sauder et al., 2016; Swartz et al., 2019), depression (Chan et al., 2016; Colich et al., 2017; Landes et al., 2018; Mori et al., 2016), and other psychiatric symptoms (Bourque et al., 2017; Lancaster et al., 2016; Maresh et al., 2019; Mikita et al., 2016; Papanastasiou et al., 2018; Stevens et al., 2018; Urošević et al., 2016; Veroude et al., 2016; von Rhein et al., 2015; Xu et al., 2017). Across these studies, a wide range of brain-behavior effects are reported. In addition to using different versions of the MID task, the studies cited above often used different univariate contrasts to derive activation maps. For example, the contrasts of choice in Chapter 3 was Big Win versus Neutral cue anticipation, but how different would the conclusions be if the All Win versus Neutral cue anticipation contrasts had been selected, as some prior neurodevelopmental studies have done (Heitzeg et al., 2014; Martz et al., 2018)? This raises the question: To what extent do analytic methods, such as variation in univariate contrast selection, inform differences and/or similarities in conclusions about psychological characteristics?

Empirical evidence suggests that analytic decisions may result in substantially different interpretations of fMRI analyses. Carp (2012) demonstrated that the analytic flexibility in fMRI can generate thousands of statistical maps that can be used in subsequent analyses. As shown by Botvinik-Nezer et al. (2020), the level of flexibility in task-based fMRI analyses can produce different outcomes even when using identical data and hypotheses. Specifically, seventy different teams analyzed identical fMRI data with pre-defined hypotheses regarding risky decision making. Despite the similarities across data and hypotheses, between-lab differences in contrast selection and region of interest specification substantially altered the interpretation of results. Thus, without a clear understanding of how analytic decisions impact our results and

interpretations, the flexibility of fMRI analyses (e.g., "researcher's degrees of freedom") may result in an unacceptable number of false positives (Gelman & Loken, 2014).

In the MID task, it is not well understood how investigators' analytic choice of contrasts (for example, defining anticipation of reward as: $5 Win Cue vs Neutral Cue, or both Win Cues ($5 & $0.20) vs Neutral Cue) may impact their inferences about the association between the neural response to reward and reward-relevant behavior. FMRI activation maps differ as a function of reward type/magnitude (Bjork et al., 2010) and recent reviews offer examples of the variability across studies in the techniques used to derive such maps (Balodis & Potenza, 2015; Dugré et al., 2018; Oldham et al., 2018). Contrast selection is important to the interpretation of the reported effect because experimental and baseline conditions are hypothesized to reveal cognitive processing components that are reflected in neural activation (Caplan, 2007). Yet, different reward contrasts, such as Big Win versus Neutral (as deployed in Chapter 3) or Big Win versus Small Win cues, may be used interchangeably in the literature. Combined with publication biases, the diverse sets of analyses may contribute to underreported contrasts and associations with behavior that may relate to the arbitrary decisions in the analytic pipeline (Simmons et al., 2011). Therefore, it is important to quantify how univariate contrast-related variation in activation maps within a given sample influences the relative utility of these maps for predicting behavioral outcomes. This would demonstrate whether there is a) stability within estimates of activation at each phase of the task (anticipation or outcome); b) consistency between conceptually-related contrasts in the level of activation in specific regions of interest (ROI; such that there is higher correlation within win than between win and loss anticipation); and c) whether choice between contrasts that, in theory, probe a shared cognitive process, such as

anticipating rewards, alter associations between neural activation and a psychological characteristic.

This would be difficult to deduce from a meta-analysis for several reasons. First, meta-analyses typically assess spatial overlap between contrasts and/or assess relations between different contrast activations and external covariates (e.g., behavioral scales or clinical disorders), but do not assess whether activations from these contrasts represent distinct versus largely overlapping individual difference dimensions. Second, most empirical studies report a constrained number of MID contrasts, while in some cases making post-hoc justifications for why a particular contrast, or set of contrasts, was included in the paper. Hence, conclusions from meta-analyses obfuscate the influence of researcher degrees of freedom linked to contrast choice and selective reporting.

## Current Study

Previous reviews of the MID task have evaluated general utilization of the task in studies of reward responsiveness (Lutz & Widmer, 2014), between-study, temporal, and phase-related differences in MID activation effects (Oldham et al., 2018), dynamics of reward versus loss (Dugré et al., 2018), and influences of substance use (Balodis & Potenza, 2015) and psychosis profiles (Radua et al., 2015) on activation differences. However, the extent to which contrast choice contributes to variability in activation maps, impacts the measurement of behaviorally relevant individual difference dimensions, and alters conclusions about associations between neural responses and behavior, is still unclear. The current study leverages a community sample of late adolescents/emerging adults to examine variability across various univariate contrast activation maps in the MID task.

To delineate variability across contrast types (which is difficult to evaluate between samples/studies), we performed multiple common analyses that focus on the anticipation, outcome, and prediction error parameters, with data from the same individuals. Due to the a) prominent role of motivation (or anticipation of reward) in this task; b) the critical role of dopamine in anticipation ("wanting") and not feedback ("liking") (Berridge & Kringelbach, 2015); c) difficulty to temporally differentiate the outcome phase (Bjork et al., 2010); and d) the drop in power during the outcome phase as each anticipatory trial is split into "hit" or "miss" trial outcome, 50% of contrasts focused on the anticipation phase of the MID task. These activation maps are thresholded to compare the degree to which statistical maps from ten contrasts a) vary within a phase (for example, anticipation Big Win > Neutral contrast) and b) vary between phases of the task (for example, anticipation vs outcome). The degree of variability is assessed at the individual- and group-level to assess the general pattern in overlap of active voxels between two given contrast's activation maps. Then, mean signal intensity values for key regions from previous reviews, such as the insula, mPFC, OFC, and VS (Balodis & Potenza, 2015; Dugré et al., 2018; Oldham et al., 2018) are extracted to evaluate whether activation in these ROIs from different contrasts index convergent or divergent dimensions of cognitive processing (such as reward anticipation). Finally, correlations between these ROI activations and self-reported measures are assessed to determine the impact of contrast choice on the prediction of psychological measures including substance use, psychosocial, and socioemotional functioning.

While meta-analyses have proposed region specific activations for positive and negative values across fMRI tasks (Bartra et al., 2013), a recent review of the MID yielded overlapping networks across positive and negative values (Oldham et al., 2018). Given the within-sample

comparison of contrasts, instead of testing specific hypotheses within a null hypothesis significance test framework in these analyses, similarities and differences are presented as an index of overlap (Jaccard's similarity coefficient), and statistical association across ROIs and behavior (Pearson's *r* coefficient; heat maps of *r* point estimates for inter-ROI relationships and posterior distributions of *r* values for associations of ROIs with behavioral covariates).

The broad goal is to improve the field's understanding of how and where there is within-task variability as a function of MID task contrast choice, and, in doing so, to inform the interpretation of existing MID studies and better guide researchers' *a priori* decisions about which specific contrasts on which the hypotheses are based in future studies. This exploratory analysis can provide inferences about how contrast selection, which typically precedes the reporting of results and increases researcher degrees of freedom, affect the activation maps. Due to the exploratory nature of the analyses, the background, methods, and analytic plan were preregistered on the Open Science Framework (https://osf.io/xh7bz).

Based on neurodevelopmental work on substance use, externalizing and sensation seeking, several brain-behavior hypotheses are proposed based on how they may fit into a nomological network. Neurodevelopmental studies (as discussed in Chapter 1 and Chapter 3) converge on the hypothesis that adolescence is marked by the motivation towards rewarding stimuli due to changes in reward circuitry (Galván, 2010). Differences in reward circuitry are believed to result in reactivity to novel and rewarding stimuli, which leads to engagement in substance use behaviors. However, given that not all adolescents develop substance use problems, it is hypothesized that externalizing symptoms is another pathway to substance use problems (Hardee et al., 2018). Genetic variants that are associated with externalizing psychopathology have been shown to be positively related to VS activity during the anticipation

of rewards (Heitzeg et al., 2014). In the same line of work, the VS activity is reported to positively relate to subsequent alcohol problems. Furthermore, sensation seeking is a subcategory of externalizing that is also considered as a pathway to substance use behaviors (Hardee et al., 2018). Drawing across these three psychological characteristics and their interrelations, it is reasonable to hypothesize that activation in key reward circuitry, such as the VS, during the anticipation of reward versus neutral cues will be positively related to these characteristics. While the effects may be strengthened or attenuated across other anticipatory reward contrasts, it is expected that the *direction* of the effects should be comparable across these psychological characteristics. That is to say, brain-behavior correlations between VS and substance use, externalizing, and sensation seeking should be consistent in the direction of the effect. It is well understood, that this point-null, or non-zero hypothesis, would be weak support for the aforementioned postulates that fill the nomological network (Grahek et al., 2021; Meehl, 1967). However, this work would be a first pass at attempting to test these hypotheses that would lay the groundwork for more precise tests of the theory.

## Methods

Participants in this study are a Phase 2 subsample ($N$ = 104; $M_{Age}$ = 19.3; $SD_{Age}$ = 1.3; 57% Female; 71% White, 14% Black, non-Hispanic, 6% Hispanic/Latinx) of adolescents from the Adolescent Health Risk Behavior (AHRB) study, as described in Chapter 2. The bulk of code used in the subsequent analyses have been made available online (https://github.com/demidenm/MIDContrasts).

### Self-Reported Psychological Measures

*Substance Use*. Substance use behaviors (marijuana and alcohol) are assessed via the item: "On how many occasions (if any) have you [used marijuana or hashish/had any alcoholic

beverage to drink—more than just a few sips] during the last 12 months?" Responses are reported on a seven-point scale ranging from 1 = "0 occasions" to 7 = "40 or more occasions". Substance use items are identical to those used in the annual, national Monitoring the Future surveys (Johnston et al., 2019). Marijuana and alcohol scores were z-scored, and then a substance use aggregate measure was created by averaging the z-scored items across Wave 1 – Wave 3.

*Impulsivity*. The Barratt Impulsiveness Scale-Brief (BIS-B) is an 8-item, unidimensional measure of impulsiveness (Steinberg et al., 2013) based on a reduced item set obtained from the Barratt Impulsiveness Scale ($BI^{S)}$, 11th revision. Items were rated on a 4-point Likert-type scale: rarely/never (1), occasionally (2), often (3), and almost always/always (4). A mean score was computed (range: 1 – 4), higher scores indicated lower self-reported impulsivity ($\alpha = .79$). BIS-B items were z-scored and then aggregated by averaging scores across Wave 1 – Wave 3.

*Sensation Seeking*. The Brief Sensation Seeking Scale (BSSS) is an 8-item self-report measure of sensation seeking (Hoyle et al., 2002) based on a reduced item set of the Zuckerman Sensation Seeking Scale (SSS). The items measure dimensions of sensation seeking: experience seeking, boredom susceptibility, thrill and adventure seeking, and disinhibition. Responses were on a 5-point Likert-scale: strongly disagree (1), disagree (2), neither disagree nor agree (3), agree (4), and strongly agree (5). A mean score was computed (range: 1–5), with higher scores indicated higher self-reported sensation seeking ($\alpha = .78$). BSSS items were z-scored and then aggregated by averaging scores across Wave 1 – Wave 3.

*Socioemotional problems.* Socioemotional problems were assessed using the Youth Self-Report (YSR; Achenbach & Rescorla, 2001) to characterize externalizing and internalizing problems. The YSR is a widely utilized, 112-item self-report measure assessing emotional and

behavioral difficulties in 11-18-year-olds. The YSR includes two broadband scales: internalizing problems (e.g., withdrawn/depressed) and externalizing problems (e.g. attentional deficit/hyperactivity problems, oppositional defiant problems). Raw scores are normalized to provide a common metric with higher scores indicating greater psychopathology. Validity and reliability of the YSR broadband, syndrome, and DSM-oriented scales are well documented (Achenbach & Rescorla, 2001; Achenbach & Rscorla, 2003) with adequate internal consistency ($\alpha$ = .70 - .86) and test-retest reliability ($\alpha$ = .67 - .88). An aggregate score was created from population-standardized z-scores for internalizing and externalizing by averaging scores across Wave 1 – Wave 3. In the present study, Cronbach's alphas of .91 and .88 were obtained for the internalizing and externalizing scales, respectively.

fMRI Task

To evaluate the neural activation of reward processing, the MID task reward (Knutson et al., 2000) was used to model the neural signatures of the anticipation of monetary reward (Bjork et al., 2010). For more information on the design, please refer to Chapter 2. As noted in Chapter 2, participants were explicitly told that their performance on the task during the scan (for example, $5 Win Cue was associated with an opportunity to win $5 and a $5 Lose cue was associated with an opportunity to not lose $5) would be associated with the compensation they can get for their cumulative earnings during the MID (Maximum $30).

The modified version in this study is currently being employed in the national Adolescent Brain Cognitive Development (ABCD) study to measure the development of adolescent reward processing (Casey et al., 2018). Identical to the task described in Casey et al. (2018), the task in this study consists of three phases: anticipation, probe and outcome (that is, feedback). A key difference between the current version of the MID (and the one used in the ABCD study) and

that used in the IMAGEN sample (Cao et al., 2019), is the IMAGEN study only includes Win and Neutral trials, excluding Loss trials. Furthermore, in the IMAGEN, study performance was rewarded with "points" that were exchanged for M&M's/candies.

### fMRI Data Acquisition

FMRI data was acquired using the same protocol as described in Chapter 2.

## Analyses

### fMRI Data Analyses

FMRI data were preprocessed using the same sequences of steps that are described in Chapter 2.

Subjects were to be excluded from analyses if a subject's mean framewise displacement (FD) values exceeded > .9 within any given run. All subjects mean post FD were < .9, thus there were no exclusions on this criterion. We focused on commonly used contrasts (Table 4.1) from a recent review (Oldham et al., 2018) and those from the review of studies using the MID (PubMed 2015 – 2019; see Appendix C, Table C1), such as reward anticipation (such as Big Win or Lose ($5), Small Win or Lose ($0.20) versus Neutral anticipation, Win outcome (such as $5 or $0.20) versus Neutral outcome, loss conditions (such as $5 or $0.20) and alternative contrasts

*Table 4.1.* Contrast Modeled in the Monetary Incentive Delay Task

| Contrasts | Phases of MID Modeled |
|---|---|
| Contrast 1 (A1) - Ant | Win (W; $5 & $0.20) > Neutral (N) (W>N) |
| Contrast 2 (A2) - Ant | Big Win (BW; $5) > Neutral (N) (BW>N) |
| Contrast 3 (A3) - Ant | Big Win (BW; $5) > Small Win (SW; ($0.20) (BW>SW) |
| Contrast 4 (A4) - Ant | Big Win (BW; $5) > Implicit Baseline (BW>IB) |
| Contrast 5 (A5) - Ant | Big Loss (BL; $5) > Neutral (N) (BL>N) |
| Contrast 6 (F6) – Out | Big Win (BW; $5) Hit > Neutral (N) Hit (BWH>NH) |
| Contrast 7 (F7) – Out | Big Loss (BW; $5) Hit > Neutral (N) Hit (BWH>NH) |
| Contrast 8 (P8) - PE | Expected Value – BW & SM Modulated (EV) |
| Contrast 9 (P9) - PE | Positive Prediction Error (PE) - BW & SM Modulated (PPE) |
| Contrast 10 (P10) - PE | Negative Prediction Error (PE) - BL & SL Modulated (NPE) |

Ant = Anticipation; Out = Outcome; P = Prediction Error; Individual contrasts modeled in FSL

that may be comparable to test for similarities within a group, for example, win or big win conditions. It should be noted that using anticipation vs outcome phase yields estimates that are often powered differently, as a function of the target accuracy of the task (60%), leading to individual variation in hit/miss trials. Furthermore, since the outcome phase is often difficult to deconvolve, or the separation from the spatiotemporal hemodynamics of proximal task events (Hinrichs et al., 2000), in the task, and modeled in various ways, we include one type of outcome contrast focusing on gain and loss, as it is not a central focus of these analyses and often not the focus in contrasts in the literature.

First-level analyses were performed by using FEAT. Time-series statistical analysis was carried out using FILM with local autocorrelation correction (Woolrich et al., 2001). Similar to other studies (Cao et al., 2019; Hagler et al., 2019; Lamm et al., 2014), both anticipation and outcome events were modeled (15 explanatory variables) and modulated prediction error signal of EV, PPE, and NPE, in addition to six motion parameters (translations and rotations in x, y, z directions) and the derivatives of the motion parameters. We included prediction error explanatory variables based on a recent review suggesting the MID is considered to be an implicit reinforcement learning (RL) paradigm (Balodis & Potenza, 2015), and others recommending use of modulators (Bjork et al., 2010; Oldham et al., 2018). However, as noted in the introduction, the MID is not a true RL design but only a proxy. To incorporate these recommendations, the RL modulators included: Expected Value (EV) and Prediction Error (PE). To derive estimates of EV and PE for this task, the behavioral data were modeled for each participant (100 trials – trial-by-trial) to calculate parametric modulators (EV for anticipation; PE for Received Reward (RR); *pGain* = probability gain, $\eta$ = learning rate (0.7)). Similar to Cao et

al. (2019), we used a RL model (equation 2) trained by reward cues and outcomes (Rescorla & Wagner, 1972):

$$\begin{aligned} EV_t &= pGain_t \times Cue_t \\ PE_t &= RR_t \times EV_t \\ pGain_{t+1} &= pGain_t + \left( \times \frac{PE_t}{Cue_t} \right) \end{aligned} \tag{4.1}$$

To average across the two runs that are used in subsequent stages, a second-level model was defined for each participant for each of the ten contrasts using fixed effect analysis in FEAT. A group-level analysis was performed using FMRIB's Local Analysis of Mixed Effects (FLAME 1) to generate a mean level activation across subjects for a given contrast. Considering the large array of contrasts that are modeled, abbreviations from the first column of Table 2.1 are referred to when referencing contrasts henceforth.

To provide a direct observation of the BOLD signal and signal-to-noise information of subcortical regions, we include complementary post-hoc analyses evaluating raw BOLD signal. We extract the mean signal for VS and mPFC in the timeseries for VS and plot it for 15 TRs. Likewise, for cortical mPFC and subcortical VS we extract and present the distribution of the signal-to-noise ratios (SNR) for each individual and run to confirm that SNR is within an acceptable range.

Individual Level and Group Estimates

To compare overlap between thresholded activation maps for each contrast at the individual and group level, we thresholded activation maps produced by the second level and group level analyses. For the individual level, subjects' second level maps (zstat) for each contrast are thresholded at $p < .01$ ($z = 2.3$) and group level contrasts are thresholded at $p < .001$ ($z = 3.1$). We selected a lower threshold for individual maps due to more variability in estimates within an individual map that may substantially alter the Jaccard's Similarity Indices. These

thresholded maps are binarized (using *fsl* -bin) and compared to derive Jaccard's Similarity Indices (described below).

## Calculating Similarity

One of the aims for this study is to compare similarity, or spatial overlap, between different activation maps of the MID task within individuals and at the group level. This is to provide an easy-to-interpret index of how similar (or different) activations are across contrast types. Similar to a previous work (Grady et al., 2020), we calculate a percent overlap using Jaccard's similarity index (JSI) (Maitra, 2010) between contrasts. The JSI calculates the number of voxels that overlap across two thresholded statistical maps. One of the major advantages of using the JSI is that the percent overlap results obtained from this technique are intuitive and physically interpretable (Maitra, 2010).

As we used JSI point estimates to evaluate activated voxels across different thresholded contrasts, we propose a bootstrapping based confidence interval calculation for identifying the 95% confidence intervals of the overlap measures across all subjects in this sample (DiCiccio & Efron, 1996). The bootstrapped JSI would provide reliable estimates of the range and shape of the distribution of percent overlap and a physical interpretation of the JSI obtained across all of the subjects. Although the thresholded maps are impacted by power in the design, similarity can be assessed within phases, such as anticipation or outcome, given the number of trials is comparable within each phase (with the exception of the all win contrast).

## Region of Interest and Behavioral Associations

Central voxel coordinates from Neurosynth.org for a priori ROIs are used to create 10mm-diameter spheres: bilateral insula, OFC, VS, mPFC, and ACC, (see Appendix C for table with MNI coordinates, in Table C2, and spheres on MNI Glass Brain, in Figure C1). For each

ROI, the voxels from each contrast mask (using z-statistics produced by Feat Second Level) are averaged to create a mean signal intensity value and extracted using *fslmeants.* Correlations (point estimates of Pearson's *r*) across ROIs were analyzed in R version 3.6.1 (R Core Team, 2019) and were visualized using a heatmap.

ROI mean level signal intensity values across ten contrast types (described above), were used to assess associations between neural activity and self-reported aggregate z-scores of a) substance use, b) sensation seeking, c) impulsivity, d) externalizing, and e) internalizing problems. Bayesian correlation analyses implemented in JASP (JASP Team, 2019; Ly et al., 2018) were used to estimate posterior distributions for the Pearson's *r* value of each predictive association. Default, non-informative priors (uniform distributions spanning the values from -1 to 1) were used for all correlation analyses. Median values of the posterior distribution, which indicate the most likely *r* value, and 95% credible intervals, which represent the lower and upper bounds of the range which has a .95 probability of containing the *r* value, are reported below to quantify the strength of, and uncertainty about, these predictive associations. As analyses are not intended to be formal tests of hypotheses, we refrain from reporting either Bayes factors or frequentist *p*-values.

Bayesian analyses are used here to give a more precise estimate of the data and report a confidence interval that is directly interpretable. Here a uniform prior was used because there was no prior belief about probabilities regarding where the effect may lie. In other words, I posed directional hypotheses based on prior belief about the direction of the parameter estimates, but I did not constrain the *a priori* range of effects (Kruschke & Liddell, 2018; Serlin & Lapsley, 1985). Hence a uniform prior was used, where there was an equal probability of the effect being between 0 and 1. Bayesian correlations with a uniform prior provide a more precise estimate of

the *r* and surrounding 95% that is easily interpretable (Cleophas & Zwinderman, 2018). Specifically, the intent of this project is to interpret what is the most probable effect across the brain-behavior measures. Unlike tradition null-hypothesis frameworks where the confidence interval is related to the *p*-value, Bayes analysis allows for interpreting what is the most probable estimate in the data is (Kruschke & Liddell, 2018) and the confidence interval around the most likely *r* indicates a more precise range of where the estimated *r* value would fall with 95% confidence (Cleophas & Zwinderman, 2018).

## Results

### Demographics, Task Behavior and General Overview

The demographic characteristics for the full sample ($n$ = 104) are provided in Chapter 2, Table 2.3. For the anticipation phase (A1-A5) and prediction error models (P8-P10), all 104 individuals were included (cf. Table 2.1 for contrast descriptions). However, for the feedback phase (F6 & F7), four subjects were excluded due to underpowered conditions resulting in anomalies in the estimated [First & Second Level] statistical maps, resulting in N = 100 for the feedback contrasts. The behavioral performance statistics from the MID task are summarized in Appendix A, in Table A1-A2 and in Figure A2-A3. Although the average accuracy for the task, 57%, was below the targeted 60%, as noted in Chapter 3, the Big Win ($5) and Big Loss ($5) conditions were at or above the target, 62% and 60% accuracy, respectively. As expected, accuracy was lower (48%) and more variable during the neutral condition. Mean response times are not reported, as the E-Prime data was not collected for incorrect (‘miss’) trials during the MID task.

JSI similarity matrices and activation maps are displayed in Appendix C, in Figure C2, and Figure 4.1, respectively. Associations between individual differences in ROI mean-level activation from each contrast are reported at https://osf.io/a5wem/ and in Figure 4.2 and are selectively reported below for clarity. Correlations between ROI activation estimates and behavioral criterion measures are reported in Figure 4.2 (subset of four regions, five anticipatory contrasts across the five

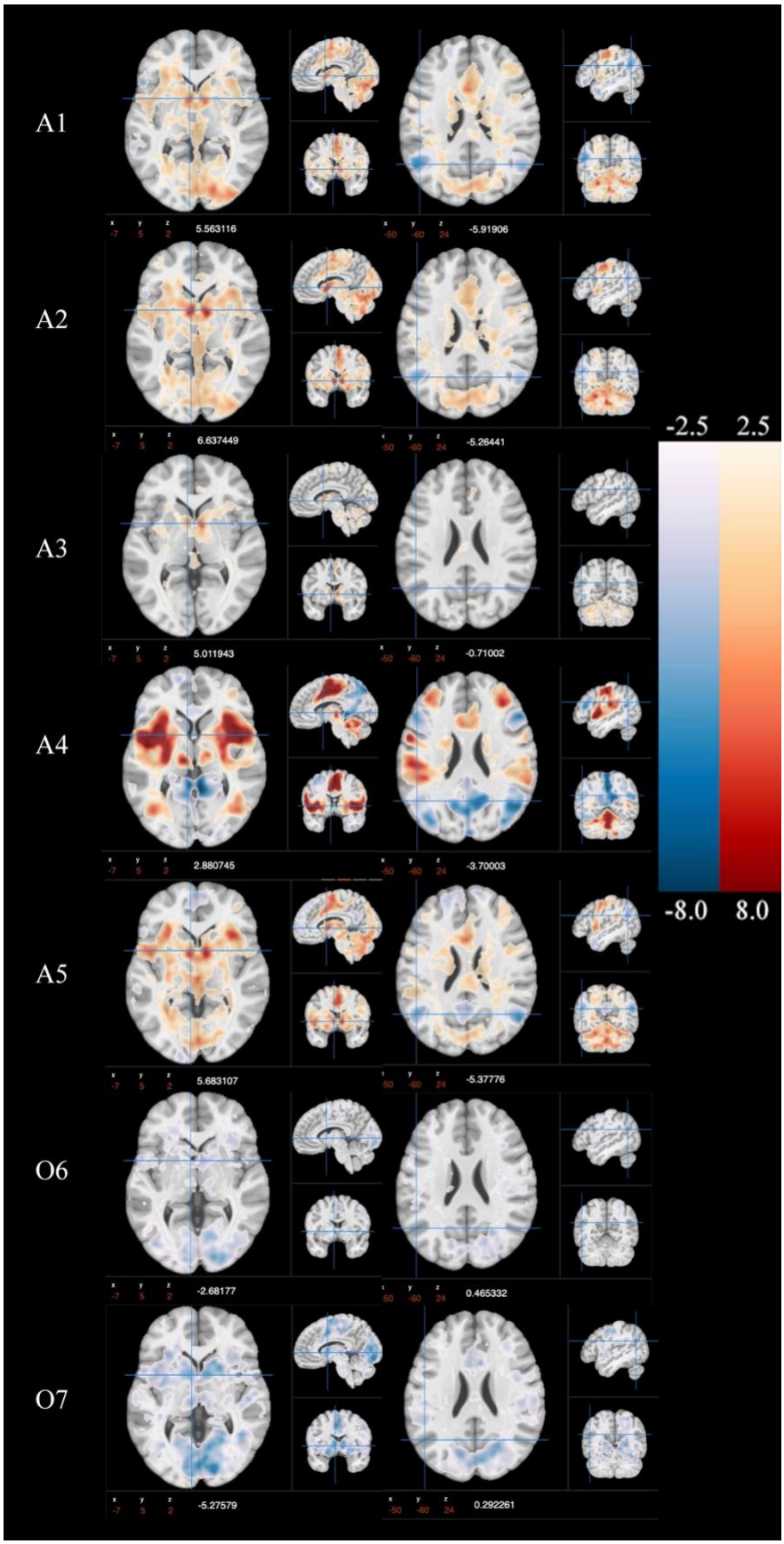


*Figure 4.1*. Mean level activation and deactivation maps for A1-A5 & O6-O7, one-sample *t*-test.

measured behaviors; full figure reported in Appendix C, Figure C3) and available at https://osf.io/d9k3v/. There were four notable patterns present in these results: 1) Win and Loss anticipation demonstrate comparable striatal/insula activation and task-negative deactivation (see NeuroVault statistical map: https://neurovault.org/images/359858); 2) outcome phase contrasts consistently imply deactivation of striatal regions (potentially due to artifact related to signal spill-over); 3) the Big versus Small Win contrast appears less meaningful than, and unrelated to, other anticipation phase contrasts; and 4) individual differences in ROI activation, across different contrasts, demonstrate relatively weak associations with behavior. The aforementioned are expanded in greater detail below. Notably, the activation maps of the prediction error models were extremely variable in activation and relatively weak in their associations with mean ROI activation from other contrasts, they are not discussed below. However, results for all contrast maps are available online and results presented in Figure 4.2 for and in Appendix C, in Figure C3.

Big Win and Loss Anticipation Engage Similar Neural Systems

The thresholded masks ($p < .001$) of **A2:**BW>N and **A5:**LB>N group maps had a Jaccard's similarity Coefficient of .16 (Appendix C, in Figure C2). This similarity is also apparent in the group level activation maps, demonstrated by shared patterns of activation (Figure 4.1). Although the peak left striatal activation in the **A2:**BW>N is greater than in the **A5:**BL>N (based on magnitude of *z*-statistic in activation maps), in their direct comparison the difference is relatively small (https://neurovault.org/images/359858/). The greatest difference between these two contrasts was increased activation in the mPFC in **A2:**BW>N as compared to **A5:**LB>N. Furthermore, contrasts **A2:**BW>N and **A5:**BL>N show similar activation of supplementary motor area (SMA), the insular cortex, thalamus and cerebellar regions. Similar to the shared

positive activation of these contrasts, they, too, share comparable deactivation in the task-negative, angular gyrus, an effect that is not seen in the **A3:**BW>SM (Figure 4.1). This activation in the striatal regions and deactivation in task negative regions is comparable to a recent meta-analysis (open source activation maps: https://neurovault.org/collections/4258/) showing similar robust patterns of activation and deactivation in both win and loss anticipation (Wilson et al., 2018).

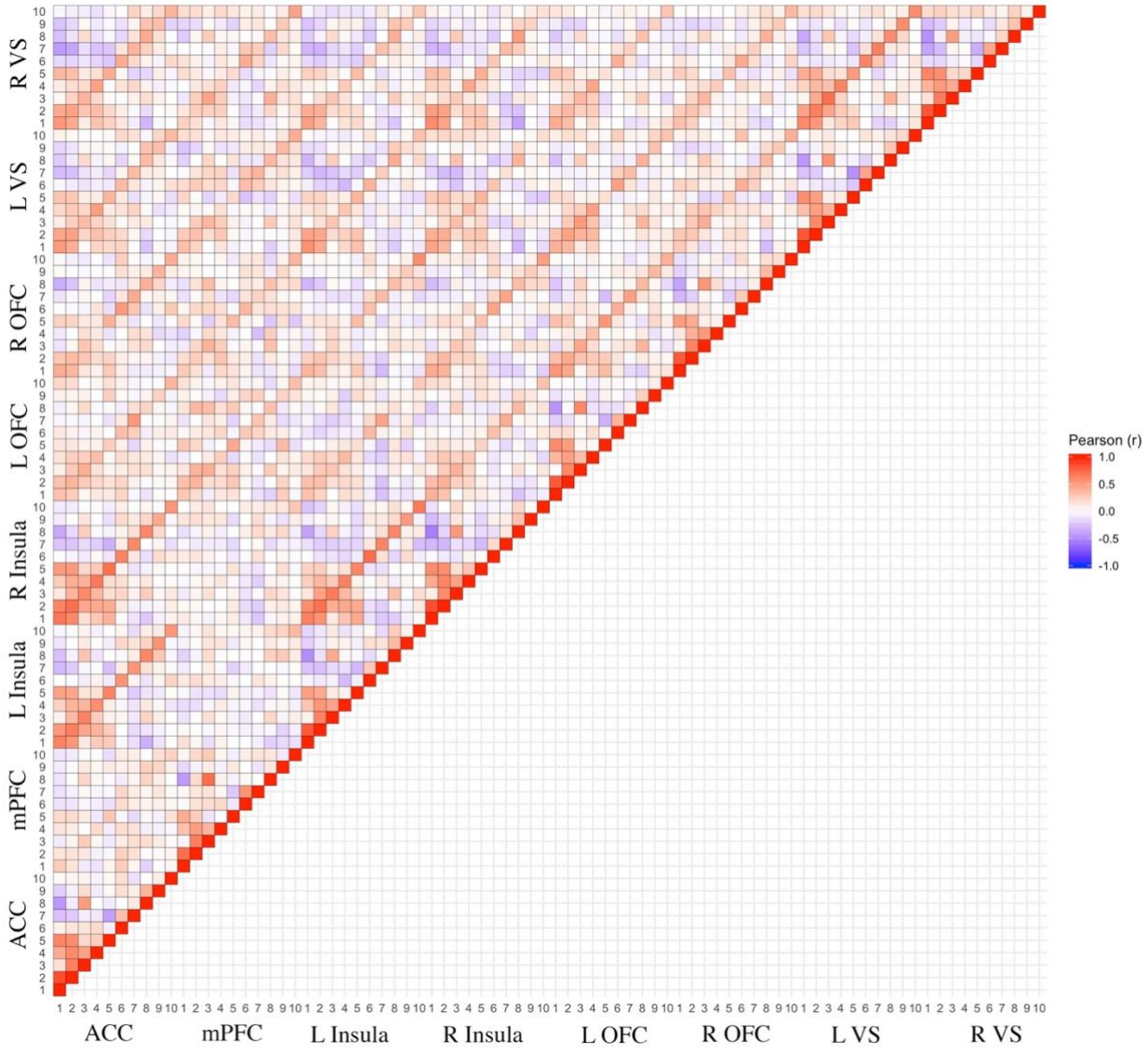


*Figure 4.2.* Pearson correlation matrix of 10 contrasts by 8 ROI's.
Color bar represents the associated Pearson's r value between the 10mm ROI across 10 contrasts. See Table 4.1 for associated contrasts information. R = Right; L = Left; VS = Ventral Striatum; OFC = Orbitofrontal Cortex; mPFC = media Prefrontal Cortex; ACC = Anterior Cingulate Cortex

Consistent with these similarity analyses in group level activation, correlations of mean signal intensity values from ROIs across **A2:**BW>N and **A5:**BL>N (Figure 4.2, full matrix available at https://osf.io/a5wem/) also suggested that neural responses from these contrasts index similar individual difference dimensions. Positive correlations in neural responses between the contrasts were identified (Figure 4.2) in the anterior cingulate cortex (ACC; $r$ = .58), medial prefrontal cortex (mPFC; $r$ = .26), bilateral Insula (Right: $r$ = .57; Left: $r$ = .44), bilateral orbitofrontal cortex (OFC; Right: $r$ = .43, Left: $r$ = .50), and bilateral ventral striatum (VS; Right: $r$ = .57, Left: $r$ = .49). The similarity between **A2**:BW>N and **A5**:BL>N is consistent with a recent meta-analyses (Oldham et al., 2018).

Reward and Loss Outcome is Paradoxically Linked to Striatal Deactivation

Contrary to past work focused on striatal activation during win conditions, the contrasts during the outcome phase, **F6:**BWH>NH & **F7:**BLH>NH, demonstrated a *deactivation* of the striatal regions. Based on the Jaccard's similarity Coefficient, .34, the regions that were deactivated were comparable in **F6:**BWH>NH and **F7:**BLH>NH (Figure 4.1 and Appendix C, in Figure C2). Although the mean level deactivation of the striatal region in the **F6:**BWH>NH contrast was relatively weak ($t$ = -2.68), in the **F7**:BLH>NH condition the deactivation was relatively robust ($t$ = -5.8). As a control comparison in change of activation, we reference the angular gyrus, which has a relatively weak mean level activation in both **F6:**BWH>NH and **F7:**BLH>NH, demonstrating that there is a more profound change in activation in the striatal region between the anticipation and outcome phase (see Figure 4.1). In a direct comparison of **F6:**BWH>NH & **F7:**BLH>NH (https://neurovault.org/images/359858/), **F6:**BWH>NH demonstrates greater activation in the left parahippocampal ($z$ = 4.3) and right nucleus accumbens ($z$ = 3.4). These two feedback contrasts demonstrated some associations (Figure 4.2)

in individual differences analyses of mean signal intensity in the ACC ($r$ = .33), mPFC ($r$ =.55), and bilateral VS (Left $r$ = .45; Right $r$ = .46). Notably, this deactivation is likely to be a function of the spill-over from the anticipatory phase given the short interval between anticipation and outcome stimuli, as can be observed in the BOLD signal change in Appendix C, in Figure C5.

Anticipation Big Win versus Small Win Contrast Is Distinct from other Anticipation Contrasts

Despite its variable use in the literature, **A3:**BW>SM was unique when compared to other contrasts in anticipation phase (Figure 4.1). The **A3:**BW>SM had the lowest Jaccard Coefficient with other contrasts modeling the anticipation phase, <.02 (Appendix C Figure C2). Further, in the group-level activation, compared to **A1:**W>N, **A2:**BW>N, and **A5**:BL>N anticipation phases, the **A3:**BW>SM had the weakest group-level striatal and insular activation, and no task-negative activation. The task-negative activation difference is unique, as all of the other contrasts demonstrate this profile of task-negative activation in the anticipation phase.

However, with respect to individual differences in ROI mean-level activation, depending on the contrast, there are similarities between **A3:**BW>SM and other contrasts. For example, the mean-level activation between **A1:**W>N and **A3:**BW>SM is negligible: ACC ($r$ = .15), mPFC ($r$ = -.05), bilateral insula (Left $r$ = .07; Right $r$ = .08), bilateral OFC (Left $r$ = .02; Right = .06) and bilateral VS (Left $r$ = .06; Right = .15). Yet, there is a strong association between **A2**:BW>N and **A3:**BW>SM in the ACC ($r$ = .64), mPFC ($r$ = .65), bilateral insula (Left $r$ = .63; Right $r$ = .58), OFC (Left $r$ = .60; Right $r$ = .62), and bilateral VS (Left $r$ = .59; Right = .66). Despite the similarity discussed between **A2:**BW>N and **A5:**BL>N above, there is a negligible association between ROI's in **A3:**BW>SM and **A5:**BL>N ($r$ = -.11 to .19). This suggests that the similarities between **A2:**BW>N and **A3:**BW>SM may arise from the shared Big Win cue in the subtraction.

Across Contrasts, Activations Show Only Weak to Negligible Correlational Relationships with Behavioral Criterion Measures

The aggregated scores for the self-reported psychological and behavioral characteristics in this sample were associated in the direction expected (Appendix C, in Table C3). More specifically, there was a strong positive association between internalizing and externalizing problems ($r$ = .51), sensation seeking and impulsivity ($r$ = .44), externalizing and substance use ($r$ = .51), and substance use and sensation seeking ($r$ = .38) and impulsivity ($r$ = .24).

Figure 4.3 shows a subset of correlational relationships between ROI activation estimates and behavioral criterion measures (for complete figure, see Appendix C Figure C3). It shows posterior medians and 95% credible intervals (CIs) of Pearson's *r* values, which represent the most likely *r* value and range in which there is a .95 probability that the *r* value falls, respectively

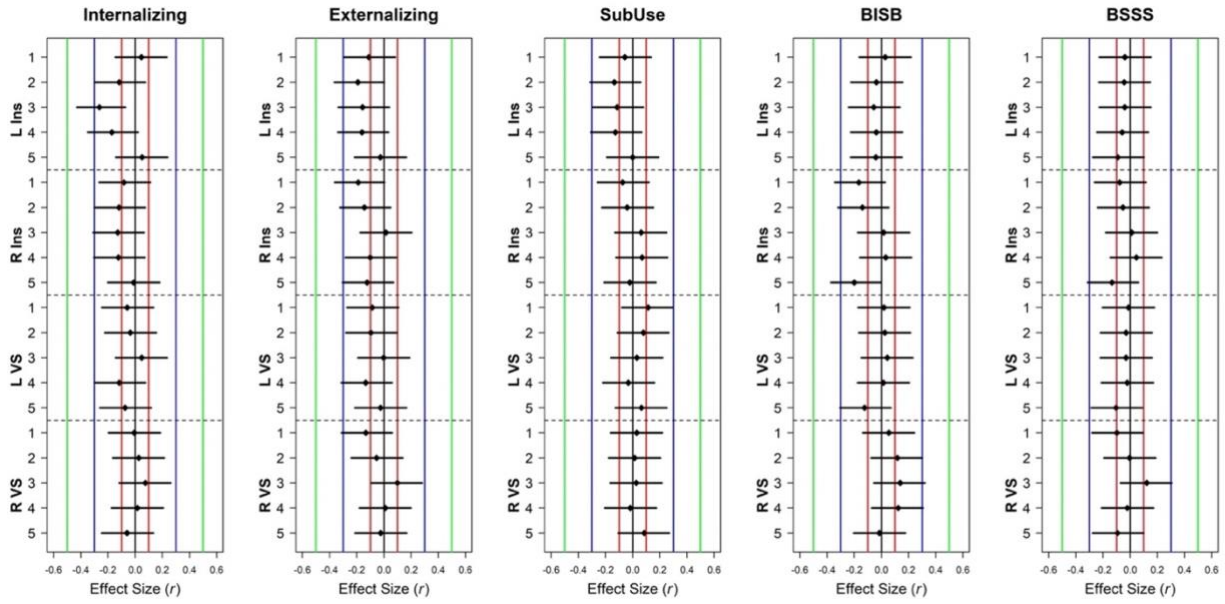


*Figure 4.3.* Forest plots displaying the most likely Pearson's r value (black diamonds) and 95% Bayesian credible internal (black lines) for correlation relationships between ROI activation estimates from each anticipatory contrast and behavioral criterion measure.
Red, blue, and green lines denote "small" (r = .10), "moderate" (r = .30), and "large" (r = .50) effect sizes. 1-5 = Five contrasts listed in Table 4.1. L = Left; R = Right; Ins = Insula; VS = Ventral Striatum; SubUse = Substance Use composite measure; BIS-B = Barratt Impulsiveness Scale-Brief; BSSS = Brief Sensation Seeking Scale. Behavioral items are z-scored.

(full results available at https://osf.io/d9k3v/; complimentary bootstrapped values are provided at https://osf.io/dr5y2/). Although the interpretation of individual associations is complicated by the large number of tests reported in Appendix C, in Figure C3, several general patterns are apparent. First, 72% of the most likely *r* values fell at or well below the threshold for what is typically considered a "small-sized" effect, |*r*| = .10 (Appendix C, in Table C4). Similarly, the bulk of most CIs also fell in this general range. In fact, there was not a single association for which the most likely *r* value indicated a "moderately-sized" effect (|*r*| >= .30), and few CIs overlapped with this "moderate" criterion. It is also notable that only a handful of CIs (less than 5%) did not overlap with 0, suggesting that even these cases, which might be interpreted as showing promising evidence for a non-negligible effect, are likely due to multiple testing rather than reflecting true relationships. Indeed, as typical Bayesian CIs do not take into account the probability that the null (*r* = 0) is true (van den Bergh et al., 2019), the effect size estimates we report are, if anything, likely to be overestimates. Hence, consistent with other emerging findings from large, diverse neuroimaging data sets (Nees et al., 2012; Paulus et al., 2019; Paulus & Thompson, 2019), these patterns of results suggest that direct associations of MID task activations with relevant behavioral criterion measures are less robust than previously thought, and that even if these associations exist, effect sizes are likely to be small.

Second, coupled with the small effects, decisions in contrasts can weaken or alter the brain-behavior results and thus the underlying interpretation. For instance, as can be observed in Figure 3, the median *r* for the relation between anticipatory win activation in the ventral striatum, and sensation seeking flips from negative to positive between **A1:**W>N (Right *r* = -.10) and **A3:**BW>SW (Right *r* = .12). This example, and the high degree of variability in median *r* between ROI and behaviors presented in Figure 3, indicates that caution should be taken when

selecting contrasts as they may invariably change interpretations even in the context of these small effects.

Post-Hoc Analyses

In light of prior meta-analytical comparisons of base contrasts within individuals, such as gain versus outcome phases (Knutson & Greer, 2008; Wilson et al., 2018), we compared these differences in the anticipation phase, **A2:**BW>N versus **A5:**BL>N; outcome phase, **F6:**BWH>NH versus **F7:**BLH>NH; win anticipation versus win outcome, **A2:**BW>N versus **F6:**BWH>NH; and loss anticipation versus loss gain outcome, **A5**:BL>N versus **F7**:BLH>NH. We provide these for reference online https://neurovault.org/collections/JVXLTPHC/. Notably, in a direct comparison of **the A2:** BW>N versus **A5:** BL>N signal we find no substantial differences in VS or Insula as a function of reward and loss.

Due to recent concerns that some multiband sequences may alter the BOLD signal in subcortical regions (Risk et al., 2018), signal-to-noise ratios and plotted time-series from the VS to provide a direct observation of signal for each anticipation condition are provided. With

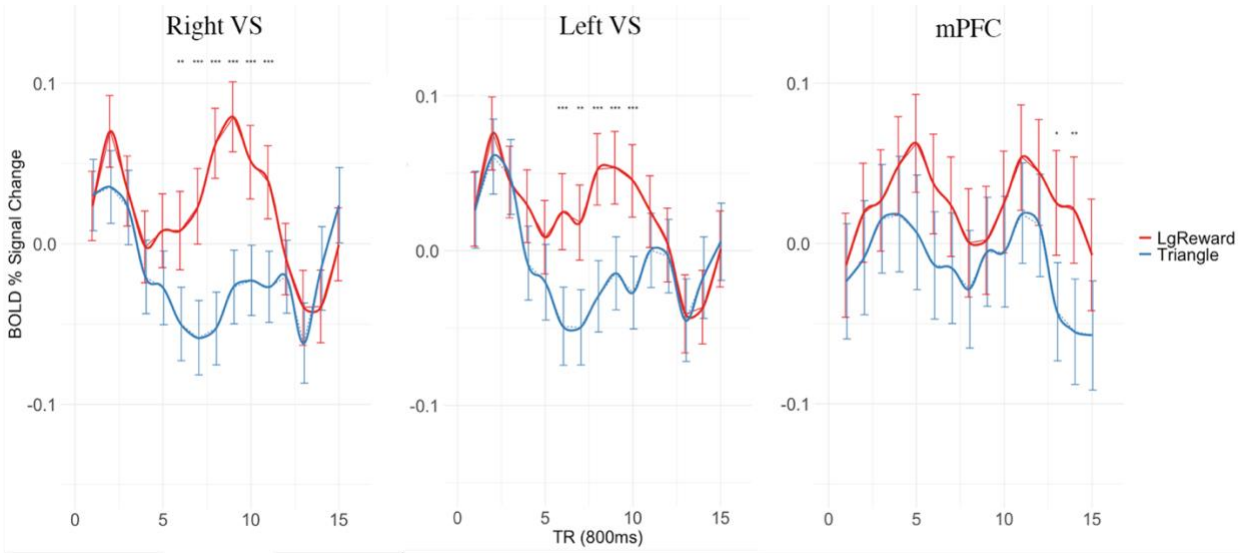


*Figure 4.4*. Direction observation of BOLD signal locked to cue onset for Big Win (Lgreward) and Neutral (Triangle) for 15 TRs (12 s) after cue onset.
mPFC = medial Prefrontal Cortex; VS = Ventral Striatum; Error bars = bootstrapped 90% confidence interval.
$p < .05$*; $p < .01$**; $p < .001$***

respect to the direct observation of the BOLD signal, we find appropriate separation in anticipation of Big Win and Neutral cues (Figure 4.4) and signal-to-noise ratio in the VS region (Appendix C, in Figure C4). With respect to the anticipation phase, we see the expected peak in BOLD separation between Big Win and Neutral cues around 7-8seconds after cue onset (Figure 4.2), such that this separation is significant from TR 6 ($p < .01$) to TR 11 ($p < .001$) in the Right VS, and TR 6 ($p < .001$) to TR 10 ($p < .001$) in the Left VS, before the undershoot at TR 14. This separation, as expected, does not occur in the mPFC. The nature of the anticipation signal bleeding into the feedback phase is apparent in the bilateral VS when the anticipation cues are locked to the feedback phase (Appendix C, in Figure C8).

## Discussion

In this study of the MID task, we performed an evaluation of similarities and differences between commonly used univariate contrasts, focusing on spatial overlap, individual differences in mean ROI signal intensity, and correlations between ROI activations and behavioral criterion measures. After identifying ten candidate contrasts that have precedent in the previous literature, this study provides the first detailed within-study comparison of these common MID task contrasts. The findings demonstrate similarity between positively and negatively arousing anticipation cues, apparent deactivation of striatal regions during the outcome phase, dissimilarity between Big Win > Small Win anticipation and other anticipation effects, and relatively weak associations between MID task activations and self-reported behaviors. These findings are generally consistent with previously reported MID task-specific conceptual findings (Bjork et al., 2010; Oldham et al., 2018) and also have implications for task-general theoretical problems (Hedge et al., 2018; Price & Friston, 1997).

A relatively similar pattern of group-level activation was observed during the Big Win anticipation and the Big Loss anticipation phase. A direct comparison of Big Win and Big Loss anticipation phases revealed negligible differences between the activation in the NAcc and insula in the group level activation maps, and only a small Win-related increase in activation in the mPFC. This similarity in activation profiles during anticipation of both positive and negative stimuli is consistent with a recent meta-analysis demonstrating that approach and avoidance behavior have considerable overlap in activation (Oldham et al., 2018), and other studies reporting similar activation patterns in young adults (Joseph et al., 2016; Murray et al., 2020) and populations at risk to substance use (Bjork et al., 2008a). The similarity in the neural activation to the anticipation of Big Win and Loss cues is also consistent with the hypothesis that certain regions may display roughly equivalent activation at the extreme ends of value (Bartra et al., 2013). This may suggest alternative cognitive processes (such as attention or motivation) that may be involved during the anticipation phase (Abler et al., 2006; Breckel et al., 2011; Krebs et al., 2012; Schouppe et al., 2014), as the NAcc may facilitate detection and attention to cues (Peters et al., 2011) as it serves as a limbic-motor interface that converts signals into action (Floresco, 2015). The overlap between win and loss group-level activation suggests the activation maps are more comparable than different which may correspond to shared cognitive processing (Price & Friston, 2005).

There was one notable instance, however, in which the analysis revealed dissimilarity between contrasts in the anticipation. Although the Big Win versus Small Win contrast activated striatal regions, the contrast demonstrated a limited association with other contrasts in the anticipation phase. Specifically, in group-level activation, there was much greater similarity between Big Win versus Neutral and Big Loss versus Neutral contrasts than the similarity

between Big Win versus Neutral and Big Win versus Small Win contrasts. Given that the MID task activates a broad set of regions involved in effortful initiation and anticipation (Suzuki et al., 2020), subtraction of cues with lower effort and greater variability (e.g., neutral stimuli) from higher effort and lower variability (e.g., Big Win), versus with those with slightly more effort (e.g., Small Win), may change the amount of preparatory signal subtracted from the contrast map. It is likely that beyond the cognitive process of 'wanting', there are co-occurring cognitive processes in these cues which may violate assumptions when using subtraction to infer reward sensitivities (Caplan, 2007).

The comparison of positively and negatively valenced reward feedback revealed widespread *deactivation* throughout the brain during the outcome phase. These patterns were counter to a recent meta-analysis, using activation likelihood estimation (based on nine studies), that reported increased activation in reward outcome (Oldham et al., 2018). Oldham et al. (2018) reported increased activation during the outcome phase in the reward hit versus reward miss or reward hit versus neutral contrasts (see Table 2 in Oldham et al., 2018, p. 3404). However, the deactivation results differed from Oldham et al. (2018) in that these analyses focused on the reward hit versus neutral hit feedback contrast. The observed deactivation of the reward hit versus neutral hit contrast during the feedback phase is likely the spill-over BOLD signal from the anticipatory phase which captures the undershoot (Buxton, 2012). In direct plots of BOLD of outcome within-condition (e.g., Big Win hit and Big Win miss signal) this undershoot is still apparent. Although comparing within condition outcomes, or more complicated contrasts (Bjork et al., 2011a; Veroude et al., 2016), are more appropriate when modeling the outcome phase, researchers should remain cognizant that these trials are still unbalanced (e.g., more hit versus miss trials) and underpowered (anticipation trial is bifurcated during outcome). Given the

undershoot, if the neural process of interest is specific to the outcome phase, designs that temporally separate the outcome phase should be considered (Bjork et al., 2010; Murray et al., 2020).

Bearing in mind that this sample is at the developmental peak of sensation seeking (Romer, 2010; Steinberg et al., 2018), a phenomenon that is hypothesized to be central to the motivation towards reward (Casey, 2015; Ernst & Luciana, 2015; Spear, 2011), it is worth to consider how the association between neural activation and sensation seeking changes across anticipatory contrasts. While we found a negligible association between sensation seeking and bilateral VS activation during Big Win versus Neutral contrast ($r < |.03|$), Big Loss versus Neutral has a notable negative association with sensation seeking. ($r$ = -.09-.10). In the latter case, this may be consistent with the hypothesis that higher sensation seekers would be less motivated by negative rewards (e.g., loss). Meanwhile, in the context of the right VS, activation during Big Win versus Small Win contrasts and sensation seeking are positively associated ($r$ = 12). The difference in association with sensation seeking across Big Win versus neutral and Big Win versus Small Win is not consistent with the hypothesis that sensation seekers are more sensitive to larger rewards elicited by this contrast. However, while these distinctions may be well reasoned from a neurodevelopmental perspective (Casey, 2015) and other work reporting neural associations with sensation seeking (Cservenka et al., 2013; Hawes et al., 2017; Tapia León et al., 2019), the similarity in the negative association between right VS activity and sensation seeking across the All Win versus Neutral ($r$ = .10) and Big Loss versus Neutral ($r$ =.09) makes it difficult discern what the key distinguishing factor is in this brain-behavior association. Considered from a nomological network perspective, the interrelationships are not as clear as one would expect them to be. Although the examples refer to the most probable $r$-values,

it is important to remember that the 95% confidence interval in all cases crossed zero, and thus in some samples the association may include results in the opposite observed direction, which should limit the confidence in the interpretation.

When the interrelations among sensation seeking, substance use, and externalizing are considered, the evidence is again inconsistent. The original hypothesis was that the brain-behavior correlations between VS and substance use, externalizing, and sensation seeking would be consistent in their direction as these criterion measures all reward-relevant behaviors. As expected, the magnitude in association between the behaviors are moderate-to-large. However, the patterns in the direction of associations are more variable. While there is similarity in the direction of effects between externalizing and sensation seeking for the right VS and externalizing and sensation seeking for the left Insula across anticipatory contrasts, there were distinct differences between externalizing/sensation seeking and substance use for right VS and externalizing/substance use and sensation seeking for the left Insula across anticipatory contrasts. These relationships were also variable for the left VS and right Insula. These differences make it difficult to clearly establish where the findings would fit into a nomological network and building theoretical frameworks that are easily interpretable across behaviors. In fact, the variability poses more questions than answers about construct validity in fMRI.

Since the task is used in a broad clinical and behavioral literature, these results indicate that it is critical to consider how patterns of activation across task phases/conditions relate to different behaviors. In the analysis using psychosocial and clinical criterion measures, we found limited evidence for associations with activations across different phases and conditions. Specifically, over 95% of associations between neural activation during the MID task and behavior were relatively small or negligible. As the original task design focused on clinical

populations (Knutson & Heinz, 2015) and reviews suggest a robust role of limbic regions in substance use (Balodis & Potenza, 2015) and psychosis (Radua et al., 2015), this may in part explain the weak effects found in the young adult community sample used here. Although it cannot be ruled out that this lack of robust associations with behavior may have been due to features of the sample or measures in this study, it stands in stark contrast to the large array of previous studies reporting associations of MID task activations with various real-world outcomes (Boecker et al., 2014; Büchel et al., 2017). Further, the findings are broadly consistent with recent work that has reported a distinct contrast between the effects found in studies with and without preregistration (median $r$ = .16 versus .36; Schäfer & Schwarz, 2019) and with findings in large, diverse data sets which indicate that neuroimaging markers often explain only very small portions of the variance in behavioral outcomes of interest (Marek et al., 2020; Nees et al., 2012; Paulus et al., 2019; Paulus & Thompson, 2019). This has led some to suggest that small effects are the "new normal" in clinical neuroscience research (Paulus & Thompson, 2019) and that MRI studies require especially large sample sizes (>2000) to identify meaningful effects in brain-behavior associations (Marek et al., 2020). However, this issue needs to be explored further, as some proposed sample sizes of >160 in univariate fMRI analyses appear to yield reasonable results (Grady et al., 2020).

One reason for discrepancy between the results reported here and prior reports of more robust MID task associations with behavior is that effect sizes may have been overestimated in previous studies with smaller samples. Some studies have reported relatively moderate to large effect sizes ($r$ > .25) with respect to brain-behavior associations (Cope et al., 2019; Karoly et al., 2015), but despite the numerous brain-behavior tests performed here that focused on related behavior constructs, the effect sizes were consistently *substantially* lower (97% out of 400

observations $r < .20$). Until recently, neuroimaging studies of individual differences have frequently been underpowered (Cremers et al., 2017; Yarkoni, 2009), with a median sample size of < 50 (Szucs & Ioannidis, 2020), which tends to cause the size and replicability of effects to be dramatically overestimated due to a combination of noise in small samples and the "statistical significance filter" (Gelman & Loken, 2014; Vasishth et al., 2018). These findings suggest that researchers should be prepared for relationships between MID task activations and clinical or real-world outcomes of interest to be of small size and design their studies accordingly. The use of large data sets from collaborative efforts (e.g., ABCD: Casey et al., 2018) may be preferable to smaller samples collected by individual labs (Beltz & Weigard, 2019; Paulus & Thompson, 2019), and would be valuable in reexamining the results presented here to understand how effects change.

Beyond the possibility that effect sizes in previous MID studies may have been inflated by small sample sizes and flexible selection of contrasts, the lack of relationships may also be attributed to problematic validity of fMRI-based tasks and the underlying assumptions about the cognitive processes involved, such as positive or negative valence. A large proportion of tasks in fMRI are experiment based, whereby conditions are manipulated to evoke excitation of a specific cognitive process (Price & Friston, 1997). Although the MID task evokes distinct neural processes that are consistent with current conceptualizations of the mesolimbic system (Knutson & Greer, 2008), the classic metric of validity is that a test measures the psychological trait that it claims to measure (Cronbach & Meehl, 1955; Kelley, 1927), and this criterion appears to be underexplored in some contemporary research. In fMRI studies of individual variation, such as behavioral differences that may be associated with neural measures of reward, the combination of experimental and correlational methods is required, work that arises from two distinct

traditions in psychology (Cronbach, 1957). Correlational approaches attempt to increase between individual variation, whereas experimental research attempts to limit the between-individual variation; the latter methodological practice has been argued to contribute to the poor predictive effect of cognitive measures in correlational research (Dang et al., 2020). A pattern that has been previously observed in the relationship of cognitive processes and cognitive ability (Keating et al., 1985). Together, the weak predictive effect of cognitive tasks and poor test re-test of fMRI (Elliott et al., 2020) can contribute to the unreliable estimates of different task contrasts and the interchangeable use of contrasts will inevitably result in playing '20 questions with nature' (Newell, 1973).

The inferential processes in task-based fMRI pose conceptual challenges. It has been argued that the standard approaches in task-based fMRI that utilize the technique of subtracting conditions are fundamentally flawed in achieving the isolation of the neural substrates of specific mental functions (for discussion, see: Cacioppo et al., 2003; Caplan, 2007; Price & Friston, 2005). Poldrack & Yarkoni (2016) suggest that there are basic conceptual difficulties within subtraction applied in task-based fMRI 'that remain widely underappreciated within the neuroimaging community' (pg. 589). This is observed in the MID task, as *conceptually* the subtraction intends to measure approach and avoidance of positive and negative conditions (Knutson & Greer, 2008), but this is not consistent in the activation patterns of valence (insula) and approach (NAcc) structures that, at the group-level, are activated similarly in both conditions (Murray et al., 2020; Oldham et al., 2018). Although using monetary value allows control of magnitude, probability, and timing (Knutson & Greer, 2008), adding a discrete step with positive or negative monetary cues (i.e., "pure insertion assumption"; Price & Friston, 1997) may not be sophisticated enough to identify valence and approach over and above processes of attention

and/or motivation within an individual. While the MID task measures distinct positive and negative valenced systems in two distinct phases, the nature to which these phenomena vary or are consistent across specific behaviors has not been well characterized. And in fact, this work in a community sample of young adults suggests that they may not significantly differ in terms of the structures that are involved. This highlights a need to precisely define the nomological network of reward designs and consider whether the predicted associations reflect the observed patterns, which is elaborated on in Chapter 6.

Although the findings suggest a high level of variability between contrast choices and behavioral associations, several measures can be taken that may improve the generalizability of results in the MID task literature. First, an immediate step that can be taken by researchers is increasing sample sizes in task-based fMRI research. Currently, a large proportion of fMRI studies are substantially underpowered for finding the effect they are testing (Szucs & Ioannidis, 2017, 2020). Second, researchers would benefit from assessing how the MID contrast values fit in a larger nomological network of neural and behavioral constructs (Poldrack & Yarkoni, 2016), beyond an abstract subtraction processes that presumes a process of motivation or consumption of reward, and preregister these hypotheses in advance. Third, multivariate methods, such as dimensionality reduction and cross-validated predictive modeling, may help with the reproducibility of theorized neural substrates of cognitive processes (Hong et al., 2019). Multivariate, cross-validated analyses can provide *a priori* activation patterns and locations that can be confirmed out of sample, reducing the possibility of exploring multiple hypotheses. Finally, if the goal is to characterize individual variability in neural function, researchers should implement functional organization techniques to explain changes in behavior and cognitive processes (Beltz et al., 2016; Yip et al., 2019; Zhang et al., 2019). Network models of task-based

fMRI may be particularly helpful for uncovering the neural architecture of cognitive processes (Greene et al., 2018; Medaglia et al., 2015). By using individual and group level estimates of connectivity patterns (Beltz et al., 2016), task-based analyses may improve the identification and replication of neural signatures that will aid researchers studying developmental and clinical differences (Yip et al., 2019; Zhang et al., 2019). I address these concerns surrounding individual variability discussed here in Chapter 6 and in the following chapter, Chapter 5.

## Study Considerations

Although the findings here pose significant implications, there are a number of limitations. First, the findings are tested only in a modified version of MID task that was administered in a young adult sample, so the implications should be considered and confirmed in separate samples to determine which effects converge between samples and which are limited to a sample. Future work should examine these associations in a larger sample and at different developmental stages using, for example, the ABCD study data. Second, the correlates between ROI activation and self-reported behavior may be underestimated, such that behavior that is collected contemporaneously with the scan acquisition or in the nature that the brain predicts behavior may produce different effects. Moreover, due to a combination of increased number of voxels and alternative methods for controlling the false positive rate, the whole brain statistical analyses exploring brain-behavior associations may reveal findings that an ROI constrained analysis may overlook. Third, only a subset of common *a priori* contrasts were selected from the literature. Alternative contrasts, such as the linear combination of winning or alternative contrasts during the outcome phase, should be considered in future work. Since the anticipation and outcome phase in this task were not jittered, we could not directly contrast these phases at the individual level (only group level), due to risk of collinearity. Finally, due to the outcome

phase containing variable number of trials as a function of 60% accuracy rate, the activation patterns may be influenced by the surprise of the event(s) (Vassena et al., 2020), which should be considered in future work.

It is worth noting that some of the differences between positive and negative cues in this and previous studies may depend on age-related factors and sample characteristics. For instance, while the results here did not demonstrate a meaningful difference in the activation of the VS or insula between Big Win and Big Lose anticipation phases, age related differences have been previously reported using this task, such that increases in activation during Big Win anticipation trials were greater in older adults (Bjork et al., 2010), and reduced activation in response to Big Lose anticipation in 9-12 year old's (Cope et al., 2019). This suggests patterns of activation during the MID task within and between sample comparisons has been considered when age-related effects are present, as qualitative differences between some contrasts may not be readily apparent. Furthermore, whereas these analyses focus on a community-recruited young adult sample, previous reviews focused on clinical populations (Balodis & Potenza, 2015; Radua et al., 2015), and these results should be considered in the future within a clinical population to assess how associations would change in light of clinical factors.

## Conclusion

Although univariate fMRI contrasts from the MID task are often used to measure neural substrates of reward processing, modeling techniques have varied substantially between studies. The structure of the task has been proposed to separately measure the constructs of arousal and valence. However, it is still unclear whether these dimensions are easily separable using different task contrasts, and whether findings from different contrasts can be easily generalized between studies. This within-sample comparison of MID contrasts during multiband fMRI revealed more

similarities than differences between positive and negative cues during the anticipation contrast, dissimilarity of the specific Big Win versus Small Win contrast during the anticipation phase, a robust deactivation effect in the outcome phase, and behavioral associations that are less robust than previously thought. These findings point to the need for caution in future work that make attempts at generalization and encourage researchers to power their studies for effects that may be smaller than previously hypothesized.

## Chapter 5 : Neural Heterogeneity Underlying Late Adolescent Motivational Processing is Linked to Individual Differences in Behavioral Sensation Seeking[3]

Adolescent risk-taking behavior, including sensation seeking, has been a central focus for developmental research, interventions, and policy largely because it is responsible for heightened death and disease seen during an otherwise healthy period of life (Kann et al., 2018). Neuroscience research has provided critical insights (Casey, 2015). As discussed in Chapter 1 and Chapter 3, there are varying degrees of support for a related set of models contending that normative changes in the cognitive control system (e.g., dorsolateral prefrontal cortex) and socioemotional system (e.g., ventral striatum and amygdala) during adolescence predispose youth to sensation seeking that most will outgrow with continued neural development (Casey et al., 2008; Ernst et al., 2006; Shulman et al., 2016; Steinberg, 2008). Although the implications of these models have been far-reaching, there is continued debate about their accuracy and applicability to all youth, potentially owing to their focus on functional localization and quantitative methods that are averaged across variable youth (Beltz, 2018; Bjork & Pardini, 2015; Willoughby et al., 2013). The goal of this study is to begin to fill that knowledge gap by creating adolescent-specific networks of the socioemotional and cognitive control systems during

[3] Chapter 5 corresponds to Demidenko et al. (2022), published in *Journal of Neuroscience Research*

a motivational mental state presumed to occur in a reward processing task and examining their associations with sensation seeking behavior.

## Neural Connectivity and Adolescent Reward Processing

There is certainly variability, but most neurodevelopmental models of adolescent risk-taking behavior (Casey et al., 2008; Ernst et al., 2006; Steinberg, 2008) broadly concern the interplay between brain regions implicated in: (a) cognitive control, such as the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (DLPFC); and (b) socioemotional processing, which can be broken down into the reward and salience subsystems. The reward subsystem facilitates approach behaviors, and includes the ventral striatum (VS), orbitofrontal cortex (OFC), and ventromedial PFC (vmPFC) (Haber & Behrens, 2014; Haber & Knutson, 2010). The salience subsystem detects the valence of stimuli, and includes the amygdala and insula (Knutson & Greer, 2008; Posner et al., 2005). Early studies evaluted differences in mean-level activation of regions thought to contribute to sensation seeking behavior during reward processing showed developmental differences between adults and adolescents (reviewed in Silverman et al., 2015), such that adolescents had greater activation than adults in the VS and insula when receiving rewards (Galván & McGlennen, 2012), but less activation than adults in the ACC and VS when anticipating rewards (Bjork et al., 2010). Some early studies also examined the associations between regional mean-level activations and risk-related behaviors, such that risk engagement and VS activation were more strongly positively related in adolescents and adults (Galvan et al., 2007).

Although informative, these early studies generally do not consider functional integration among the multiple regions that constitute each system or network (Pessoa, 2017), and they rarely consider individual differences in activation. Connectivity studies, however, have the

potential to map patterns among integrated neural networks (Beltz, 2018; Lydon-Staley & Bassett, 2018). Specifically, connectivity analyses overcome limitations of functional localization by evaluating the covariation, or functional dynamics, among regional activations, which is emphasized in most theories of the neural underpinnings of adolescent risk-taking behavior (Beltz, 2018; Meisel et al., 2019). While prior studies have used connectivity analyses, methods have often averaged across adolescents in an attempt to describe normative development. Person-specific connectivity takes an individual differences approach, though, by modeling at the subgroup, or even at the individual, level. This is important because there is growing evidence of extreme individual differences in both neural function (Becht & Mills, 2020; Gordon et al., 2017; Finn et al., 2017; Poldrack, 2017) and in adolescent brain development (Lydon-Staley & Bassett, 2018).

To date, several studies have considered the relation between mean (or group-level) connectivity and sensation seeking. For instance, connectivity between the amygdala and the OFC during resting state using seed-based functional connectivity (i.e., detecting associations between a candidate region and all other brain regions) have been shown to be inversely related to sensation seeking (Crane et al., 2018). Also, connectivity between VS and motor areas during incentivized trials during a task using psychophysiological interaction (i.e., combining seed-based correlations and task regressors) have been shown to be positively related to sensation seeking (Crane et al., 2018; Weiland et al., 2013). Finally, mean-level connectivity patterns in the OFC and ACC using correlations matrices (i.e., Pearson's correlations) from resting state data were reported to reliably predict ($r$ = .30) sensation seeking in adults (Wan et al., 2020). Together, these studies suggest that there are links between neural connectivity and sensation seeking.

Nonetheless, significant questions remain about the association between connectivity and sensation seeking during adolescence, as participants in the studies reviewed above ranged in age from 18 to 85 years (Crane et al., 2018) or only included young-to-mid adults aged 21 to 35 years (Wan et al., 2020). Questions about adolescent-specific motivational processes and behavior are important to answer because the developmental peak in sensation seeking seems to be between ages 14 to 20 (Harden & Tucker-Drob, 2011; Romer, 2010). Although one study examined functional connectivity patterns and sensation seeking in an adolescent sample (18 to 22 years old), the study only looked at mean-level connectivity in a sample of adolescents exposed to higher rates of adversity (Weiland et al., 2013). This is important, but it is unclear the extent to which those findings generalize to other samples. Thus, there is empirical evidence for meaningful associations between functional connectivity and sensation seeking, but there remains a need for research on adolescents that captures individual differences.

## Person Specific Connectivity

One promising way to accurately capture individual differences in the neural networks underlying adolescent motivational processing is to use a person-specific connectivity approach that avoids assumptions about uniformity (Beltz, 2018; Lydon-Staley & Bassett, 2018). Given the heterogeneity of functional networks (Finn et al., 2017) and adolescent behaviors (Bjork & Pardini, 2015), modeling person-specific covariation among regional activations may capture effects that are stronger (or present) for one subset of individuals than another or even that are unique to an individual (see Beltz & Gates, 2017).

Group Iterative Multiple Model Estimation (GIMME; Gates & Molenaar, 2012) is one such modeling approach. GIMME creates sparse person-specific networks specifying data-driven connections (or edges) among brain regions of interest (ROIs) that can occur at multiple levels:

group, subgroup and individual (Beltz & Gates, 2017; Gates et al., 2017). First, GIMME estimates group-level connections that are meaningful for at least 75% of individuals. Second, subgroups are identified using the Walktrap community detection algorithm (Orman & Labatut, 2009), which clusters into a community individuals based on the similarity of their group-level connection magnitudes (Gates et al., 2016), and then subgroup-level connections that are meaningful for only individuals in the same subgroup are estimated. Third, individual-level connections that are unique to a person (and estimated after group- and subgroup-level connections, which improves their reliability; Gates et al., 2017) are estimated. While the final networks characterize both homogeneity (in the group-level connections – without averaging across individuals) and heterogeneity (in the individual-level connections) in a sparse network, subgroup-level connections represent both homogeneity and heterogeneity. Simulation studies have demonstrated that GIMME effectively identifies the presence of connections between ROIs and is an accurate method for modeling network patterns in functional timeseries data, especially compared to other approaches when participants are heterogeneous (Gates et al., 2017; Mumford & Ramsey, 2014; Smith et al., 2011).

GIMME has been successfully used to delineate person-specific networks in developmental and clinical research (reviewed in Beltz & Gates, 2017; Beltz & Weigard, 2019). For instance, during an alcohol-related inhibition task in young adults, the number of connections within the cognitive control system changed across the transition to college in accord with alcohol use behaviors (Beltz et al. 2013). Moreover, during resting state, network connectivity patterns in subgroups effectively delineated communities of children with different clinical diagnoses (e.g., autism spectrum disorder and attention deficit hyperactivity disorder) and healthy controls (Henry et al., 2019), such that children with diagnoses were characterized

by connections between the default mode, salience and ventral attention networks, whereas controls were largely characterized by within-network connections. Likewise, resting state network connectivity patterns revealed subgroups of adolescents who varied in levels of childhood violence exposure (Goetschius et al., 2020), which is particularly noteworthy because it illustrates how GIMME can differentiate - in adolescence - brain networks of children with certain experiences of adversity in a purely data-driven fashion. The ability to capture both neural homogeneity and heterogeneity in neural network features is critical in the study of adolescent sensation seeking because risk-taking tendencies may only represent a subset of youth and not all adolescents (Bjork & Pardini, 2015).

## Current Study

In the current study, we examine whether person-specific network connectivity during a motivational processing task meaningfully relates to individual differences in self-reported sensation seeking behaviors. Given our interest in modeling the dynamic complexity of the brain and the precedent in prior studies using GIMME with task fMRI (Beltz et al., 2013; Duffy et al., 2021; Hillary et al., 2014; Weigard et al., 2018), we do not consider modulating effects of task regressors but rather focus on comprehensively evaluating connectivity during a *motivational state*, or a state of being continuously engaged in a task in which possible gains and losses are evaluated and received. In other words, we uniquely capture relations among a broad set of ROIs to understand systems-level neural integration during continuous motivational processing, but we do not explicitly estimate contrasts (e.g., gain > loss) as in traditional analyses of the Monetary Incentive Delay (MID) task; thus, our GIMME networks may not reflect reward processing *per se* (Balodis & Potenza, 2015; Dugré et al., 2018).

Specifically, we applied GIMME to two separate runs of the MID task (Knutson et al., 2000) in a sample of late adolescents, focusing on 12 ROIs that reflect the cognitive control, reward and salience networks (e.g., bilateral OFC, DLPFC, Insula, Amygdala, VS, and ACC and vmPFC). As described above and in the neurodevelopmental literature (Demidenko et al., 2020; Sherman et al., 2018; Silverman et al., 2015; Steinberg, 2010), we focus on these ROIs given evidence for the role of DLPFC and ACC in cognitive control processes (Apps et al., 2016; Szczepanski & Knight, 2014); the role of VS, OFC and vmPFC in motivational processes and economic decision making (Haber & Behrens, 2014; Knutson et al., 2014; Padoa-Schioppa & Conen, 2017; Roy et al., 2012); and the role of the insula and amygdala in valence and affective processing (Knutson et al., 2014; Posner et al., 2005). Although we use network labels, such as cognitive control, reward and salience, as heuristics, brain regions are rarely localized to specific networks (Rolls, 2014) or affective processes (Berridge, 2019); instead, they play a dynamic part in a complex interacting system (Pessoa, 2021). Thus, these network labels are intended to serve as conceptual links to the neurodevelopmental models from which the hypotheses below are derived (Casey et al., 2008; Ernst, 2014; Steinberg, 2010).

We implement GIMME's subgroup community detection algorithm to uncover potential communities of adolescents who share neural features during motivational processing, and then we examine how these features relate to adolescent sensation seeking behavior. Given that reported poor within-participant reliability in task-based fMRI may be attributed to habituation (Elliott et al., 2020), or waning vigilance or novelty in reward systems triggered by fMRI tasks (Ekhtiari et al., 2020; Plichta et al., 2012), we also consider the network connectivity during the combined and individual MID run time-series.

Our study is comprised of three aims. In Aim 1, we map person-specific connectivity in reward processing regions separately for each run of the MID task, exploring whether there are data-driven subgroups during a presume motivational state. In Aim 2, we examine whether there are meaningful associations between network features (such as subgroup membership and connection strength) and sensation seeking separately by run. In Aim 3, we compare estimated connections between Run 01 and Run 02 to detect potential habituation across runs and repeat Aims 1 and 2 for the combined runs to evaluate the robustness of findings from the individual runs for the combined time-series. We expect to find substantial individual differences in motivational processing, evidenced by person-specific networks, but given the novelty of this approach, we do not have expectations about whether data-driven subgroups will exist. Nevertheless, we do hypothesize that connectivity strength between reward and cognitive control ROIs will be related to sensation seeking based on common neurodevelopmental models that implicate regions, including the VS, OFC, vmPFC and/or DLPFC, in the relationship to sensation seeking (Casey et al., 2008; Casey et al., 2019; Ernst et al., 2006; Shulman et al., 2016; Steinberg, 2008).

## Methods

### Participants

Participants in this study are a Phase 2 subsample ($N$ = 104; $M_{Age}$ = 19.3; $SD_{Age}$ = 1.3; 57% Female; 71% White, 14% Black, non-Hispanic, 6% Hispanic/Latinx) of adolescents from the Adolescent Health Risk Behavior (AHRB) study, as described in Chapter 2.

### Procedures

All study procedures were approved by the University of Michigan Institutional Review Board. Upon arrival for Phase 2 neuroimaging, research staff reviewed instructions of the MID

task. Participants were informed of the cue-related outcomes and completed a practice trial. Participants were explicitly informed that their performance, or cumulative earnings during the MID (maximum of $30), would be associated with the compensation they received at the end of the visit.

Measures

*Sensation Seeking*: Participants completed the Brief Sensation Seeking Scale (BSSS) at Wave 3, which is an 8-item self-report measure of novelty seeking behaviors (Hoyle et al., 2002). Participants responded on a 5-point Likert-scale for 8 items: (1) "strongly disagree" to (5) "strongly agree." Example items are "*I would like to explore strange places*" or "*I would like to try bungee jumping*". The BSSS is a revised version of the earlier SSS (Horvath & Zuckerman, 1993; M. S. Zuckerman et al., 1978) that updates behavioral descriptions and language, and that removes similar items (e.g., related to alcohol) (Arnett, 1994; Hoyle et al., 2002). The composite variable is the average of the 8 items, such that higher scores reflect higher sensation seeking.

In order to leverage the longitudinal sensation seeking data from Phase 1 of this study, growth curves were used to estimate behavior at Wave 3 (most proximal to the scan) for all participants. Specifically, SAS 9.4 PROC NLMIXED (SAS Institute Inc., Cary, NC) was used to fit mixed-effects growth curve models to the three waves of BSSS data treating the intercept as a random effect and using an unstructured error covariance matrix; the intercept was calculated at Wave 3. Across the three waves, 100% ($N$ = 104; $M$ = 3.29, $SD$ = .76), 77% ($N$ = 80; $M$ = 3.26, $SD$ = .72) and 89% ($N$ = 93; $M$ = 3.33, $SD$ = .56) of participants provided BSSS data. Full information maximum likelihood (FIML) estimation was used in combination with empirical Bayes estimates to provide intercepts for all 104 participants in the sample (Rubin, 1976). As

expected, the individual BSSS intercept estimates were highly correlated with the observed Wave 3 self-reported BSSS, $r$ = .82.

*FMRI Task:* The MID task (Knutson et al., 2000) was used to measure brain activity during a motivational state that comprised both monetary gains and losses. For more information on the design, please refer to Chapter 2. As noted in Chapter 2, participants were explicitly told that their performance on the task during the scan (for example, $5 Win Cue was associated with an opportunity to win $5 and a $5 Lose cue was associated with an opportunity to not lose $5) would be associated with the compensation they can get for their cumulative earnings during the MID (Maximum $30). Two MID runs were administered; each lasted 5:42 min and consistent of 407 volumes.

### fMRI Data Acquisition

FMRI data was acquired using the same protocol that is described in Chapter 2.

## Analyses

### fMRI Data Analyses

FMRI data were preprocessed using the same sequences of steps that are described in Chapter 2.

Several steps were completed to extract the timeseries data for GIMME analyses. First, central coordinates for 12 ROIs (see Figure 5.1; Appendix D, in Table D1, for specific MNI coordinates) were selected using Neurosynth

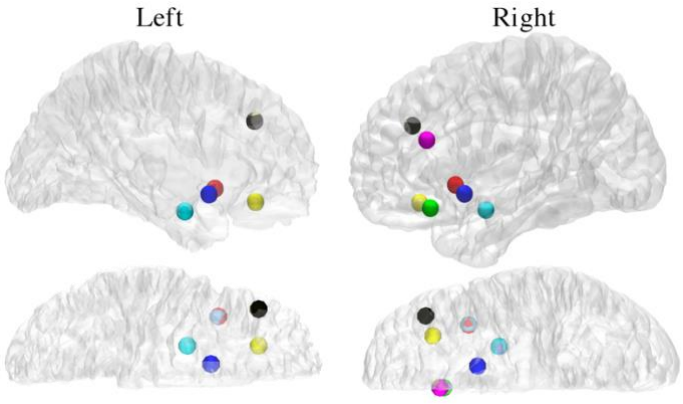


*Figure 5.1*. Twelve ROI coordinates projected onto an MNI glass brain.
Blue = Ventral Striatum; Green = Ventromedial Prefrontal Cortex; Pink = Anterior Cingulate Cortex; Yellow = Orbitofrontal Cortex; Red = Insula; Cyan = Amygdala; Black = Dorsolateral Prefrontal Cortex

(Neurosynth.org) based on previous literature (Galvan, 2010; Sherman et al., 2018). These regions belong to three networks: the cognitive control network, which consists of the bilateral DLPFC, and ACC; the reward network, which consists of the bilateral VS, vmPFC and OFC; and the salience network, which consists of the bilateral amygdala and insula. For each ROI, a 10mm sphere around the central coordinate was used to extract the mean signal intensities at each volume for each of the two runs. For Aims 1-2, the timeseries from each separate run was used, but for Aim 3, the concatenated timeseries across the two runs was used. Due to the rapid volume acquisition (800ms), each run was down-sampled (retaining every other volume) after preprocessing, as has been suggested (Beltz & Gates, 2017) and used in other fast-acquisition methods, such as functional near-infrared spectroscopy (Pinti et al., 2019).

GIMME Analyses

GIMME version 0.6-0 in R version 3.6.1 (R Core Team, 2020) was used to estimate time-lagged (*t*-1) and contemporaneous (*t*) network connections in unified structural equation models (uSEM), which combine vector autoregressions and structural equation models, respectively, for each individual within a grouping algorithm that contains subgrouping via community detection. GIMME estimates network connections through a data-driven search process that uses Lagrange multiplier tests to select connections at the group, subgroup and individual level that most improve model fit. The sequential steps of the GIMME search process are summarized in Figure 5.2. At the beginning of these steps, we estimate autoregressive connections as part of a "null" model, as this search strategy has been demonstrated to improve recovery of other connections in temporally dense data (Lane et al., 2019). Then, starting with this null model, group-level connections that best improve fit for the at least 75% of the sample are iteratively estimated for all participants. After the estimation of the group-level connections,

GIMME uses this *a priori* model to inform subgroup detection. Subgroups are estimated using a data-driven community detection technique to cluster individuals with common sets of interconnected ROIs via Walktrap. For each subgroup, connections that improve fit for at least 50% of individuals in the subgroup are iteratively estimated for all participants in the subgroup (Gates et al., 2017). After subgroup detection and connection estimation are complete, the group and subgroup *a priori* models are used in the iterative data-driven estimation of individual-level connections that uniquely characterize participants and improve their model fit. At each of these three steps, the algorithm stops its search when: a) the model fits well according to two out of four fit statistics: Comparative Fit Index (CFI) ≥ .95, Non-Normed Fit Index (NNFI) ≥ .95, Standardized Root Mean Square Residual (SRMR) ≤ .05 and Root Mean Square Error of Approximation (RMSEA) ≤ .05; or b) modification indices indicate no additional connections will significantly improve fit– whichever comes first. The former is a stopping rule implemented to avoid overfitting. Given that the connections are inferred through the data-driven process from

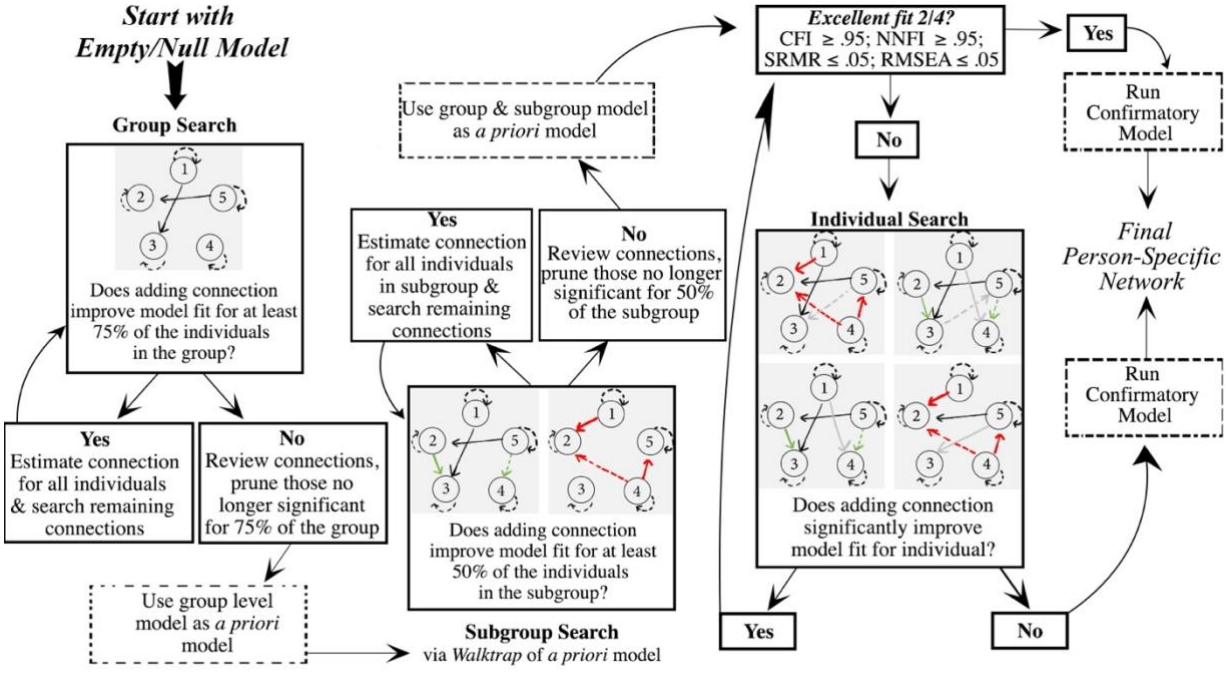


*Figure 5.2.* GIMME Model Flow Chart.
Lines represent: Group connections= Black; Subgroup connections = Green; Individual connections = Grey; Solid = Contemporaneous; Dashed = Lagged; Green = Subgroup 1; Red = Subgroup 2

the temporal information in the fMRI data, the final maps reflect estimates of directed functional connectivity (Beltz & Gates, 2017; Friston et al., 2013).

To characterize individual differences in GIMME-derived networks, we focus on subgroup membership and individual coefficients from the networks when examining links to sensation seeking behavior. Subgroups are identified in GIMME (if they exist) and reflect neural network similarities among some sets of participants during the MID continuous motivational state. Each subgroup is characterized by a set of unique network connections, and each has a person-specific beta estimate that reflects its strength and magnitude. These individual subgroups and connection estimates can be examined in relation to the BSSS.

## 2.8 Analysis Plan

Event-related designs are often insufficiently powered to estimate the effects of specific task conditions (e.g., anticipation or feedback in the MID) on neural connectivity (see Beltz, 2018; Di & Biswal, 2017). This is especially true for *rapid* event-related designs, such as the current study's design, because the HRF is longer than the inter-stimulus interval. It is also borne out by simulations using GIMME on task data (Duffy et al., 2021; Gates et al., 2011) and in empirical studies that modeled task regressors in GIMME and found little evidence for their substantial modulating effects on connectivity (Hillary et al., 2014; Price et al., 2020). Given this evidence, we focus on the connectivity among regions during a *motivational state* rather than modeling modulation by specific task phases (e.g., during individual gain or loss events).

To test Aim 1, which was to examine whether there are data-driven subgroups during motivational processing, we use GIMME to map person-specific connectivity in reward ROIs separately for each run of the MID task, and then examine whether data-driven subgroups are identified. If subgroups are found, we will proceed to Aim 2.

To test Aim 2, which was to examine whether there are meaningful associations between network features (e.g., subgroup membership and connection strength) and sensation seeking, we use logistic regression to evaluate whether BSSS (i.e., Wave 3 empirical Bayes intercepts from the growth curve models) is significantly ($p < .05$) associated with the subgroups detected from the first and second runs, separately. Specifically, we predict subgroup membership from BSSS, controlling for age, sex, and head motion (mean framewise displacement, or FD). To determine which subgroup connections may be driving links with sensation seeking, significant associations are followed-up with exploratory multiple regression analyses – conducted within each subgroup separately – to examine associations between specific connection strengths that are meaningful to the subgroup and BSSS.

Finally, to test Aim 3, we i) compare estimated connections between Run 01 and Run 02 to detect potential habituation across runs and ii) repeat Aims 1 and 2 for the concatenated time-series to evaluate the robustness of neural connectivity and its BSSS associations in the full time-series. Specifically, we: (a) examine whether data-driven subgroups are identified, and then if subgroups are identified, we (b) use logistic regression to evaluate whether BSSS is significantly ($p < .05$) associated with the subgroups and evaluate which subgroup connections may be driving links with BSSS with follow-up multiple regression analyses, as we did in Aim 2.

We set the alpha cut-off ($p < .05$) that is conventionally used in null-hypothesis significance testing for each of the regression analyses because of the novelty of these analyses. This is consistent with recommendations for new analyses and recent perspectives on multiple comparison corrections (e.g., Rubin, 2021; Thompson et al., 2020).

## Results

Demographic characteristics, task accuracy in Appendix D and in-scanner motion during the MID task for participants are reported in Appendix D, in Tables D2-D5, respectively. No participants had mean head motion (Post FD) greater than .20, and so based on prior recommendations (Park et al., 2018), no participants are excluded from analyses for this reason; specifically, maximum mean FD was .07 (*M* = .02, *SD* = .01) for Run 01 and .11 (*M* = .02, *SD* = .01) for Run 02. Furthermore, BSSS was not significantly associated with mean post FD for Run 01, *r*(102) = .02, or Run 02, *r*(102) = - .05.

### Aim 1: Person-specific Connectivity Networks by Run

For all 104 participants, GIMME networks fit the data well (see Appendix D, Table D5), and a summary of the final networks is shown in Figure 5.3. Specifically, network connections for the group (black), subgroup (Subgroup01 = red; Subgroup02 = green) and individual (grey) connections are presented for each run of the MID in Figure 5.3. Solid lines represent

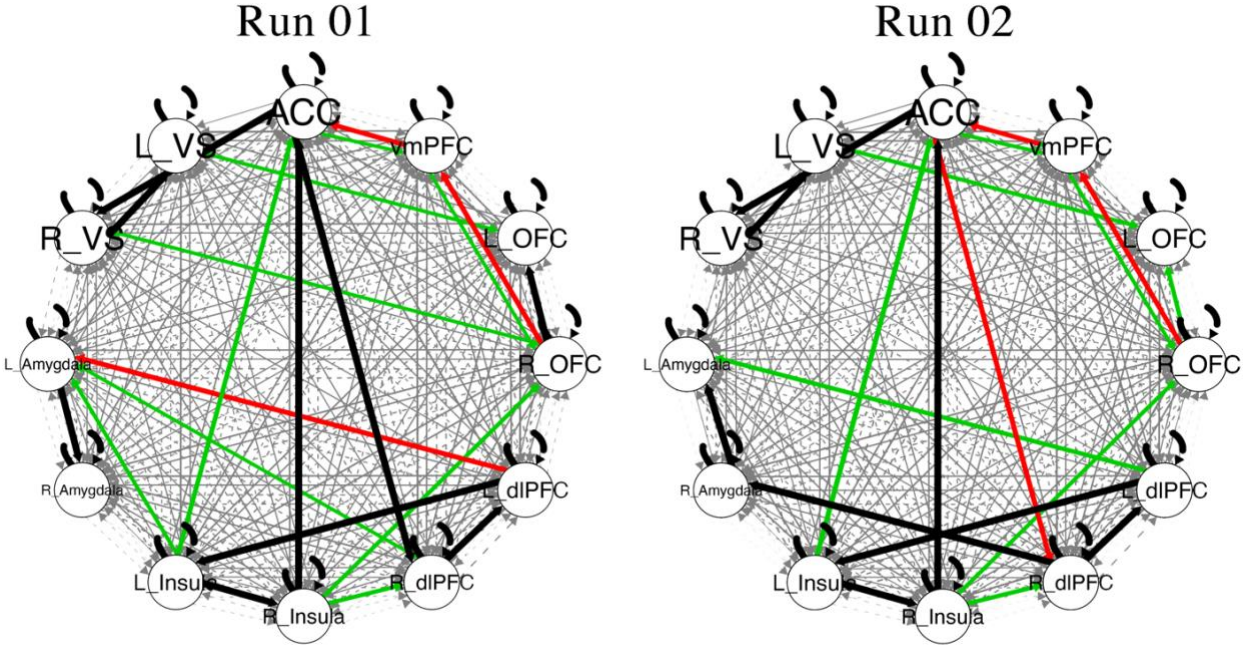


*Figure 5.3*. GIMME Connectivity Networks for Each Run.
Black = Group connection; Red = Subgroup01 connections; Green = Subgroup02 connections; Solid = Contemporaneous; Dashed = Lagged (*t* – 1); dlPFC = dorsolateral prefrontal cortex; OFC = orbitofrontal cortex; vmPFC = ventromedial PFC; VS = ventral striatum

contemporaneous connections, dash lines represent lagged connections, and the weight of each line reflects the proportion of participants with that connection.

There were some similarities and some differences in the GIMME group-level networks for each run. For instance, there were consistent connections among the bilateral VS, amygdala and insula regions, L VS and ACC, L insula and L DLPFC, and R insula and ACC regions of reward, salience and cognitive control networks, but different connections between ACC and R DLPFC regions of cognitive control network at the group-level. The GIMME community detection algorithm also identified two subgroups in each run of the MID, but the number of participants in each subgroup and the subgroup-level connections differed.

For Run 01, 61 participants were in Subgroup01 and 43 participants were in Subgroup02. For Run 02, 56 participants were in Subgroup01 and 48 participants were grouped into Subgroup02. For each run, the more homogeneous subgroup, Subgroup02, was represented by dense within-reward network connections and a greater number of connections between cognitive control, reward and salience networks than the heterogeneous subgroup, Subgroup 01, which had few subgroup connections. With respect to subgroup connections, patterns were relatively consistent across runs. Participants in heterogeneous subgroup, Subgroup01, had three subgroup-level connections during each run; two were the same and one differed, such that R OFC → vmPFC and vmPFC → ACC connections reoccurred across the two runs, but L DLPFC → L Amygdala was unique to Run 01 and ACC → R DLPFC was unique to Run 02. Participants in the more homogeneous subgroup, Subgroup02, had nine and eight connections per run, respectively; they were similar except L Insula → L Amygdala, R DLPFC → L Amygdala, R and OFC → R VS only occurred in Run 01 and R OFC → L OFC, L DLPFC → L Amygdala only occurred in Run 02 (see Appendix D Table D8).

Aim 2: Subgroup and Connection Strength Associations with Sensation Seeking

For Aim 2, we evaluated whether the subgroups identified in Aim 1 were related to BSSS. In a logistic regression model, there was a significant association between subgroup and self-reported BSSS for Run 01 (*b* = 1.1), OR = 3.1 (see Table 5.1), such that a unit increase in BSSS was associated with 3.1 odds increase in the likelihood of being in Subgroup02, which is represented by several subgroup level connections among reward and salience regions. The model that included BSSS (AIC = 126.9) fit the data significantly better than the model without BSSS (AIC = 131.4), $\Delta\chi^2(1) = 4.7$, $p = .03$. Subgroups did not differ in age or sex, but they did differ in FD, such that there was greater motion observed for participants in Subgroup02 ($p < .01$). This effect is unchanged with (Table 5.1) and without the covariate of motion (e.g., mean Post FD) in the model (Appendix D Table D9).

*Table 5.1* Logistic Regression: Sensation seeking associated with GIMME-derived subgroup from MID task data, by run, with and without Post FD (N = 104)

| | *Run 01* | | | *Run 02* | | |
|---|---|---|---|---|---|---|
| | *b* | SE | *p* | *b* | SE | *p* |
| Age | - .18 | .17 | .28 | - .11 | .16 | .48 |
| Sex | .28 | .43 | .52 | .80 | .42 | .06 |
| PostFD | 48.8 | 18.24 | .008 | 29.4 | 15.84 | .06 |
| BSSS | 1.1 | .55 | .04 | .58 | .51 | .26 |

PostFD = Post Preprocessing Framewise Displacement; BSSS = Brief Sensation Seeking Scale

There was not, however, a significant association between subgroup and self-reported BSSS from Run 02 (*b* = .58), OR = 1.8 (see Table 7), such that the model that included BSSS (AIC = 135.1) did not fit the data significantly better than the model without BSSS (AIC 136.4), $\Delta\chi^2(1) = 1.3$, $p = .25$. Even though the direction of the effect was the same as in Run 01, such that sensation seeking was greater in Subgroup02, the size of the effect was attenuated in Run 02. Subgroups also did not differ in age, sex, or FD.

Given the significant prediction of subgroup classification from BSSS in Run 01, with Subgroup02 being linked to increased BSSS, we explored whether BSSS was associated with person-specific beta weights (i.e., connection strength) of subgroup-level connections in Subgroup02 for Run 01. Exploratory multiple regression analyses revealed that the strengths of the vmPFC → R OFC connection, $b$ = .21, $p$ = .02, and the R OFC → R VS connection, $b$ = -27, $p$ = .01, (see Figure 5.4 and Appendix D, Table D11) were significantly associated with BSSS. Hence, increased self-reported sensation seeking was positively associated with connectivity strength between the vmPFC and R OFC (Figure 5.4B), and sensation seeking was negatively associated with connectivity strength between R OFC and R VS (Figure 5.4C) – which are regions that are associated with reward processing.

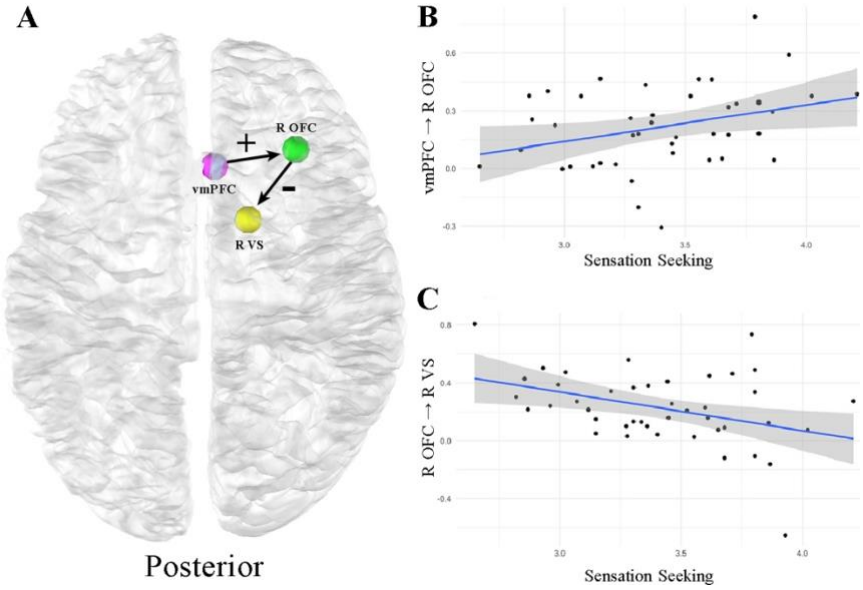


*Figure 5.4.* Meaningful associations between connection strength and sensation seeking in Subgroup02 during Run 01.
(+) = sig. positive association; (-) = sig. negative association.

Aim 3: Subgroup Associations with Sensation Seeking in Combined MID Runs

We compared and contrasted GIMME results between the runs with GIMME results from the combined MID runs. Regarding comparisons between Run 01 and Run 02, there were notable differences (Figure 5.3). Although the group-level connections do not appear completely disparate between the two runs, only 55% of the group-level contemporaneous connections (solid black lines) re-occurred across both runs. Then, the number of participants classified into a

Subgroup01 and Subgroup02 are statistically significant between runs, $\chi(1) = 18.1$, $p < .001$, $\Phi = .41$, such that 72% ($N = 44$) of the participants were consistently grouped into Subgroup01, and 72% ($N = 31$) of participants were consistently grouped into Subgroup02 (Appendix D, D6).

Regarding analyses of the combined runs, the GIMME networks fit the data well for all participants except one (see Appendix D, Table D12 and Figure D2). For this participant, the model did not converge. As for the analyses conducted separately per run, two subgroups were identified. The number of participants differed across each subgroup, with 34 in Subgroup01 and 69 in Subgroup02. Subgroups were comparable in the number of subgroup-level connections estimated for Subgroup01 and Subgroup02, with 19 and 16 connections, respectively. Both Subgroup01 and Subgroup02 had connections within the reward and salience networks as well as dense between reward, salience and cognitive control network connections. When examining whether self-reported BSSS predicted subgroup membership, there was not a significant effect ($b = -51$; Appendix D Table D13), such that the model that included BSSS (AIC = 129.6) did not fit the data significantly better than the model without BSSS (AIC 130.5), $\Delta\chi^2(1) = 0.9$, $p = .33$. This suggests that the positive association between sensation seeking and subgroups that was present for Run 01 was not observed when the runs were combined.

## Discussion

We used a person-specific network connectivity approach, GIMME (Gates & Molenaar, 2012), to evaluate a central question in adolescent risk-taking: Do individual differences in neural network connectivity during a continuous motivational processing task meaningfully relate to self-reported sensation seeking behavior? Specifically, we examined whether and how connectivity during two runs of a commonly used reward task (i.e., Monetary Incentive Delay; Knutson et al., 2000) differed between data-derived subgroups of late adolescents in ways related

to sensation seeking (calculated as the endpoint intercept of a 3-wave behavioral trajectory across adolescence). To examine possible habituation effects, we considered how neural subgrouping and behavioral associations varied across runs and across analyses that combined the runs. We found that there were two data-derived subgroups in each run, and that subgroup network connections were meaningfully associated with sensation seeking, although inferences depended on how the runs were modeled. To my knowledge, this is the first investigation of adolescent-specific network connectivity mapping during a motivational state with significant links to risk-relevant behavior.

In light of evidence for the neural habituation to reward across time (Plichta et al., 2012; Ekhtiari et al., 2020), we examined person-specific connectivity during continuous motivational processing separately for runs of the MID task in a sparse network of 12 ROIs representing cognitive control, reward processing, and salience networks. We found that the majority of group-level connections reoccurred across runs reflecting some level of stability across connections meaningful to all individuals. Then, for each MID run the GIMME algorithm identified two subgroups. Specifically, Subgroup01 had greater heterogeneity (only three subgroup connections during each run) than the more homogeneous Subgroup02, which had nine and eight connections across Run 01 and Run 02, respectively. This suggests that while there is heterogeneity in adolescent brain activity during motivational processing, there are also some meaningful commonalities across groups of adolescents.

With respect to sensation seeking, when modeling each run separately, we found a significant association between community-based subgroups and self-reported sensation seeking. Specifically, these analyses revealed that the more homogenous subgroup, Subgroup02, had significantly higher sensation seeking than Subgroup01. However, this effect was significant

only during the first run, suggesting that changes in subgroup membership across the runs may have impacted associations with sensation seeking. Similar to prior work that found associations between OFC connectivity and reward traits (Crane et al., 2018; Wan et al., 2020), we found a significant positive association in connectivity strength between vmPFC—Right OFC and sensation seeking, and a negative association in connectivity strength between Right OFC—Right VS and sensation seeking for Subgroup02 during Run 01, but not Run 02. This suggests that the OFC, which is important for stimulus-value representations, tracking internal values, and goal-directed and affective behavior (Haber & Behrens, 2014; Padoa-Schioppa & Conen, 2017; Szczepanski & Knight, 2014), may in part be relevant for individual differences in reward seeking. It also has implications for the potential that habituation may have to impact findings, when the total experimental exposure time is substantial. However, given the exploratory nature of this finding, it requires further exploration and replication in future work.

There were important differences across runs. Although 72% of participants maintained their subgroup assignments across runs (i.e., were in the homogeneous subgroup in both runs or the heterogeneous subgroup in both runs), the differences between runs were meaningful because the association with sensation seeking decreased from the first to the second. This is consistent with recent findings, indicating that some of this decrease may be attributable to habituation (Elliott et al., 2020; Plichta et al., 2012), which is especially relevant to reward regions modeled here (Ekhtiari et al., 2020). Specifically, motivation towards approaching and receiving rewards may be attenuated with repeated runs due to strategic changes in attentional processes (Failing & Theeuwes, 2018); this might be reflected in the dynamics of reward, salience and cognitive control networks that consequently decrease the association with reward-relevant behaviors.

When the analyses were repeated using the combined MID runs, we found changes in subgroup memberships (reflecting homogeneity and heterogeneity) as well as with subgroup associations with sensation seeking. While two subgroups were detected in combined runs, these two subgroups were both more homogeneous and represented by more connections between reward, salience and cognitive control networks than when the runs were analyzed separately. Moreover, the subgroup association with sensation seeking was not significant, and in fact was negative; this is a striking deviation from the significant and positive association in Run 01 and even the positive (but non-significant) association in Run 02. This stark difference might reflect methodological artifacts, such as signal quality or stability with a longer duration scan (Gordon et al., 2017) or the limitations of task-based fMRI, as test-retest reliability is underwhelming (Elliott et al., 2020). Differences across runs could reflect meaningful individual differences. For example, connectivity patterns have been shown to reflect some variability in individuals across runs in both static and dynamic networks (Fong et al., 2019). Moreover, it is tenable that the variability across runs may have influenced both subgroup partitioning (Gates et al., 2016; Pons & Latapy, 2005) and the association between network connectivity and sensation seeking. Future work should reconsider these associations in the context of test-retest of network connectivity metrics (Beck & Jackson, 2020), the features and assumptions of GIMME, and the effect of different fMRI protocols, such as non-multiband data, different head motion corrections, and alternative reward, salience and cognitive control ROI coordinates.

An important consideration in study is that participants were in a presumed general *motivational state* during the MID task, in which neural mechanisms involved in the processing of both gains and losses were consistently engaged, with potentially overlapping neural perturbations. Our reported estimates of directed functional connectivity during the MID task is

therefore distinct from the field's common focus on average contrasts of anticipatory or outcome reward cues or the comparison of neural activation during gain versus loss trials (Demidenko et al., 2021b; Dugré et al., 2018; Oldham et al., 2018). Thus, the ways in which our specific findings map onto established findings in the field regarding reward processing is currently unclear. It is important, however, to highlight that there is empirical support for examining motivational processing as we did because gain and loss cues in the MID design exhibit substantial overlap in neural activation (Murray et al., 2020; Oldham et al., 2018), and brain function involves continuous time-lagged brain states (Munn et al., 2021), with "carryover" effects that are often assumed to be random (e.g., if jitter is implemented correctly) – but this is rarely examined. Nevertheless, the complex issue of reward circuitry and motivational processing during task-based fMRI requires careful theoretical and empirical future work to understand and disentangle.

In addition to generalizing the results reported here, future work should consider how the variability in task length, number of runs and task type impact findings. Some researchers have proposed that increasing the amount of data, or task length (Gordon et al., 2017), and aggregating across modalities (Elliott et al., 2019) may improve reliability and generalizability. Although these suggestions certainly have merit, there may be an inherent trade-off between the possible measurement improvements to reliability that result from increasing the length of a task, and possible measurement decrements that occur due to habituation or other state-related changes linked to longer tasks. Furthermore, cognitive states induced by different tasks have been shown to be characterized by different connectivity patterns explaining different amounts of variance in behavior (Greene et al., 2018). Hence, considering how group-, subgroup- and

individual-level network patterns may vary across reward tasks and its impact in explaining variation in sensation seeking may increase understanding of adolescent risk-taking.

## Study Considerations

The findings reported here are not without limitations. First, major issue in fMRI is the effect of head motion on the quality of the underlying neural signal (Parkes et al., 2018; Power et al., 2014; Siegel et al., 2014). Although we used standard task-based fMRI motion correction (Park et al., 2018), motion may still have impacted the underlying signal. This is especially of concern given that head motion was significantly related to the Subgroups identified. However, we compared our models with and without the covariate of head motion and the moderating effect of motion on the association between sensation seeking and subgroups and found our interpretations did not meaningfully change. Nonetheless, future work should consider how different head motion correction strategies may influence the estimation of person-specific networks.

Second, although the main sample used here is two times greater than the median sample used in neuroimaging studies (Szucs & Ioannidis, 2020), the analyses focused on the brain-behavior associations for Subgroup02 were smaller, and therefore, may be less robust than results involving the full sample. Given the issues of reliability and power in fMRI analyses (Button et al., 2013; Elliott et al., 2020; S. Noble et al., 2019; Szucs & Ioannidis, 2017), we cannot extrapolate our exploratory analyses examining the association between specific connection strengths and BSSS. As such, these results warrant replication in an independent sample. The issue of power was also critical to consider when weighing the pros and cons of modeling the coactivation of brain regions during a *motivational state* rather than the modulating effect of specific task regressors. Ultimately, choosing not to model task regressors during

functional connectivity sacrifices the knowledge about the effects of different phases of reward processing. However, as in most analyses, we had to consider the conceptual and statistical trades-offs of our decision. Our goal was to assess the dynamic engagement of respective brain regions during motivational processes that are important to neurodevelopmental heuristics (Casey et al., 2019). Our related, statistical goal was to model coactivation among regions in a way that was informed by prior literature and adequately powered. Although task regressors are included in psychophysiological interaction analyses (PPI; McLaren et al., 2012), it has been reported that most modulating effects are small and statistically noisy, and therefore, require substantial power accomplished through task lengths and sample sizes in fMRI studies (Di & Biswal, 2017). Consistent with these group-level analyses in PPI, simulation studies of GIMME demonstrate that issues of power can prevent the detection of small task modulating effects, especially in rapid event-related designs like that used in the current study (Duffy et al., 2021; Gates et al., 2011). Thus, we encourage future studies to build on our empirical findings by considering the effect of task modulation in designs that are well powered to do so, such as through the creation and implementation of a slow-event-related MID task.

Third, the networks are based on several key *a priori* ROIs. Although GIMME simulations have demonstrated that omission of variables (i.e., the third variable problem) does not greatly impact recovery of connections (Gates et al., 2017), future work should consider how subgrouping and connection strength are altered when using different combinations of regions.

Fourth, due to some missing sensation seeking data, we used full information maximum likelihood to estimate a sensation seeking score at Wave 3 (closest to when neuroimaging was conducted) for all individuals. This strategy may have introduced additional noise into our models, especially if missingness was related to an unaccounted variable. However, the strategy

also allowed us to maximize our sample size (i.e., by not excluding participants with missing Wave 3 data), and our estimated intercept was significantly related to the observed data increasing our confidence in the observed associations.

Although our study is based on a tenet of the imbalance hypothesis and we found a significant brain-behavior relation, findings cannot be seamlessly extrapolated to other datasets, modeling sequences, or to real-world risk-taking behavior and age-related differences without further research. This is because we used a partially data-driven approach when fitting neural networks and did not have a second, similar dataset available for cross-validation. Indeed, recent evidence in fMRI demonstrates that brain parcellations (Bryce et al., 2021), analytic pipelines (Botvinik-Nezer et al., 2019; X. Li et al., 2021) and other potentially subjective researcher decisions (Bloom et al., 2021; Steegen et al., 2016) impact results; hence, it is imperative that future work replicates these results in other adolescent samples, with other tasks that probe motivational processing, and using other preprocessing pipelines. Second, associations between self-reported sensation seeking and real-world risk-taking are often small-to-medium in adolescent samples (Demidenko et al., 2019). Instead, our findings represent the link between brain function during motivational processing and a psychological trait hypothesized to relate to real-world risk-taking behaviors. While there were not meaningful associations between age and connectivity patterns in this work, prior work has reported developmental differences in connectivity patterns (Marek et al., 2015; Oldham & Fornito, 2019) which future studies should consider. Moreover, while both habituation and reliability issues are plausible explanations for the difference in the association between subgroups and sensation seeking across runs, we cannot delineate which is more probable, given that this version of the MID task did not capture all mean response times and the reliability of fMRI connectivity (generally) and GIMME

(specifically) are still being evaluated. This will be an important consideration in future work modeling functional connectivity across multiple runs of reward tasks.

## Conclusions

This study is among the first to evaluate a central tenant of the imbalance hypothesis (and related hypotheses) using a data-driven person-specific network connectivity approach that contains group-, subgroup- and individual-level connections. In a sparse network of cognitive control and socioemotional ROIs during motivational processing, two subgroups were uncovered – one "homogenous" with a greater number of shared connections, and one "heterogeneous" with fewer shared connections – with the homogeneous group having higher self-reported sensation seeking than the heterogeneous group. Further, the strengths of select homogeneous subgroup connections, such as the Right OFC-Right VS and vmPFC-Right OFC, were negatively and positively associated with self-reported sensation seeking, respectively. This implies that reward-related behaviors are meaningfully related to connectivity patterns derived from person-specific networks. However, brain-behavior relations varied by experimental trial run, such that connectivity between reward regions was only significantly related to sensation seeking during the first run, but not the second run, nor when the runs were combined. These findings underscore that young adults whom report greater sensation seeking may share unique patterns of network connectivity during motivational processing, and that these patterns may attenuate with repeated exposure.

# Chapter 6 : Findings, Limitations, and Future Directions: A Nomological Network Perspective

As discussed at the end of Chapter 1, the goal of this dissertation is to evaluate different relationships in a nomological network that are postulated by the neurodevelopmental models. Across the three studies (summarized below), I evaluated three issues that are salient to the network: (1) How well does the hypothesis that risk takers have increased activation in reward regions generalize; (2) how analytic flexibility of task contrasts alters the observed associations among neural activation and behaviors; and (3) whether novel functional connectivity approaches help reconcile limitations of traditional univariate approaches (discussed in Chapter 5). For example, in the first study (Chapter 3), I evaluated the core postulate of the neurodevelopmental framework that risk-taking during adolescence is driven by heightened activation in response to rewarding stimuli in reward-relevant neural regions. The empirical evidence in that chapter demonstrated that the relationship postulated by a nomological network is not supported. This brings a critical problem, noted in Chapter 1, to the forefront. How do we explain why this hypothesis from the neurodevelopmental model did not generalize?

Theoretical models often suffer from well-reasoned assumptions (Hull, 1952) and generalize beyond what is being measured (Lerner, 2006). The neurodevelopmental models are no exception. Similar to other psychological theories (Eronen & Bringmann, 2021), the

neurodevelopmental models lack precision which make it difficult to test and falsify the postulated phenomena (Pfeifer & Allen, 2016). In this regard, it is difficult to say whether the hypothesis in Study 1 (Chapter 3) was not supported because a) the deduction that risk-taking adolescents are more sensitive to rewards is a mischaracterization; b) the chosen measure of the phenomenon quantifying the construct of reward sensitivity did not appropriately capture the domain in the nomological space; or c) it was a failure in the analytic approach, whereby a static process is measured in Study 1 (as in most reported investigations in the research literature), but a dynamic process is hypothesized by neurodevelopmental models like the Imbalance Model (Casey et al., 2008). While this dissertation cannot answer these questions in full, the findings from the three studies provide substantial evidence that researchers should give greater attention to issues of generalizability, validity, and reliability when it comes to the methods used to measure brain, behavior, and brain-behavior associations.

In this concluding chapter, I will discuss more holistically the findings from the studies presented in Chapter 3 to Chapter 5 and propose ways to evaluate the associations among postulated constructs. I will contextualize the issues and findings using the nomological network framework (Cronbach & Meehl, 1955; Pfeifer & Allen, 2016) that takes into account the topology of validity (Cook & Campbell, 1979; Shadish et al., 2002). While a brief definition for the nomological network framework was provided in Chapters 1, 3, and 4, I start this chapter by providing a detailed description of the nomological network framework. Within the scope of this definition, I then revisit and consider the findings presented in Chapter 3 to Chapter 5. I discuss the implications of these findings and their limitations given that "*every solution to a problem tends to create new problems*" (Shadish et al., 2002, p. 35). Considering that this dissertation focuses specifically on the aspects of neural activation derived from task-based fMRI measures

of reward processing, I discuss several issues in task-based fMRI and propose some future directions that are consistent with the nomological network framework.

## Nomological Network: Definition and Description

Science is a method that allows researchers to systematically interpret observations from nature (Cowles, 1989). The accumulation of observations gives rise to theories that help give structure to interrelated constructs (Muthukrishna & Henrich, 2019) and propose an integral set of postulates, or hypotheses, that express relationships among phenomena in the natural world (Miller, 2009; Oberauer & Lewandowsky, 2019). Once we have a theory that we can articulate, it becomes possible to systematically test and falsify that theory which is rooted in the measured attributes and observations. By measuring the underlying phenomena, the relationships among the constructs can be embedded within a nomological network (Pfeifer & Allen, 2016). The nomological network can be viewed as "*a metaphor to emphasize the structure of the system*" (Meehl, 1978, pp. 813–814), whereby the *nodes* of the network represent the postulated theoretical components (e.g., neurocognitive measures of reward), which are connected to other nodes in the network via *strands* that constitute the relationships (e.g., association between neurocognitive measures of reward and substance use). The network is comprised of interlocked relationships that constitute a theory (Cronbach & Meehl, 1955).

From the neurodevelopmental models discussed throughout this dissertation, such as the Maturation Imbalance Model (Casey et al., 2008; see Figure 1.2 in Chapter 1), several properties can be deduced from a nomological network (Figure 6.1). Importantly, while the neurodevelopmental models are often labeled as 'heuristics' or 'frameworks' for interpreting findings, the information within the models gives structure to findings and observations which may be thought of as constituting a theory or, as some would label it, a "soft-theory" (Fried,

2020; Meehl, 1990).

Nevertheless, using the neurodevelopmental model framework, we can postulate relations between observations and phenomena or different measures of phenomenon within a construct, by the nodes and strands from the nomological network.

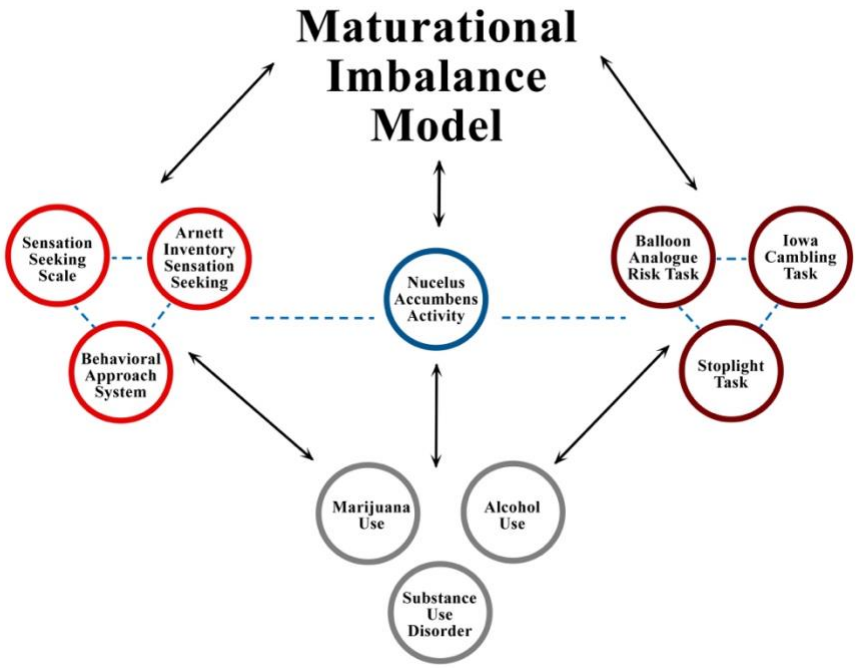


Figure 6.1. Abbreviated Example of Nomological Network for Maturational Imbalance Model
Solid lines = theory implied relationships among nodes.
Dashed lines = construct implied relationships among nodes.

The network may relate observations to one another, such as adolescents engaging in greater substance use and higher reward seeking at a certain age. It can also relate theoretical measures of phenomena to observations, such as performance on a reward task or neural activation in the nucleus accumbens (NAcc) to self-reported substance use. Then, in the nomological network, a researcher can relate a specific construct measured via distinct phenomenon, such as performance on two different reward tasks or reward seeking measures. The confidence among the relationships (i.e., strands) between units of measurement or observations (i.e., nodes) is heavily influenced by the underlying measures and their underlying theories (Cronbach & Meehl, 1955). In some instances, the strands that emphasize *postulated* relationships, such as the operationalization of the construct of reward sensitivity via a measure like the BART task, may be problematic as they are susceptible to interpretation (Meehl, 1978) and may empirically

demonstrate poor construct validity (Demidenko et al., 2019; Eisenberg et al., 2019). In scenarios where construct validity is poor, interpolating and extrapolating findings is quite challenging because the basis for the relationships is unclear. Therefore, it is difficult to know what is, in fact, being measured or related (Shadish et al., 2002).

Clark Hull argued that, "*The typical procedure in science is to adopt a postulate tentatively, deduce one or more of its logical implications concerning observable phenomena, and then check the validity of the deductions by observation. If the deduction is in genuine disagreement with the observation, the postulate must be either abandoned or so modified.*" (1952, p. 15). The discordance between the postulate and observation can be caused by issues of construct validity, the theoretical network, or the design (Cronbach & Meehl, 1955). The former issue, construct validity, imposes major constraints on interpretations of relationships in the nomological network (Shadish et al., 2002) both in traditional measures within psychology (Flake et al., 2017; Flake & Fried, 2020) and measures within cognitive neuroscience (Pfeifer & Allen, 2016; Poldrack & Yarkoni, 2016). As described in Flake & Fried (2020), a construct (or measure) can be "*any approach that researchers take to create a number to represent a variable under study*" (p. 458). Because constructs are not directly measurable, such as reward sensitivity or self-regulation, measures of the phenomena, such as self-reported sensation seeking or neural activation during reward tasks, serve as the primary indirect measure of the construct. Given the abstract nature of many constructs in adolescent research, such as how we define reward sensitivity during the MID task, errors in constructs have major implications as they "*can mislead both theory and practice*" (Shadish et al., 2002, p. 65). For example, if I believe I am *explicitly* measuring neural substrates of reward anticipation during the MID task in the NAcc (Figure 6.1) but that process is confounded by interrelated components, such as attention, this

can impact my conclusions. This confounding variable may impact both the theoretically implied associations (Figure 6.1: solid lines) and measurement-implied nodes (Figure 6.1: dashed lines). When the goal is to use the correlational design to generalize from the narrow-to-broader population of adolescents (Cronbach, 1957), and when the relationships among constructs in the nomological network fail to materialize, it becomes onerous to generalize about what the measured neural process of reward means and how it relates in the broader network. With this in mind, it is imperative to understand the limitations of constructs and the narrow-to-broader generalizations for the neurodevelopmental models (Shadish et al., 2002). While researchers proclaim the importance of construct validity and cite research on construct validity at an exceeding rate (Fiske & Campbell, 1992), they often give it little attention in their work (Proulx & Morey, 2021).

The nomological network may help us structure and answer these very important questions about our theories. The network helps contextualize how theoretically similar constructs are interconnected in the system and how findings *may* generalize across persons, measurement variables, and settings. Shadish, Cook & Campbell (2002) describe several threats to construct validity that can cause the strands of the network to break down. For instance, (1) constructs can be defined in a manner that is incongruent with the phenomenon (i.e., approaching substances may be incongruent with anticipation of monetary reward during the MID task; see for example, Modak et al. (2021)); (2) constructs may be confounded by other processes which are often operationalized using single measures of constructs containing irrelevant information (i.e., MID task measure of reward is confounded with attention; see Caplan (2007)); and (3) in most scenarios, only single, abstract components of a construct may be studied, which makes the traditional psychometric approach more difficult for disaggregating relevant and irrelevant

processes in the measures (Campbell & Fiske, 1959). These three issues interact with elements of the study (e.g., normative or atypical populations), differences in outcomes (e.g., alcohol initiation or retrospective alcohol use), or congruency in effect sizes (e.g., similar magnitude or direction of effects). Thus, understanding constructs is difficult but it is an essential part of research (Shadish et al., 2002) that helps expand the nomological network (Cronbach & Meehl, 1955). In fact, construct validation is considered by Flake and colleagues (2021) as a major step towards assuaging the generalizability crises that permeates psychology (Yarkoni, 2020). As these issues are discovered, researchers will have to face the complexities of psychological measures and wrestle with the lack of precision in their theories (Proulx & Morey, 2021).

In the next section, I will synthesize and elaborate the empirical work in Studies 1, 2, and 3 and expand on the nomological network.

## Chapter 3 to Chapter 5: Findings and Limitations

The purpose of the studies in this dissertation (Chapter 3 to Chapter 5) are to drill-down into the nomological network, particularly the neural component, and consider where and why deviations from the broader neurodevelopmental models may arise. In this section, I describe how one may test the network of relationships postulated by the Maturational Imbalance model, synthesize the findings from the context of the nomological network, and provide some limitations that were not already discussed in Chapter 3 to Chapter 5.

One way to assess an existing nomological network is to start with a theory or a framework, such as the Maturational Imbalance model. This framework can be simplified into its nodes, such as self-report risk-taking behaviors and neural substrates of reward (Figure 6.1). Then, it can be deduced that the postulated strands of the theory are apparent in the observations. If one (or more) of the postulates in the network do not generalize, it is worth considering

whether the failure is attributable to an alternative definitions of the construct (Cronbach & Meehl, 1955; Shadish et al., 2002) or an issue with the analytic design. This is especially true in task-based fMRI where cognitive processes are implied and rarely confirmed. Moreover, traditional experimental designs may not appropriately test the postulates of a theory. For example, tests of the neurodevelopmental models that place too much emphasis on one-to-one mapping of brain regions (Pfeifer & Allen, 2016) and group averages (Beltz, 2018), rarely consider the dynamics, or interplay, among brain regions as discussed in those models. In which case, alternative designs may be appropriate to consider the support for the strands in the nomological network.

The purpose of Study 1 (Chapter 3) was to evaluate whether there was a strand in the broader neurodevelopmental framework associating neural substrates of reward with risk-taking behaviors. Instead of spanning multiple decades of development, the emphasis was placed on the developmental peak in risk-taking that occurs during mid-to-late adolescence (Bjork & Pardini, 2015; Willoughby et al., 2013) to make a more precise prediction (Pfeifer & Allen, 2016). If the postulate of neurodevelopmental models holds true—adolescents that have greater motivation towards reward will report increased risk-taking tendencies (Galván, 2010)—this would be evident in a sample of adolescents that were specifically sampled to differentiate high risk and average/low risk-taking profiles. This would evaluate the central strand that connects neural substrates and behavioral nodes in the nomological network (Figure 6.1). Despite the narrow sampling of adolescents during the developmental peaks in risk-taking and using a reward task that is employed by major consortium studies to measure reward processing (Casey et al., 2018; Schumann et al., 2010), there was no empirical evidence in the study to support the Maturational Imbalance model's postulate of adolescent neurodevelopment. We found no significant

association between Wave 1 or multi-wave risk-taking profiles (e.g., high risk versus average/low risk) and activation in pre-selected neural regions during the anticipation of large rewards in the MID task. While this study used both a whole brain and ROI analysis, the analyses were restricted to a single construct of reward. Thus, failure to generalize may be a function of how reward was characterized during the MID task. For instance, the decision was to opt for the Big Win versus Neutral cue contrast. While this decision was based on prior research, it was not always congruent with contrasts that were used to operationalize reward during previous use of the MID task (Büchel et al., 2017; Cope et al., 2019; Schwartz et al., 2019).

The purpose of Study 2 (Chapter 4) was to evaluate how the arbitrary operationalization of the reward construct during the MID task may have impacted the underlying findings in Study 1. If the construct was defined incorrectly in Study 1, thus being inconsistent with the phenomenon being measured, this may systematically alter the observed relationships that are postulated by the neurodevelopmental models. While there are numerous reward tasks that can tap the construct of reward during task-based fMRI (Richards et al., 2013), there are also several ways that a construct can be defined *within* a given task. In Study 2, ten different constructs of reward were evaluated within the MID task, spanning anticipation, feedback, and prediction error. In addition to testing the patterns of the whole brain activation during different contrasts, relevant to the nomological network, the systematic associations (strands) among select contrast and psychological characteristics (nodes) were also examined. As previously reported (Marek et al., 2020), results from similar studies suggest that most brain-behavior effects are likely to be small. Relevant to the nomological network, in Study 2, there was little-to-no consistent empirical evidence for relationships among constructs of reward and psychological characteristics that are theoretically linked. For instance, while self-reported substance use and

sensation seeking and substance use and externalizing were strongly associated in the adolescent sample, there were few, if any, consistent patterns among the associations between these behavioral characteristics and the neural constructs of reward that were modeled. The findings from Study 2 suggest that there may have been differences in neural activation across risk-taking profiles in Study 1 if the construct of reward were defined differently. This difference, however, would not have been easily interpretable. This raises the concern that there are likely to be construct misidentifications in task-based fMRI that mislead interpretations (Shadish et al., 2002), and, in some scenarios, rationalization may be used in place of appropriate construct validation (Cronbach & Meehl, 1955) which likely results in vague definitions of reward.

Characteristic of the broader neurodevelopmental literature, both Study 1 and Study 2 utilized a traditional univariate approach which may not necessarily be an appropriate design to examine the neural strands of this nomological network. As discussed in Chapter 5, adolescent neurodevelopment and behavior is not uniform. Furthermore, traditional univariate analyses use one-to-one mappings that do not address the dynamics of brain function that the neurodevelopmental models, such as the Maturational Imbalance model, refer to (see Casey et al., 2019). If neural function in brain regions is averaged across individuals that are heterogeneous in their development and behaviors, the theoretical association (strand) between brain and behavior (nodes) may be hindered.

The purpose of Study 3 (Chapter 5) was to use an empirical design that would be more reflective of the Maturational Imbalance model. Unlike Study 1 and Study 2 that averaged neural activation of brain regions, Study 3 evaluated the neural coactivation (or dynamics) of brain regions that would approximate the hypothesis posed by the Maturational Imbalance model (see Chapter 1, Figure 1.2). Consistent with Study 1 and Study 2, Study 3 evaluated the theoretical

association (strand) between self-reported sensation seeking and neural coactivation during the MID task (nodes). The findings in Study 3 illustrate that there was empirical evidence supporting the theoretical association (strand) between self-reported sensation seeking and person-specific connectivity among reward regions (nodes) during motivational processing. However, the strength of these associations waned as a function of how the fMRI time-series data was modeled (perhaps reflecting habituation and/or reliability) and due to the length of the time-series (reflecting power). While the first run during the MID task reflected the strongest associations between brain and behavior, the association during the second run was attenuated, although similar in direction. While this study demonstrated some theoretical support for relationships within a networking of findings, similar to Study 2, there are distinct differences that must be considered in the context of the MID task, such as attention, attenuation of reward, reliability, and power to model an effect. Ultimately, these concerns may impact the underlying interpretation(s).

When considering the neurodevelopmental frameworks from a nomological network perspective, it is important to acknowledge the difference in using the person-specific approach in Study 3 and group average approach in Study 1. When testing the nomological network as it relates to the Maturational Imbalance model, the associations are based on group averages. As presented in Figure 1.2 in Chapter 1, the neurodevelopmental framework's assertion is that there is an *average* trajectory of when reward regions are sensitized during mid-adolescence. However, as mentioned in previously, adolescent development and behaviors are heterogeneous. While adolescence is marked by the onset of puberty, it is well recognized that the onset of puberty differs in age between males (~12 years old) and females (~10 years old; Dahl et al., 2018). This suggests that males and females may have unique neurodevelopmental trajectories as

a result of the "social re-orientation of adolescence" that may contribute to the rise in engagement in rewarding experiences (Forbes & Dahl, 2010, p. 67). Hence, instead of an average trajectory there may be a multitude of trajectories that reflect different onsets and tempos of development in motivational processing. Thus, the use of group averages in Study 1 may be more equipped to answer the strand between brain-behavior as it relates to the average but the person-specific analysis may inform new strands that relate to an individual and not adolescent development in aggregate. Person-specific approaches, whether across weeks, months or years, that model trajectories of an individual may provide insights as to why mortality from unintentional injuries rise substantially higher during mid-to-late adolescence in males than in females (Centers for Disease Control and Prevention, 2020). Ernst (2022), the curator of the Triadic model in 2006, recently suggested a prediction based approach that may bridge both the group and person-specific models. In essence, Dr. Ernst argued that if we define key features of neurodevelopmental models, such as brain activation in key brain regions, connectivity between brain regions and self-report measures of key psychological characteristics, perhaps researchers may be able to predict which individuals engage in risk-taking behaviors. Such an approach would be agnostic to the age along the developmental trajectory but instead focus on the predictive features of the model in the context of behaviors.

The three studies summarized here provide an example of how a "drill-down" approach can be used within a sample to illustrate what strands may be supported within a nomological network. By using the identical sample and task, subtle modifications to the construct (e.g., contrasts used during the MID task, such as in Study 2) and the empirical design (e.g., traditional univariate versus a dynamic model, such as in Study 3) allow for a comprehensive understanding of the strands and nodes of a nomological network for the prevailing neurodevelopmental models

(Chapter 1, Figure 1.2). While using a different sample and task for each study would have allowed for comparisons across populations and tasks, the differences between persons, settings, and measurement variables would have made it difficult to discern the reason for the differences (Shadish et al., 2002). For instance, it would be difficult to determine whether the association between neural activation of reward and behavior in the network is attributable to the abstract decision at each definition or analytic step, or to differences in sampling and measurement characteristics that arise when using different samples. Across three studies, this dissertation tested distinct limitations of the neurodevelopmental framework by evaluating brain-behavior associations for a specific subset of the population. For the initial phase of this work, constraining the potential sources of empirical differences was the logical approach. In future iterations (proposed below), multiple samples and tasks may help build on these findings.

While taking a single sample and task to drill-down into a network is informative, there are several limitations that should be considered. Referring to the sampling characteristics and interview design discussed in Chapter 2, there are explicit decisions made in the design that could introduce sampling biases that are present in each of the three studies due to the "drilling down" approach. These decisions carry similar implications as the "researcher degrees of freedom" discussed in Chapter 3. I will discuss five of these limitations and their implications below.

First, across the three studies in this dissertation, there are a number of research degrees of freedom in deciding which self-report measures to use. For example, Study 1 used the BMS scale as metric of risk-taking, Study 2 used self-reported substance use and several psychology characteristics (e.g., sensation seeking and externalizing symptoms) and Study 3 used sensation seeking. In general, for Study 1 and Study 3, the literature highlights that risk-taking peaks

between 18-23 (Bjork & Pardini, 2015; Willoughby et al., 2013) and sensation seeking – which is moderately related to substance use (Demidenko et al., 2019) – peaks between 14-20 (Harden & Tucker-Drob, 2011) or 18-20 (Steinberg et al., 2018), depending on the sample and operationalism of the variable. The decision to focus on risk-taking in Study 1 was to measure the neurodevelopmental model's generalizability to real-world risk-taking in the focal age range, however, the focus on sensation seeking in Study 3 was to measure the association of trait level motivational towards rewards and coactivation during a presumed state of motivational processing. It is apparent from the brain-behavior variability between substance use and sensation seeking in Study 2, that differences in whole brain and ROI activation across risk-taking in Study 1 (which is strongly related to substance use) would likely differ from sensation seeking. While we did not analyze differences in brain coactivation during motivational processing across risk-taking profiles in Study 3, the results would likely vary given sensation seeking demonstrates only a moderate correlation with risk-taking in the full sample (Demidenko et al., 2019). This further supports the need for research studies to test different theoretical strands of the nomological network to gain a nuanced understanding for brain-behavior associations as they relate to neurodevelopmental models.

Second, the imaging sample was recruited to test distinct differences in behavioral and cognitive associations of risk-taking behaviors. Thus, the subsample selected to maximize risk-taking individual differences would not reflect a typical adolescent population, as the prevalence in risk-taking behaviors in this sample is higher than a fully representative adolescent population (Johnston et al., 2019). Likewise, the distinction made in this recruitment strategy was to sample categories of high risk and average/low risk-taking profiles based on a latent factor score of several risk-taking measures. While this approach is recommended in a prior review (Sherman et

al., 2018), this study may not fully capture the history of exposure to substance use (Bjork, 2020) or family history (Cope et al., 2019) that may be relevant to the neural underpinnings of reward or motivational processing. Nevertheless, these sampling procedures for high risk and average/low risk-taking profiles were necessary to make the appropriate comparisons and were derived from a larger sample that was consistent with the population from which it was drawn.

Third, the recruitment strategy may misappropriate the cause and effect that is postulated in the neurodevelopmental models. The neurodevelopmental models propose that the sensitivity to rewarding stimuli increases adolescents' motivation to approach salient behaviors that often incur risk. This view may suggest that increased activation in reward regions would *prospectively* predict risk-taking tendencies. The samples for all three studies utilized self-reported behaviors that were *retrospective* and proximal to the scan. Self-reported data was not available to evaluate whether activation was prospectively associated with self-reported risk-taking behaviors. While this is a limitation of each of the study's conclusions, retrospective and cross-sectional analyses of neurodevelopmental models are common in the field, and so this remains an unresolved issue (Sherman et al., 2018).

Nevertheless, the retrospective nature of self-reported measures is especially important in the context of substance use. For example, the neurodevelopmental models hypothesize that adolescence is marked by the increased sensitivity of reward regions which may increase engagement in risk-taking behaviors, however, research has reported that the reward systems, in particular the NAcc, are blunted in response to reward in problematic drug use (Volkow et al., 2010) and more normative marijuana use (Martz et al., 2016). This argument was posed in response to Study 1 by Bjork (2020). However, the evidence from Study 2 suggests a more nuanced understanding in which task and what contrast this occurs and why. This is especially

important given the fact that animal and human studies of drug self-administration converge on the finding that the dopamine response *increases* rather than a *decreases* in to drug cues (Samaha et al., 2021).

Fourth, a major tenant of the neurodevelopmental models is the difference in neural activation that occurs *across* development. Reviews often compare differences in activation to rewards in adults, adolescents, and children (Galván, 2010; Silverman et al., 2015) to derive adolescent emergent characteristics that coincide with risk-taking behaviors (Casey, 2015). The purpose of our studies was to ask a more precise question within a narrow developmental range regarding the neural substrates of risk-taking. While there was a lack of generalizability (Study 1) and increased variability (Study 2) in the findings that did not provide empirical support for certain strands of the nomological network, the theoretical strand specific to the developmental trajectory may still hold true. In this case, the nomological network encompassing the theory may be retained, however, some hypothetical links (strands) of the network may need to be modified.

Fifth, there are ongoing discussions in fMRI related to power and reliability that the work here cannot fully evade. As discussed in Chapter 4, the work here has the strength in using a sample size ($N = 104$) that is substantially larger than the median sample size ($N < 50$) that is common in fMRI (Szucs & Ioannidis, 2020). Marek and colleagues (2022) have argued that sample sizes of $N > 2000$ may be necessary to uncover meaningful brain-behavior effects and multivariate approaches would be better powered than traditional univariate methods. Similarly, Grady and colleagues (2022) have reported that multivariate methods may be more sensitivity to brain-behavior effects than univariate methods. Unlike the findings in Marek and colleagues (2022), Grady and colleagues (2020) report that brain-behavior correlations may be inflated at

smaller sample sizes but multivariate correlations between brain-behavior stabilized at N > 80. With respect to Study 1, the sample size we used here is superior to the some of the prior work but may still incur rates of Type II errors given the lack of power to find significant mean differences between groups based on self-reported behavior. Nevertheless, the issue of power is not unique to this study as the early neuroimaging that provided evidence for the neurodevelopmental models were often severely underpowered. For example, one study estimated the neural correlates of risk-taking in 26 participants that ranged in age from 7 to 29 years (Galvan et al., 2007). Notably, the focal age range used in the studies in this dissertation increases the precision with which the hypotheses may be answered in Study 1 over prior work that used samples with broad age ranges which limit the datapoints per age group. Conversely, in the case of Study 2, the sample may be sufficiently sized to reflect the stability of correlations as Grady and colleagues (2020) suggest that univariate methods may perform marginally worse than multivariate methods. But the field continues to grapple with issues relating to power and reliability, so more evidence is needed.

For example, Elliott and colleagues (2020) reported poor test-retest reliability across a number of fMRI tasks that used univariate methods. A commentary on this work argued that multivariate methods may provide biomarkers that in some cases may be more reliable in prediction modeling (Kragel et al., 2021). The latter perspective converges with the opinions in Marek and colleagues (2022) that fMRI studies may benefit from moving to brain-wide association studies (BWAS) which is similar to the shifts observed in genomic research that uses genome-wide association studies (GWAS; Witte, 2010). Nevertheless, more work is necessary to understand the issues of power and reliability in fMRI studies examining the associations between the brain and psychological characteristics. While some task-based fMRI studies have

been reported to have poor test-retest reliability, the strength of this work is the use of the MID task which has been reported to have reasonable test-retest reliability in the NAcc that is central to motivational processing (Wu et al., 2014). Moving forward, more research using larger samples, numerous runs and sessions will help appreciate the test-retest reliability in the MID task.

I applaud recent calls for increased reliability in task-based fMRI (Elliott, Knodt, Caspi, et al., 2021). Reliability for brain-behavior research, however, is necessary but not be sufficient. At the heart of all these procedures is the question: What does the neural activation mean? I elaborate on this and propose some recommendations in the next section.

## Implications to Neurodevelopmental fMRI Research

Neurodevelopmental models play a pivotal role in how we think about adolescent neural and socioemotional development. Nevertheless, as references throughout this dissertation have made clear, there are prevailing issues in psychological measures (Flake et al., 2017, 2021; Flake & Fried, 2020; Hussey & Hughes, 2020; McNeish, 2018; Muthukrishna & Henrich, 2019; Shadish et al., 2002), cognitive neuroscience (Baker et al., 2021; Caplan, 2007; Price & Friston, 2005), and task-based fMRI (Elliott et al., 2020; Elliott, Knodt, & Hariri, 2021; Poldrack, 2010; Snow & Culham, 2021). These issues make it difficult to interpret accumulating findings and make sound predictions about adolescent behaviors.

Given the large number of reward measures used in the neurodevelopmental literature (Flannery et al., 2020; Richards et al., 2013) and the tendency to use proxies of stimuli and behaviors in fMRI (Baumeister et al., 2007; Snow & Culham, 2021), there is often too much heterogeneity between reward and cognitive control tasks to aggregate across studies. While meta-analytic clustering techniques are helpful (Flannery et al., 2020), the highlighted

discrepancies in Study 2 pose several conceptual challenges as they relate to noisy measures of brain and behavior. This aligns with the commentary that task-based fMRI must pay greater attention to psychometric properties, particularly reliability (Elliott, Knodt, Caspi, et al., 2021). However, as mentioned earlier, I would argue that resolving reliability is only one component of moving fMRI forward in brain-behavior research. Of course, it is crucial that researchers can reliability measure neural activation in fMRI research but there needs to be sound evidence for both reliability and validity for us to produce relationships that are meaningfully interpretable (Clifton, 2020).

Currently, there is an assumption in task-based fMRI studies that misappropriates traditions from experimental designs to correlational research. For instance, in Chapter 2, I discussed that the MID task is an experimental design that taps reward specific regions. As such, it is not a robust approach to testing cognitive control in risk-taking behaviors. This locationist perspective (Lindquist et al., 2012) distinguishes which neural regions are explicitly tapped by functionally relevant processes in a task-based fMRI experimental design. This convention is used in fMRI research to distinguish relevant brain regions for different tasks (Casey et al., 2018; Elliott et al., 2020) and is often the primary justification for the utility of the task when studying a particular behavior (as in the studies reported here). How can we claim that the elicited neural activation during the task represents an attribute that is both latent and in the domain of interest? This technique of validating a construct for brain-behavior research suffers from similar limitations, such as using internal consistency (i.e., Cronbach's α) in social psychology studies to reflect a measure's validity (Flake et al., 2017).

Currently, the common method used to determine what an fMRI task measures can be defined as content or face validity (Clifton, 2020), which may be adequate for experimental but

not correlational research. Traditionally, to define mean-activation of a *construct* during task-based fMRI, such as the MID task, a one-sample t-test is often performed to identify where "robust" activation is present. In experimental designs, the goal is to control or reduce the source of variance (Dang et al., 2020) and increase the signal (or activation) in task-relevant brain regions. However, as stated by Paul Meehl, "*one psychologist's subject matter is another's error term*" (1967, p. 808). In correlational research, the variability in task-irrelevant regions not shown during mean-level activation in a one-sample *t*-test, such as cognitive control regions during the MID task, does not necessarily preclude them from being assessed in brain-behavior associations. The covariation is, in fact, the central component of the measured effect in correlational research, such as Pearson's correlation. Furthermore, integrative neuroscience perspectives would argue that these task-irrelevant brain regions may still play a role in dynamic processes (Pessoa, 2017) and so they do not lay dormant. Cognitive neuroscientists are reconsidering traditional sequence processes using an interactive framework, whereby processes such as decision making include neural feedforward and neural feedback steps since participants are "*not simple stimulus-response devices*" (Pessoa et al., 2022, p. 8). Therefore, simple mean-level activation maps in experimental designs may not be adequate to define the construct of interest.

Experimental designs in task-based fMRI are effective at eliciting neural function for pre-specified experimental conditions. However, the way in which they have been used to date in correlational research provides little information about the similarity in constructs within a nomological network. A recent meta-analysis assessed task-based fMRI to determine whether there is consistent spatial location and direction for the hypothesis that hyperactivation in reward regions and hypoactivation in cognitive control regions is associated with substance use

behaviors (Tervo-Clemmens et al., 2020). Across the 22 studies that the authors evaluated, they found a large range of reward and cognitive control tasks that reflected the dominating neurodevelopmental theories. In their meta-analysis of 190 foci, they found evidence that activation in striatal regions relates to substance use but only during motivational/reward processing. While this evidence provides support for the prevailing hypothesis of hyperactivation in reward regions, the authors noted, "*the specific components indexed by the contrasts were quite diverse (e.g., winning rewards – neutral condition; risky – safe decisions…)*" (Tervo-Clemmens et al., 2020, p. 8). This doesn't necessarily provide support for the theory, given that there is limited evidence linking these measures in fMRI (Pfeifer & Allen, 2016). Like the results suggest in Study 2 (Chapter 4), the associations across these different designs and contrasts may not be theoretically meaningful. In fact, when convergent validity of comparable constructs was evaluated outside of fMRI, there was little support for links in the nomological network (Eisenberg et al., 2019). This suggests that task-based fMRI would benefit from attending more to psychometric issues, such as construct validity, to allow for intuitively clear brain-behavior associations. In other words, the focus on internal validity, that is the hallmark of experimental approaches, and the focus on external validity, that is the hallmark of correlational approaches (Cronbach, 1957), must both be honored in order to provide valid assessments of brain-behavior associations.

The American Psychology Association (APA) recommended that construct validity be a part of the scientific process in the 1950s to improve the interpretability of findings (Cronbach & Meehl, 1955). Historically, the measurement of attributes has been a complex matter (Briggs, 2021). Publications since have highlighted the importance of establishing relevant and irrelevant properties of constructs (Campbell & Fiske, 1959; Edwards & Bagozzi, 2000; Eronen &

Bringmann, 2021; Grahek et al., 2021; Shadish et al., 2002; Strauss & Smith, 2009), risks (Shadish et al., 2002) and trade-offs in validity (Clifton, 2020), and questionable measurement practices (Flake & Fried, 2020). Psychometric properties, such as construct validity, help establish a belief that "*an instrument reflects a particular construct to which a meaning is attached*" (Cronbach & Meehl, 1955, p. 290). Without establishing adequate construct validity, what we can conclude, especially when using noisy fMRI data, is appropriately summarized by Dr. Patrick Curran, "*If you blow construct validity, dude, you're done. […] There is individual variability in developmental trajectories of crap. Let's slap some lipstick on this pig and get it out the door*." (Curran & Hancock, 2021, 53:44). While this comment was said in jest during the recording of a podcast, there is a level of candor to the statement that is relevant to both psychology and task-based fMRI.

Support for the neurodevelopment models is comprised of constructs that appear to be loosely defined given the empirical findings from literature reviews (Richards et al., 2013; Sherman et al., 2018) and meta-analyses (Tervo-Clemmens et al., 2020). To date, affective paradigms in task-based fMRI are in jeopardy of surface similarities (Shadish et al., 2002), or the "jingle fallacy" (Flake & Fried, 2020). Two tasks that have similar names or share a domain, such as the MID task or the Wheel of Fortune (WoF) task, are assumed to be comparable given the monetary stimuli or the regions that they activate (e.g., NAcc). Evidence from a contrast in the WoF task can be used to corroborate or contradict findings from a contrast in the MID task, as was recently published (Del Giacco et al., 2021). Likewise, different contrasts within a similar task, such as the MID task, can be used in a similar fashion and depending on the reader, this approach may incur less caution. Study 2 shows that, even within a study where all other factors are held constant, subtle differences in how the phenomenon of the motivation towards rewards

is measured, such as Big Win versus Neutral and Big Win versus Small Win, can produce brain-behavior relationships that are notably different. What this means for the field more broadly is still unclear.

If task-based fMRI continues to be used in correlational research, it will be of utmost importance to work towards improving its psychometric properties. In addition to improving test-retest reliability (Elliott et al., 2020) and using appropriately large sample sizes (Szucs & Ioannidis, 2020), I argue that the task-based fMRI literature would significantly benefit from a comprehensive understanding of the underlying constructs. While fMRI may show promise in correlational research, until all of these issues are understood, it's best seen as a biomarker (Kragel et al., 2021) with properties that are not fully defined.

In addition to reliability, there are several important questions that need to be addressed with respect to construct validation. How do contrasts differ within a task? Do they differ in a meaningful way that is specific to the phenomenon being measured? Are convergence and divergence present across tasks that are *postulated* to belong to a shared nomological network? Most importantly, how do these different elements impact brain-behavior associations? The nomological network consists of a number of stages, such as a theory, construct, or phenomenon, and these have imbedded assumptions and auxiliary theories that impact their reliability (Meehl, 1967). Although large consortium studies like the IMAGEN and the ABCD are equipped to answer some of these questions, they may be unable to answer important questions relating to construct validity. Specifically, the types and quantity of fMRI tasks are limited in the studies mentioned here. Oftentimes, the fMRI tasks are constrained to select reward and cognitive domains due to valid reasons, such as cost and participant burden. Because consortium differences in tasks will limit the tests of construct validity, alternative studies and analytic

techniques may have to be used. I propose two potentially fruitful approaches to address some of the construct validity concerns in the next section.

## Futures Directions via the Nomological Network

There are several paths that may help researchers improve construct validity in task-based fMRI that are not solely dependent on surface similarity (Shadish et al., 2002). I will put forth two approaches: one that can be adopted by using existing data and another that is an emerging area of research that leverages "dense-sampling". As noted earlier, "*every solution to a problem tends to create new problems*" (Shadish et al., 2002, p. 35) so the proposals suggested here will not resolve the underlying issues. However, I hope they may serve as a path forward to understand both constructs and individuals during task-based fMRI in a comprehensive manner that increased power alone will not resolve.

In Chapter 4, I noted that *"… some suggest that small effects are the "new normal" in clinical neuroscience research (Paulus & Thompson, 2019) and that MRI studies require especially large sample sizes (>2000) to identify meaningful effects in brain-behavior associations (Marek et al., 2020).*" When this problem is considered solely from a null-hypothesis framework, it is somewhat misguided (Cohen, 1994) given the weak signal-to-noise ratio in brain-behavior effects. During the last half century, Paul Meehl stated that, "*everything in the brain is connected with everything else*" (1967, p. 110) and "*everything correlates to some extent with everything else*" (1990, p. 204), so it is highly unlikely that experimental effects would show no effect on psychological phenomena. This is especially true in noisy data, such as fMRI. If we continue to increase the sample size, as a function of the "crud factor", trivial significant (i.e., $p < .05$) correlations will emerge in task-based fMRI (Cohen, 1994).

In large brain imaging samples, such as the ABCD study (N > 11,000; Volkow et al., 2018) or the UK Biobank study (N > 100,000; Alfaro-Almagro et al., 2018), the issues surrounding small effects or the population parameters that reflect meaningful importance will become a critical point of discussion. In the ABCD data, it has been reported that the effect sizes are small by traditional standards (Dick et al., 2020) and that brain-behavior relationships are likely to be smaller (Marek et al., 2020). Yet, increasing power will not help us understand the relationships being observed in the data because small effects that are observed in the brain-behavior correlations may stem from some systematic error which is central to measurement concerns (Clifton, 2020). In adolescent research, there are perspectives that suggest conceptual relationships can override weak empirical support (Steinberg et al., 2018). To avoid *ad hoc* explanations using an existing theoretical framework, researchers should place an emphasis on construct validity in task-based fMRI to understand what constructs are being measured. This is not to say that large datasets, such as the UK Biobank study, will not meaningfully inform our understanding of the brain. In fact, the results coming out of the UK Biobank study are beginning to inform age-related standards for MRI research (Bethlehem et al., 2021). Instead, we need to develop and systematically evaluate theoretical frameworks to guide our interpretations. This is especially true in regards to small effects, as described by Davis-Stober and Regenwetter, "*if a small effect is simply a 'prediction with many exceptions,' then we need to worry about the degree to which exceptions accumulate across multiple predictions.*" (2019, p. 870).

Fortunately, a theoretical framework exists for domains of approach and valence systems in affective processing that can be put to the test using a nomological network approach. Approach and valence systems have been proposed to underlie core aspects of the motivation system which can modify the rate of engagement in risk-taking behaviors during adolescence, including substance use (Steinberg, 2008; Zuckerman, 1979). These two systems are organized across a multidimensional plane (Figure 6.2) where the motivational response (e.g. whether to approach or avoid) for a given stimuli can be judged on its a) valence, whether a stimulus is good or bad, and b) arousal, whether stimuli causes a state of high or low alertness (Posner et al., 2005). A stimulus that elicits positive valence and high arousal triggers an approach state in the organism resulting in engagement of the salient behavior. These processes are believed to be evoked by cues that signal monetary value (Knutson et al., 2014; Knutson & Greer, 2008) and affective stimuli, such as emotional words and faces (Russell & Bullock, 1985; Stevenson et al., 2007). Theories of reward and affective stimuli suggest that the anticipation of winning money is marked by activation in the NAcc and losing money by the insula (Knutson et al., 2014; Knutson & Greer, 2008). Fearful and happy faces are marked by the amygdala, disgust by the insula, anger by the orbitofrontal cortex (OFC) and sadness by the anterior cingulate cortex (ACC)(Lindquist et al., 2012). Be that as it may, recent meta-analyses have reported that similar brain functional parcels are involved in winning and losing rewards (Oldham et al., 2018) and processing positive and negative affective stimuli

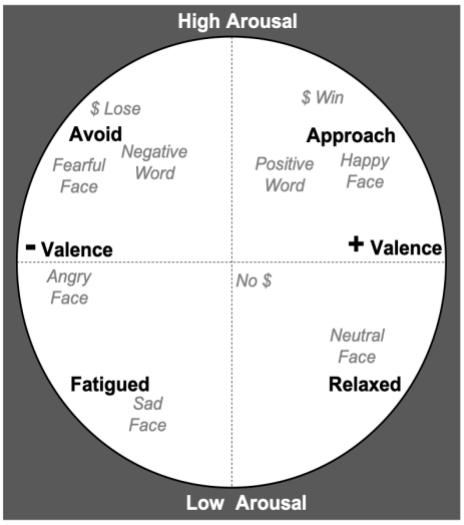


*Figure 6.2.* Multidimensional scale of valence and approach systems

(Lindquist et al., 2012), which gives rise to the question: When and how do brain regions converge on comparable constructs when engaged during different states?

For task-based fMRI, general linear models utilize traditional subtraction techniques to generate hypothetical measures of approach or avoidance in neural activation within domains of reward and affective processing. When abstract subtraction techniques are used, it is difficult to conclude whether overarching constructs exist within domains of reward and/or affective processes. Furthermore, if these constructs do exist, it is unclear how stable they are across samples. Research has shown that certain cues ($5 win) elicit a certain activation (increased NAcc) during the MID, but it is unclear whether an approach and avoidance construct is distinguishable across the many combinations of arousal (Big ($5), Small ($0.20), or No gain cues) and valence (win and loss). Despite reward and affective processing sharing a hypothesized multidimensional scale (Figure 6.2), it remains to be seen whether there is convergence and divergence between high approach reward states and high approach affective states across neural regions in the directions that a nomological network would propose.

One way to answer part of this question is to identify existing samples that share at least two tasks that represent a phenomenon of reward and affective processing. The AHRB study (described in Chapter 2), the ABCD study (Casey et al., 2018), and the Michigan Longitudinal Study (MLS; Zucker et al., 2000) are adolescent samples that include monetary and emotional processing paradigms (Figure 6.3) that offer a preliminary attempt to ask several construct validity questions. The MID tasks and multiple versions of affective processing allow several definitions for constructs of approach and avoidance to test the construct validation between reward and affective processing. The traditional subtraction approach in task-based fMRI can generate multiple definitions of approach and avoidance, both of which can be used in the evaluation of the underlying construct. Then, by using the resulting neural signal, it is possible to consider how the signal in specified ROIs are related within and between

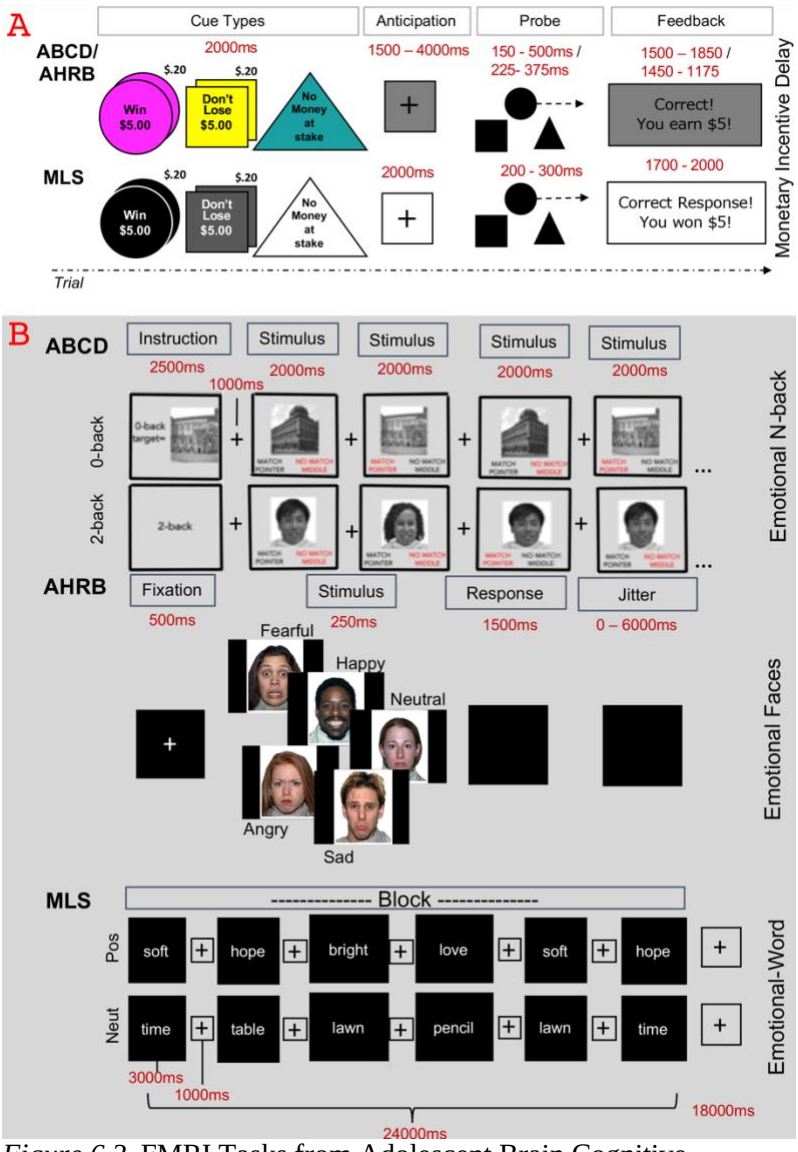


*Figure 6.3.* FMRI Tasks from Adolescent Brain Cognitive Development (ABCD), Michigan Longitudinal Study (MLS) & Adolescent Health Risk Behavior study (AHRB)

different domains. Ultimately, this can fill the nomological space and theoretical models can be used to explain the associations.

Although Study 2 showed that approach activation in the MID task revealed variability across contrasts, it is unknown what the resulting convergence and divergence is between two tasks that measure both approach and avoidance constructs, and how this effect changes across multiple developmental samples. With this data, it is possible to ask several construct validation questions. First, how do different contrasts tap domains that are conceptually related using a multidimensional framework (Figure 6.2)? Second, do these relationships significantly differ across samples that would require updating the nomological network? Third, by using comparable psychological characteristics from each sample, do brain-behavior relationships remain stable or do they change across developmental samples for a given construct?

This approach is a feasible first step that takes advantage of already collected data to evaluate the associations among *postulated* constructs within studies and changes across studies. While the way that construct validity is tested is not consistent with traditional multimethod-multitrait methods (Campbell & Fiske, 1959), it does offer insights into the fluctuation of covariance matrices among task fMRI and behavioral measures that can inform what assumptions researchers can make when they adopt conclusions from other studies to corroborate their own findings. Nonetheless, to understand the nuance of these differences, future efforts would require data collection that permits a comprehensive assessment of the constructs within individuals.

A more comprehensive approach would be to evaluate construct validity of task-based fMRI within individuals. As discussed above, traditional fMRI analyses, such as the univariate methods used in Study 1 and Study 2, analyze a group of participants by transforming their

brains into a standard space from which brain-behavior relationships are probed. Increasing attention has been given to the analysis of individual brains, such as dense-sampling, that would account for measurement error and within-subject variability (Laumann et al., 2015). Dense-sampling collects longer durations and repeated measures of fMRI data on participants to evaluate changes in the neural architecture of each individual brain. Original work using dense-sampling of a single subject used network analyses to provide a reference for how connectivity patterns changed across visits due to self-reported behaviors, experiences, and biological factors (Poldrack et al., 2015). While this work generated interesting new hypotheses, given the minimum sample size (N = 1) and issues of test-retest reliability of functional connectivity (S. Noble et al., 2019), larger samples sizes would be necessary to meaningfully answer specific construct validity questions. Since then, the Midnight Scan Club (MSC) has provided evidence of functional connectivity using the dense-sampling approach (Gordon et al., 2017). The MSC study recruited ten study participants and collected five hours of resting state and six hours of task-based fMRI data for each participant. Their work informed two sources of measurement issues in fMRI: reliability and validity. The authors reported that a larger quantity of data (>30-minute scans) improves test-retest reliability of network features in fMRI. The authors also demonstrated that there is correspondence in person-specific functional connectivity between resting state and some fMRI tasks, such as motor and perceptual processing. The information on reliability and validity from the MSC study have been highlighted as an exemplary step towards scientific measurement in fMRI (Poldrack, 2017).

Future efforts can build on the dense-sampling approach from the MSC study to inform a nomological network using different constructs in task-based fMRI. The MSC study collected a large amount of data on three distinct tasks for ten participants, but the constructs were not

sampled strategically from domains that are hypothesized to exhibit convergent or discriminant processes. Future efforts should sample participants for repeated durations using a rich dataset of fMRI tasks. By including tasks from each domain, such as reward, cognitive control, emotional, spatial, and/or working memory tasks, researchers can build matrices that can satisfy a traditional multimethod-multimethod matrix in order to evaluate construct validity (Campbell & Fiske, 1959). By including more than one task from each domain, researchers can alleviate issues stemming from the mono-operation bias (Shadish et al., 2002), or single measures that underrepresent or contain irrelevant properties for a given construct.

Relevant to neurodevelopmental models, researchers can strategically sample the proposed domains to include neurocognitive and psychological characteristics that have different representations of constructs, which would avoid monomethod/method covariance issues (Shadish et al., 2002). Examples of these efforts have been previously proposed by cognitive researchers, such as Dr. Molly Simmonite and Dr. Thad Polk at the University of Michigan and Dr. Russell Poldrack at Stanford University. At this time, the National Institute of Mental Health has funded a project that is collecting this type of data. Dr. Poldrack's study, "*Characterizing cognitive control networks using a precision neuroscience approach"*, is in the process of collecting fMRI data where, over a six-month period, each of the 55 participants will complete 12 hours of fMRI. To answer construct-related questions, Dr. Poldrack is collecting eight tasks that span several domains within cognitive control. This work may provide meaningful information about similarities and differences between tasks and promote more research on measurement issues in fMRI.

## Concluding Remarks

I hope this dissertation has stimulated some important issues pertaining to the modern neurodevelopmental models, tools, and methods used to test current postulates. I hope, too, that I provided justification as to why we must revisit rather than ignore traditional measurement questions in task-based fMRI. Historically, descriptive trends of adolescent development and behavior have remained fairly stable (Casey, 2015; Hall, 1904a; Kann et al., 2018; Rogers, 1969). However, the cause-and-effect relationship between neurobiological changes and health risk behaviors remains elusive. The neurodevelopmental models have been important to the field of development psychology and resonate century-old heuristics. In some ways, the field has progressed rapidly without careful consideration of major limitations of measurement in fMRI and their implications in predicting adolescent risk-taking behaviors. Notably, psychology researchers using fMRI have acknowledged issues of spurious correlations in brain-behavior studies (Vul et al., 2009), problems relating to test-retest reliability (Elliott et al., 2020; Noble et al., 2019), and repeated publications commenting on issues stemming from small sample sizes (Button et al., 2013; Szucs & Ioannidis, 2017, 2020; Varoquaux, 2018; Yarkoni, 2009).

Nevertheless, more work needs to be done with regards to construct validity to effectively generalize about adolescent populations and have a comprehensive understanding of cause-and-effect relationships between neural activation and health risk behaviors. It is inevitable that different studies will produce results that may contradict one another. Davis-Stober and Regenwetter (2019) argue that a framework's inability to predict individual behaviors consistently is a *paradox* of the framework and is immune to falsification. I do agree that heuristics, similar to the neurodevelopmental models, have been immune to falsification. However, the lack of convergence across studies is an opportunity to understand the nuance of

our constructs and measures that are central to the neurodevelopmental literature. If we cannot be certain about what we are measuring using an fMRI task and do not have a precise mapping of how brain activation during a reward task relates to other phenomena in the nomological network, the conclusions we draw may be jeopardized.

Perhaps one way forward is for neurodevelopmental researchers to step back and incorporate these concerns into future research. As expressed in a recent opinion piece, the publish or perish climate has negative effects on both the researcher and research (Frith, 2019). The pressure to publish, or more specifically the pressure to publish *novel findings* (Proulx & Morey, 2021), might produce more publications but not necessarily quality publications. Perhaps by restricting the output of publications, the reduced pressure to publish may enable researchers to increase collaborative efforts with other researchers from different disciplines, different perspectives, and different expertise on methods/topics. This is especially critical for neurodevelopmental science which often attempts to bridge methods and theories from developmental science, psychometrics, cognitive neuroscience, biopsychology, and statistics. Having to bridge all these areas may, in part, explain why measurement issues have not been thoroughly considered—the level of training in each area isn't always clear. Over time, some suspect that, in addition to coding (Juavinett, 2022) and computational methods, theory will become critical in neuroscience research (Poldrack, 2019). As the emphasis on theory unfolds, perhaps there will be developments in psychometrics that will help inform the nomological networks of neurodevelopmental models. If the goal in neurodevelopmental psychology is to understand why adolescents engage in health risk behaviors at a higher rate than any other age group, having a better understanding of how we measure these behaviors will help reduces bumps along the way.

# APPENDICES

## Appendix A : Phase 2 Wave 1 Sample and fMRI Task Performance

This appendix consists of information pertaining to the duration between P1W1 and P2W1 visits, behavioral performance (accuracy and mean response times), and head motion information during the Monetary Incentive Delay Task.

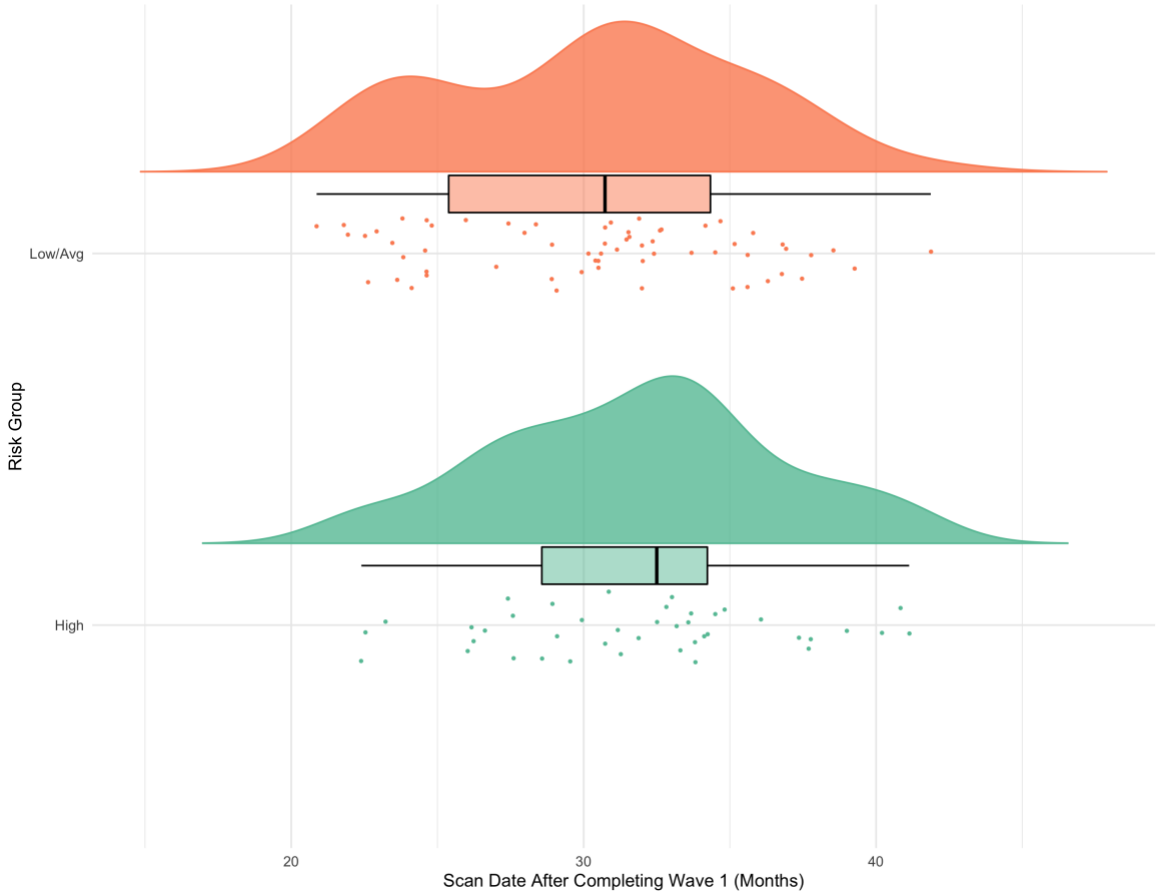


*Figure A.1* Distribution of months for Average and High-risk adolescents between P1W1 completion and P2W1 Scan Date.

There was no significant difference ($p > .05$) between months since Wave 1 and Scan Date competition between High (Mean = 31.8, SD = 4.8) and Low/Average Risk (Mean 30.4, SD = 5.1).

*Table A.1* MID Accuracy

| | *M (SD)* |
|---|---|
| Overall Acc. % | 56.9 (3.2) |
| Win Big | 62.7 (9.2) |
| Win Small | 57.8 (9.6) |
| Neutral | 47.7 (14.5) |
| Lose Small | 56.4 (8.8) |
| Lose Big | 59.9 (10.4) |

The mean response times in the Table A2 and Figure A3 are limited as a function of a flaw in the E-prime design. Mean response times (MRT) were NOT logged by E-Prime for early or late responses, therefore, reported are only MRTs collected by E-Prime for **'hit' (correct) responses**. This is a limitation of these behavioral data.

*Table A.2* Mean response times of full sample completing the MID task

| | *M (SD)* |
|---|---|
| MRT (*ms*) | 296.5 (24.4) |
| Win Big | 293.4 (22.9) |
| Win Small | 296.4 (26.4) |
| Neutral | 300.4 (28.3) |
| Lose Small | 296.1 (24.5) |
| Lose Big | 296.8 (23.7) |

MRT = Mean response time; ms = milliseconds

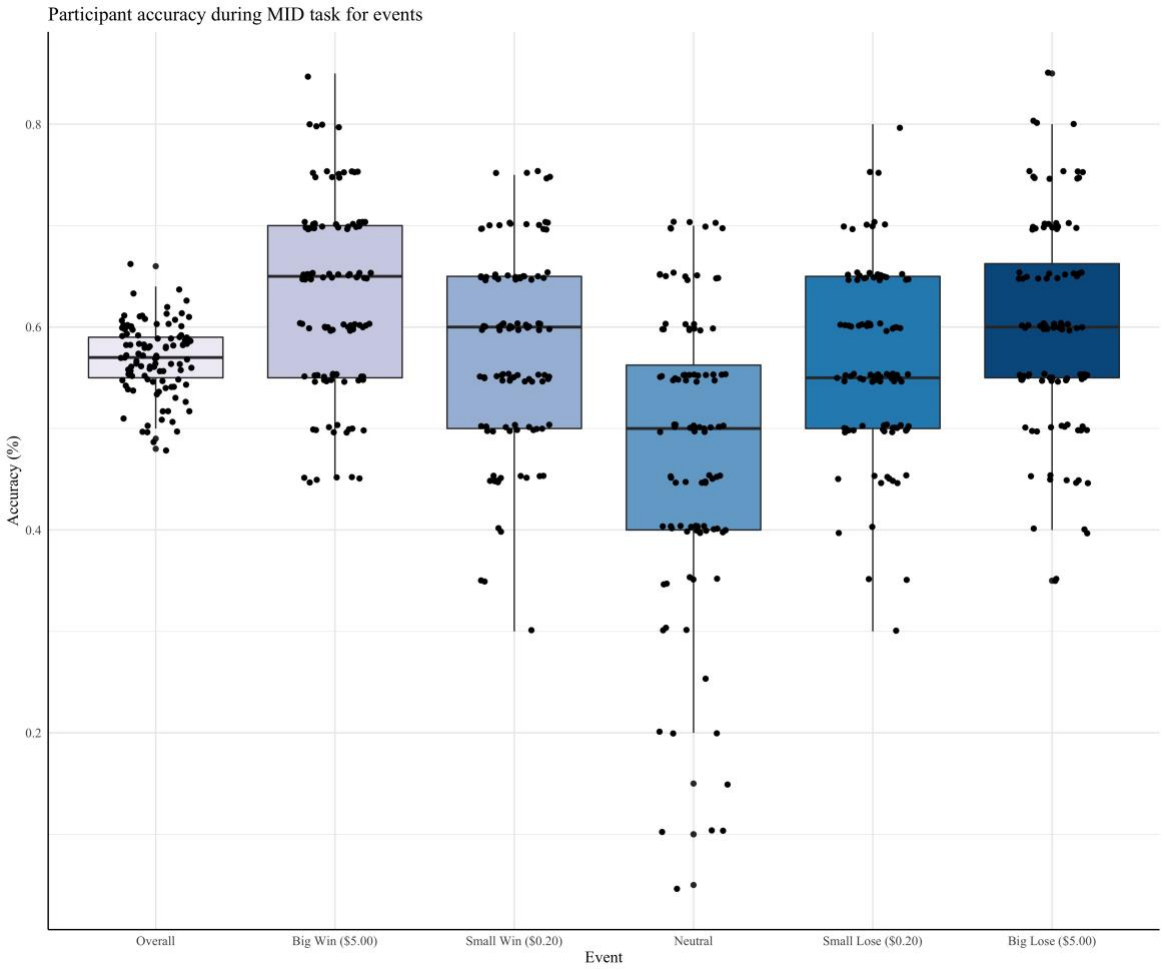


*Figure A.2* Distribution of accuracy by condition for the MID task

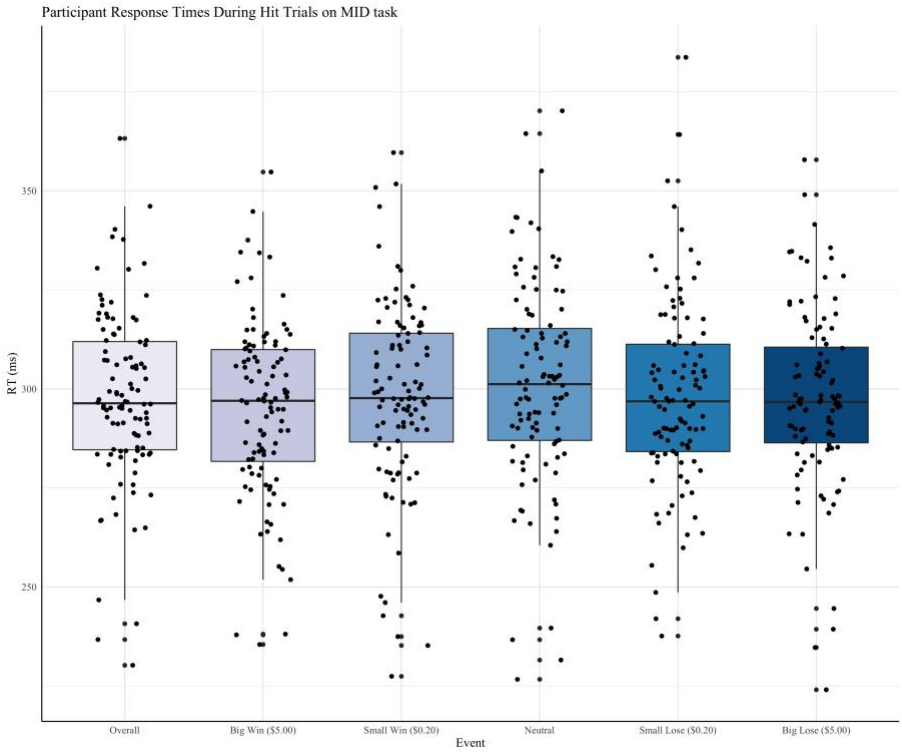


*Figure A.3* Distribution of response times by condition for the MID task

*Table A.3* Motion: Mean Framewise Displacement (FD)

| | *M (SD)* |
|---|---|
| Run 01 – Pre FD | .11 (.05) |
| Run 02 – Pre FD | .11 (.06) |
| Run 01 – Post FD | .02 (.01) |
| Run 02 – Post FD | .02 (.01) |

## Appendix B : Supplemental Information for Study 1 (Chapter 3)

This appendix includes information pertaining to study one in Chapter 3. It includes several tables and figures that summarize: the non-exhausting ROI meta-analysis of studies used to derive a list of *a priori* coordinates, the ROI and whole brain masks used in the FSL analyses, whole brain one-sample t-test activation for all participants (N = 104), the nonparametric whole brain activation for the high risk (N = 41) and average/low risk (N = 63), and the results from the ROI and continuous BMS sensitivity analyses.

### Defining Regions of Interest and Literature Search of Brain Regions

*Table B.1* A prior MNI coordinates based on Neurosynth peaks and those

| Region of Interest | MNI Coordinate (x, y, z) | | |
|---|---|---|---|
| Right Ventral Striatum | 15 | 8 | -9 |
| Left Ventral Striatum | -12 | 8 | -8 |
| Ventromedial Prefrontal Cortex | 2 | 40 | -8 |
| Left Amygdala | -22 | -5 | -19 |
| Right Amygdala | 26 | -4 | -18 |
| Anterior Cingulate Cortex | 3 | 29 | 21 |
| Left Orbitofrontal Cortex | -22 | 34 | -14 |
| Right Orbitofrontal Cortex | 32 | 33 | -14 |
| Right Dorsolateral Prefrontal Cortex | 43 | 37 | 29 |
| Left Dorsolateral Prefrontal Cortex | -42 | 34 | 28 |
| Right Insula | 38 | 13 | -4 |
| Left Insula | -38 | 12 | -9 |

| | | | |
|---|---|---|---|
| Right Posterior Parietal Cortex | 19 | -65 | 54 |
| Left Posterior Parietal Cortex | -23 | -64 | 59 |

*Table B.2* Coordinates information from 18 studies evaluating risk and reward processing in adolescents

| Publication (year) | Left/Right | Region associated with coordinate | MNI x,y,z | | | Type of Behavior Assessed |
|---|---|---|---|---|---|---|
| Bjork et al. (2004) | Left | VS | -9 | 13 | -4 | Age differences (adolescents/young adults); and excitement for cue (button box rating (one to four) feeling when seeing cues on Likert scale - (e.g., how "happy," "tired," or "tense" each cue made them feel) (p. 1794) |
| Bjork et al. (2004) | Right | VS | 12 | 15 | -4 | |
| Bjork et al. (2004) | | mPFC | 2 | 59 | -5 | |
| May et al. (2004) | Left | lOFC | -44 | 40 | -10 | Main effect of cue in adolescents |
| May et al. (2004) | | mOFC | -3 | 51 | -8 | |
| May et al. (2004) | Left | VS | -10 | 9 | -10 | |
| Ernst et al. (2005) | Right | NAcc | 10 | 4 | -6 | Age differences (adults/adolescents); ratings of satisfaction/dissatisfaction in outcome in WOF task (5-pt self-rating) scale; |
| Ernst et al. (2005) | Left | NAcc | -12 | 12 | -6 | |
| Ernst et al. (2005) | Right | Amygdala | 20 | -2 | -14 | |
| Ernst et al. (2005) | Left | Amygdala | -14 | -4 | -8 | |
| Galvan et al. (2006) | Right | VS | 7 | 8 | -6 | Age differences between children, adolescents and adults in activation on two-choice task. |
| Galvan et al. (2006) | Left | VS | -8 | 9 | -6 | |
| Galvan et al. (2006) | Right | OFC | 48 | 34 | -3 | |
| van Leijenhorst et al. (2010a) | Right | Insula | 30 | 27 | 0 | Age differences, preadolescents, adolescents, young adults; anticipation, receipt and omission of rewards on child-friendly Slot Machine Task. |
| van Leijenhorst et al. (2010a) | Right | Insula | 30 | 15 | -15 | |
| van Leijenhorst et al. (2010a) | Left | NAcc | -9 | 9 | -3 | |
| van Leijenhorst et al. (2010a) | Right | ACCg | 3 | 30 | 15 | |
| Bjork et al. (2008) | Right | VS | 15 | 6 | -12 | Adolescents of alcohols and adolescent health control; differences in activation to reward magnitudes on MID task and affect-by-cue self-report ratings |
| Bjork et al. (2008) | Left | VS | -10 | 11 | -9 | |
| Bjork et al. (2008) | Right | VS | 8 | 14 | -7 | |
| Bjork et al. (2008) | | mPFC | 3 | 51 | -5 | |
| Nees et al. (2012) | Left | Caudate | -4 | 16 | 2 | Adolescent SEM model of: factors **personality** (novelty seeking, impulsivity, sensation |
| Nees et al. (2012) | Right | Amygdala | 18 | -1 | -14 | |
| Nees et al. (2012) | Left | Insula | -30 | -20 | 11 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Nees et al. (2012) | Right | VS | 11 | 11 | 0 | seeking, extraversion), **behavior** (delay aversion, risk adjustment, risk-taking on Cambridge Gambling Task), and **brain** (MID task) activation (NAcc, PFC, amygdala, insula, nucleus caudatus, putamen, cerebellar vermis, thalamus) predictors of alcohol intake. |
| Nees et al. (2012) | | dACC | 5 | 42 | 12 | |
| Braams et al. (2016) | Right | Putamen | 15 | 11 | -5 | Age related differences in adolescents and adults; activation on heads/tails gambling task in NAcc and testosterone with average glass per night, total glasses last month and lifetime classes of alcohol consumption |
| Braams et al. (2016) | Left | Caudate | -9 | 15 | -5 | |
| Braams et al. (2016) | Left | ACC | 0 | 50 | -2 | |
| Galvan, et al. (2007) | Right | VS | 7 | 8 | -6 | Age related differences, children, adolescents and young adults. Activation during two choice task (NAcc) association with self-reported likelihood in engaging in risky behavior (Cognitive Appraisal of Risk Activities), and Benthin Risk Perception Measure |
| Galvan et al. (2007) | Left | VS | -8 | 9 | -6 | |
| Galvan et al. (2007) | Right | OFC | 48 | 34 | -3 | |
| Galvan et al. (2007) | Right | dlPFC | 45 | 32 | 26 | |
| Galvan et al. (2007) | | vmPFC | 2 | 36 | -2 | |
| Galvan et al. (2007) | | ACC | 6 | 29 | 36 | |
| Kahn et al. (2015) | Right | VS | 3 | 6 | 3 | Adolescents completed Stoplight Task; risk measured by risks made on task; brain activation during Stop > Go decisions & Go > Stop contrasts, extracted ROI and correlated with self-reported Sensation-seeking and Sensitivity to Punishment and Sensitivity to Reward Questionnaire |
| Kahn et al. (2015) | Right | vlPFC | 45 | 30 | 9 | |
| Cservenka et al. (2015) | Right | VS | 13 | -6 | -14 | Adolescent naïve recent binge drinking (Wave1) brain predictors (WOF task) of Wave 2 self-reported binge drinking. |
| Cservenka et al. (2015) | Left | VS | -12 | -8 | -8 | |
| Pfeifer et al. (2011) | Left | VS | -6 | 16 | 0 | Developmental transition from early childhood (10 years) to early adolescent (13 years) during Faces task predicting Resistance to Peer Influence scale and Positive Youth Development survey |
| Pfeifer et al. (2011) | | vmPFC | -8 | 54 | -6 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Qu et al. (2015) | Left | vlPFC | -27 | 59 | -8 | Longitudinal changes during adolescents related to parent-child relationships, risk-taking (BART) and brain activation to rewards during risk (BART) |
| Qu et al. (2015) | Right | vlPFC | 30 | 56 | 10 | |
| Qu et al. (2015) | Left | dlPFC | -33 | 41 | 38 | |
| Qu et al. (2015) | Right | dlPFC | -33 | 41 | 38 | |
| Qu et al. (2015) | Left | VS | -9 | 8 | -2 | |
| Qu et al. (2015) | Right | VS | 15 | 11 | -8 | |
| Qu et al. (2015) | Left | Insula | -36 | 11 | 1 | |
| Qu et al. (2015) | Right | Insula | 33 | 20 | 4 | |
| Qu et al. (2015) | | ACC | -6 | 8 | 28 | |
| Eshel et al. (2007) | Left | vlPFC | -38 | 22 | 4 | Differences in adolescent and adult risk-taking during task (WOF task) and brain activation. |
| Eshel et al. (2007) | Right | vlPFC | 52 | 24 | -4 | |
| Eshel et al. (2007) | Right | ACC | 2 | 36 | 20 | |
| Eshel et al. (2007) | Left | dlPFC | -26 | 24 | 46 | |
| van Leijenhorst et al. (2010b) | | dmPFC | -12 | 51 | 18 | Age differences children, adolescents, and young adults; and High risk and low risk choices in a gambling task, Cake Gambling Task. |
| van Leijenhorst et al. (2010b) | | vmPFC | -6 | 60 | -6 | |
| van Leijenhorst et al. (2010b) | Right | dlPFC | 39 | 24 | 36 | |
| van Leijenhorst et al. (2010b) | | mPFC | -3 | 45 | -6 | |
| van Leijenhorst et al. (2010b) | Left | NAcc | -9 | 9 | -9 | |
| McCormick & Telzer (2017) | | dACC | -6 | 20 | 31 | Adolescent sensitivity to positive versus negative feedback in decision making during risk-taking context (BART); brain activation with positive versus negative feedback, and self-reported risk-taking behavior (Mod. Adolescent Risk-Taking Scale – frequency engaged in variety of risk behaviors). |
| McCormick & Telzer (2017) | Left | Insula | -45 | 11 | -5 | |
| McCormick & Telzer (2017) | Right | Insula | 54 | 11 | -2 | |
| McCormick & Telzer (2017) | Left | VS | -21 | 14 | -5 | |
| McCormick & Telzer (2017) | Right | VS | 21 | 11 | -2 | |
| Telzer et al. (2015) | Left | Insula | -24 | 24 | -5 | Adolescent peer relationships (support/conflict; Wave 1 & Wave 2) and brain during risk-taking (BART; Wave 3) and self-reported risk-taking behavior (Adolescent Risk-Taking Scale; Wave 3) |
| Telzer et al. (2015) | Right | Insula | 38 | 20 | 0 | |
| Telzer et al. (2015) | Left | VS | -10 | 5 | -10 | |
| Cascio et al. (2015) | | vmPFC | 5 | 53 | -20 | Peer influences on adolescent driving in driving simulation, and relationships with brain |
| Cascio et al. (2015) | Left | Putamen | -21 | 21 | 4 | |
| Cascio et al. (2015) | Left | Caudate | -13 | 21 | 6 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | | response inhibition during Go/Nogo |

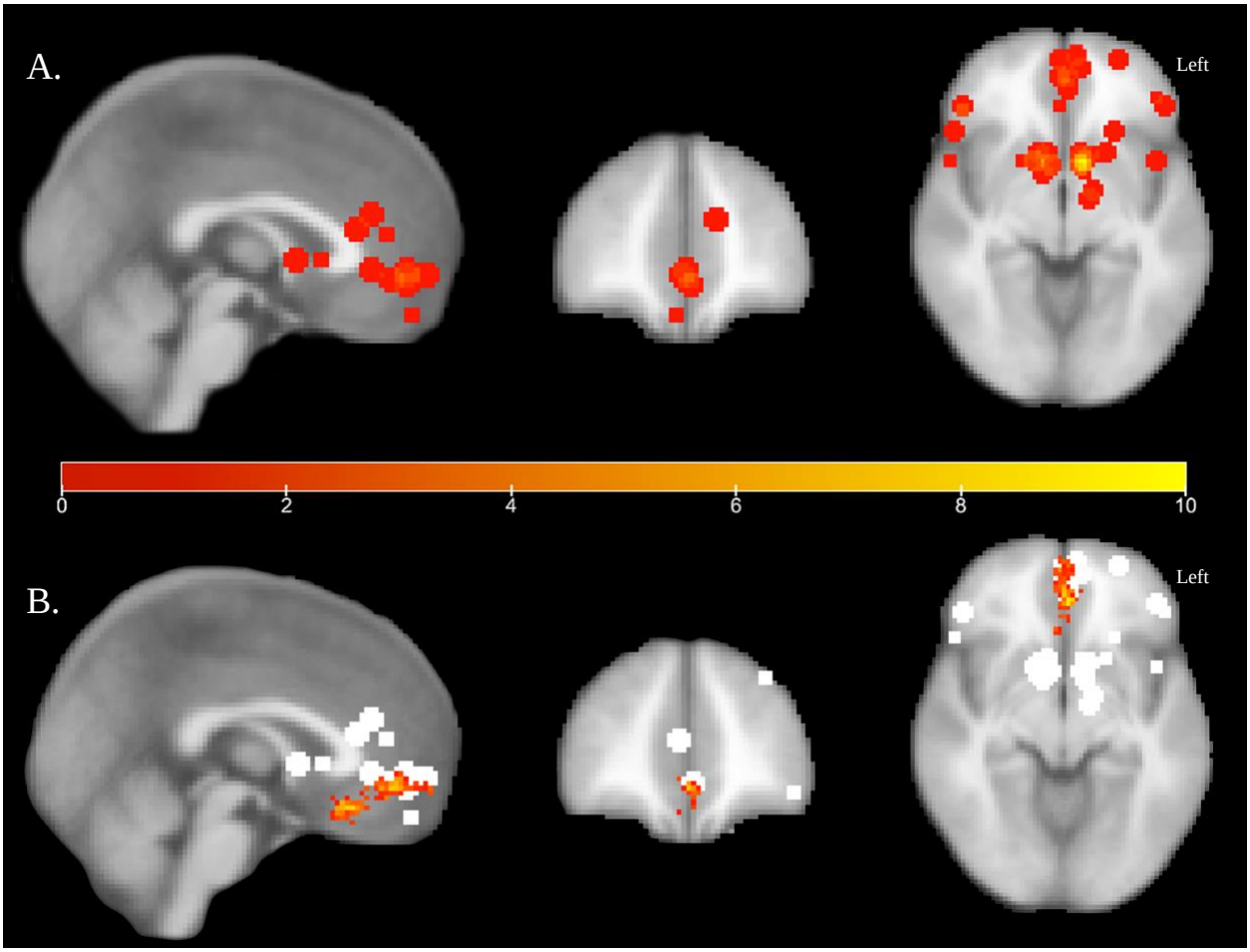


*Figure B.1* Representation of overlap of ROIs from 18 studies along x = 0

**A.** Seventy ROIs from Table S1 were created using 10mm spheres and added into a single aggregated mask. The thresholding represents number of studies that had overlapping coordinates. The majority of spheres were represented one time, shown in red, with increasing numbers representing a greater intensity of yellow. VS/NAcc were most frequently represented, Right NAcc = 10, with vmPFC represented four times.

**B.** As a result of variability in both 18 studies and Neurosynth coordinates defining the vmPFC, Neurosynth NIFTI files were extracted and thresholded at 95$^{th}$ percentile, that were overlayed with bin ROIs from 20 studies, that presented a critical peak in the ventral/rostral section.

**Results**

The group level mask was derived by the FEAT higher-level analysis GUI calculating a similar mask that would be included in an alternative FSL analysis using FLAME. The mask excludes portions of the superior sagittal sinus, and areas of extensive sinus dropout, such as the ventral-caudal portion of the vmPFC. Parcellations of the cerebral spinal fluid from mask were not excluded as the BOLD signal is represented in these boundaries for regions in the medial walls that include the motor areas, cingulate and prefrontal regions.

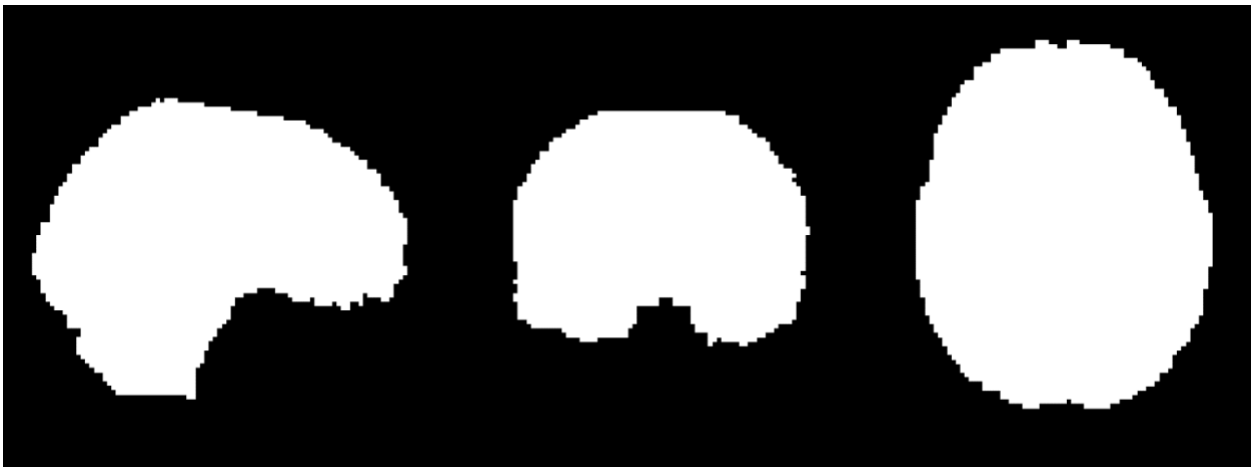

*Figure B.2* Group level mask input to the randomise nonparametric analysis

*Whole Brain Map*

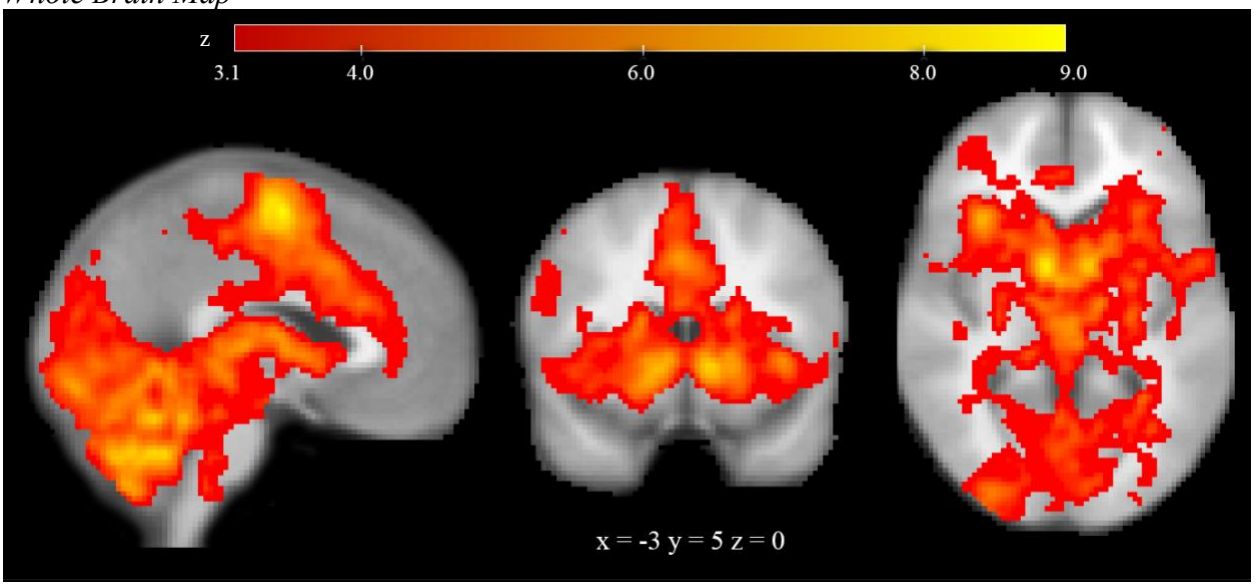


*Figure B.3* Mean level activation to anticipation of Big Reward vs Neutral contrast for 104 subjects, One-sample T-test

Mean level maps produced using FSL Feat, Mixed Effects Flame1. Activation is presented as z-statistics, thresholded at $p < .001$, range 3.1 to 9.0. Robust activation is present in areas previously referenced with this task and anticipation contrasts (Bjork et al., 2011b; Büchel et al., 2017)

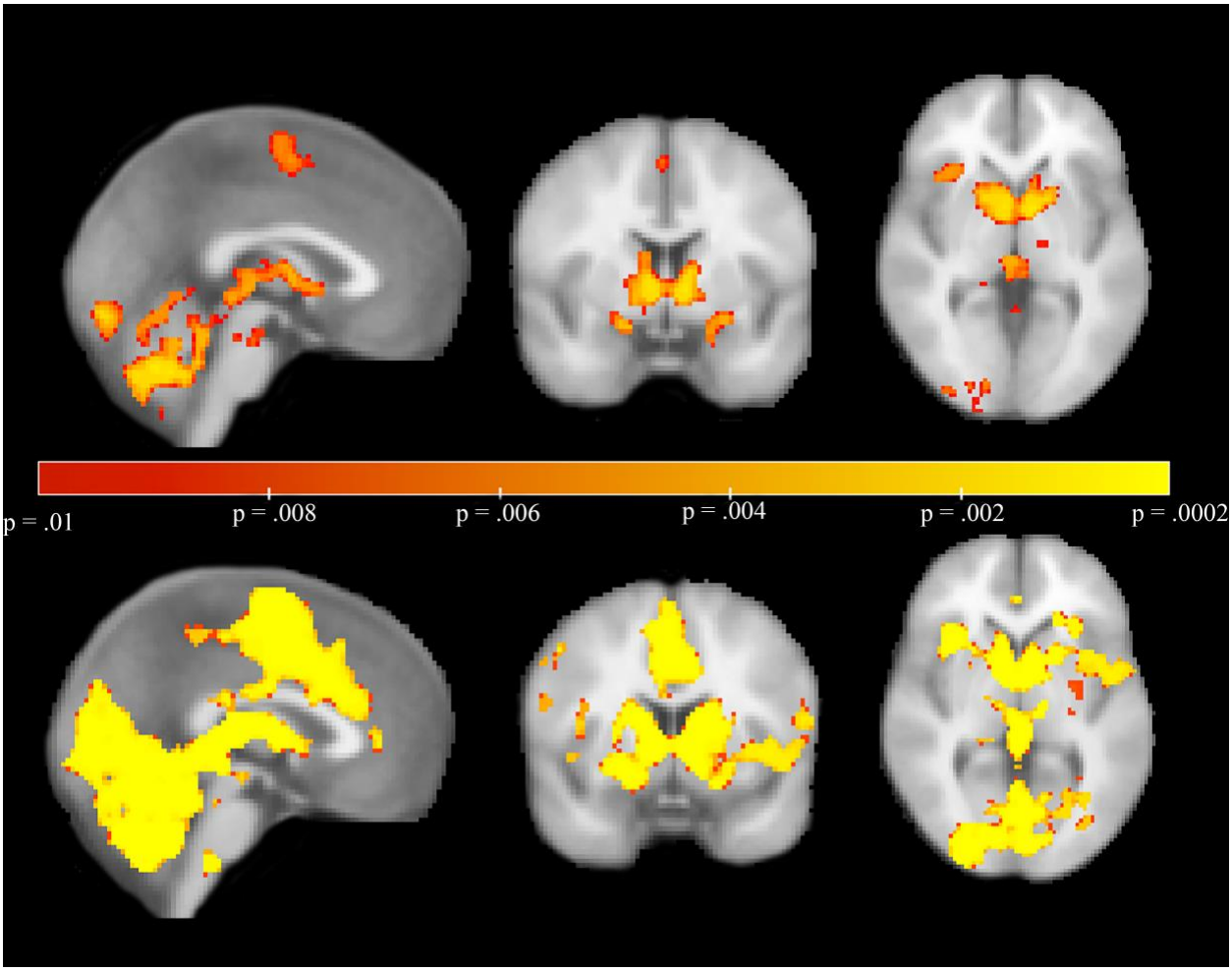


Figure B.4 Overall activation to anticipation of Big Reward vs Neutral contrast for (A) High Risk One-sample t-test (N = 41) and (B) Average Risk One-sample t-test (N = 63) adolescents

Activation is represented as the output of TFCE output image overlayed on MNI 152 2mm brain, thresholding output maps at minimum activation (p = .01) to maximum (p = .0002). Maximum threshold is constrained to the upperbound $\alpha$ for 5000 permutations (1/5000 = .0002)

*Table B.3* Risk profile (High vs average) predicting Region of Interest during anticipation of Big win vs Neutral contrast for Wave 1 and Multi-wave stable risk profile

| Region of Interest | $p$ Uncorrected | $p$ FDR |
|---|---|---|
| | Wave 1: High vs Average Risk-Taking Profile | |
| Anterior Cingulate Cortex | .29 | 0.80 |
| Ventromedial Prefrontal Cortex | .80 | 0.86 |
| Left Orbitofrontal Cortex | .45 | 0.86 |
| Right Orbitofrontal Cortex | .67 | 0.86 |
| Left Dorsolateral Prefrontal Cortex | .02 | 0.14 |
| Right Dorsolateral Prefrontal Cortex | .13 | 0.61 |
| Left Posterior Parietal Cortex | .51 | 0.86 |
| Right Posterior Parietal Cortex | .02 | 0.14 |
| Left Insula | .27 | 0.80 |
| Right Insula | .37 | 0.86 |
| Left Ventral Striatum | .78 | 0.86 |
| Right Ventral Striatum | .76 | 0.86 |
| Left Amygdala | .96 | 0.96 |
| Right Amygdala | .66 | 0.86 |
| | Longitudinally Stable Profiles: High vs Average Risk-Taking | |
| Anterior Cingulate Cortex | .68 | 0.85 |
| Ventromedial Prefrontal Cortex | .98 | 0.98 |
| Left Orbitofrontal Cortex | .77 | 0.85 |
| Right Orbitofrontal Cortex | .40 | 0.85 |
| Left Dorsolateral Prefrontal Cortex | .13 | 0.51 |
| Right Dorsolateral Prefrontal Cortex | .04 | 0.35 |
| Left Posterior Parietal Cortex | .48 | 0.85 |
| Right Posterior Parietal Cortex | .007 | 0.09 |
| Left Insula | .66 | 0.85 |
| Right Insula | .34 | 0.85 |
| Left Ventral Striatum | .94 | 0.98 |
| Right Ventral Striatum | .75 | 0.98 |
| Left Amygdala | .35 | 0.85 |
| Right Amygdala | .79 | 0.85 |

*Sensitivity Analyses:* In a post-hoc comparison, the continuous variability of brain and Behavioral Misadventure (Wave 1) was evaluating using FSL randomise. When using the continuous score of BMS, there was not significant association ($p < .05$) between brain activation (positive or negative) and individual BMS scores. However, the nature of activation was comparable to that Table 3.2 in the manuscript at a lower bound threshold.

*Table B.4* Whole Brain Analyses: Negative association in activation between Behavioral Misadventure (continuous) and anticipation of big reward versus neutral contrast (Nonparametric, 5000 Permutations with Threshold-Free Cluster Enhancement)

| Wave 1 Brain Negative Association with BMS ($p < .08$) | | | | |
|---|---|---|---|---|
| Cluster Index[a] | Cluster peak x, y, z | # of Voxels | Cluster Label [b] | *p* |
| 8 | *-13, -3, 17* | 680 | Left-Caudate | .06 |
| 7 | *16, -82, 6* | 43 | Right Primary Visual | .07 |
| 6 | *20, -61, -14* | 28 | Right Cerebellar | .08 |
| 5 | *50, -72,20* | 18 | [c] Right Angular Gyrus | .07 |
| 4 | *-32, -34, -24* | 10 | Left-Parahippocampal | .07 |
| 3 | *-22, -72, 2* | 4 | Left Primary Visual | .08 |

Clusters obtained using FSL's *cluster* on TFCE activation maps from randomise, threshold .92 (i.e., .08)
**[a]** Cluster index identified using fsl command *cluster* that identified peak clusters in volume, index 1 not reported due to number of voxels = < 3, clusters plotted on MNI brain in Figure 3.2.
**[b]** To identify region for cluster label, we used a combination of reverse inference on neurosynth.org/locations to identify top association with cluster activation and cross-referenced with *FSL Harvard-Oxford Cortical Structural Atlas*
**[c]** Cluster unique to this tresholded map, region not represented in Table 3.2.

## Appendix C : Supplemental Information for Study 2 (Chapter 4)

### Region of Interest Identification & Definition

The below table summarizes the studies from the meta-analysis of contrasts for published work on PubMed from 2015-2010 using the MID. This type of contrasts the proportion of studies using these contrasts are noted below the table.

*Table C.1* Paradigm Contrast Reviews PubMed 2015-2019

| Study | N | age ranges | Paper Focus | Target % Acc | Type of Contrast (Anticipation = Ant; Feedback = FB) | MID version |
|---|---|---|---|---|---|---|
| (Dhingra et al., 2019) | 54 | 22-74 | Age related effect of reward activation | 67% | **Ant:** Big Win v. Neutral, Big Win vs Small Win, Small Win vs Neutral | modified MID |
| (Schwartz et al., 2019) | 15 | 15.29 (2.4) | Social vs non-social reward | 66% | **Ant** : Reward vs No Reward | Youth friendly - MID - Pinata task (non-social) |
| (Swartz et al., 2019) | 262 | 16.8 (.58) | Mexican origin, alcohol | - | **Ant:** Reward v. Neutral **FB**: Reward Hit v. Neutral hit | MID |
| (Maresh et al., 2019) | 99 | 13-19 | EEG-Bipolar Disorder | 70% | Average each trial | MID |
| (Nestor et al., 2019) | 36 | 16.2 (most male) | cannabis dependence | 50% | **Ant**: Win v. Neutral | MID |
| (Aloi et al., 2019) | 150 | 16.1 (1.1) | Diff. in alcohol and marij. Exposure | 66% | ***Modulator: reward value outcome and win vs loss*** | Altered version, trails: Neut 12; Win 48; Loss 48 |
| (Cope et al., 2019) | 34 children (10.5) | 16 | substance use -- eternalizing and FH | 60% | **Ant:** Big Win v. Neutral Large Loss v. Neutral | MID - modified Mich. Long. Study |

| | | | | | | |
|---|---|---|---|---|---|---|
| (Cao et al., 2019) | 1510 | 14yr | sensation seeking, reward anticipation. [Reward = candy] | 66% | **Ant**: Big reward v. Neutral **FD**: Big Reward Hit v. No Reward; Big Reward Hit > Neut Reward Hit | MID [IMAGEN] -- No loss cue |
| (Stevens et al., 2018) | 151 | 12-18 | ADHD | 66% | **Ant**: Big Win v. Small Win | Modified Knutson ($0, $1, $5) |
| (Papanastasiou et al., 2018) | 298 | 14 & 19 | psychotic like experiences | | **Ant**: Big Win v. Neutral | Knutson? Not specified…. |
| (Landes et al., 2018) | 54 | 12-17 | major depressive disorder-ERP/EEG | 50% | Average each trial | altered MID |
| (Martz et al., 2018) | 57 | ~20 | psychosocial/neural resilience in FH SU | 60% | **Ant**: Win v. Neutral | MID - modified Mich. Long. Study |
| (Chronaki et al., 2017) | 32 | 10-16 | Reinforcement effects | 66% | Average each trial | modified versoin, shapes, colors. |
| (Navas et al., 2018) | 68 | 16.5 (1.5) | Body fat | NR | **Anticipation** linear: big>medium>low>neutral. **FB**: Win Hit vs Win Miss | modified colors, shapes, etc. |
| (Garrison et al., 2017) | 14 & 28 | 17 (1.3) | Smoking Behavior | 66% | **Ant:** Win v. Implicit Baseline Loss v. Implicit Baseline | Modified Knutson MID -- no paradigm example |
| (Colich et al., 2017) | 76 (38 pairs) | 9-15 | Risk for depression | 75% | **Ant:** Win v. Neutral Loss v. Neutral | modified - Kid MID task (replaced money w/ points of Knutson 2008 version |
| (Xu et al., 2017) | 1129 | 14.4 (.4) | ADHD | 66% | **Ant**: Win v. Neutral | MID [IMAGEN] -- No loss cue |
| (Bourque et al., 2017) | 246 & 1196 | 14.3 (.4) - | Symptoms at 16 - Psychotic like experi. | 66% | **Ant**: Win v. Neutral | MID [IMAGEN] -- No loss cue |
| (Duka et al., 2017) | 1299 | 14.4 (.4) | gene & brain response correlates | 66% | **Ant**: Big Win v. Neutral | MID [IMAGEN] -- No loss cue |
| (Gonzalez et al., 2016) | 83 | ~25 | Neighborhood quality on brain | 66% | **Ant:** Win v. Neutral | MID (27 reward, 27 punish, 18 neutral cues) |

| | | | | | | |
|---|---|---|---|---|---|---|
| (Büchel et al., 2017) | 144 | 14 (16 f/u) | Novelty seeking and substace use | 66% | **Ant**: Big Win v. Small Win | MID [IMAGEN] -- No loss cue |
| (Veroude et al., 2016) | 328 | 17.6 (3.3) | Callous-unemotional, ADHD, oppositional defiant | 33% | **Ant**: Win v. Neutral<br>**FB**: {reward hit.- reward miss} > {non-reward hit-non_reward miss} | MID modified - colored cues (green/red), NO LOSS condition |
| (Mikita et al., 2016) | 1472 | 14.4 | Autism | 66% | **Ant**: Big Win v. Neutral<br>**FD**: Big Win Miss v. Miss Neutral;<br>Big Win Hit v. Neutral Hit | MID [IMAGEN] -- No loss cue |
| (Urošević et al., 2016) | 47 | 13 - 19 | bipolar disorder | 70% | **anticipation**: gain vs neutral; large gain > small [compensated $ for 10% of winnings] | MID - 60 trials |
| (Richards et al., 2016) | 429 | | Plasticity genes & social environments | 33% | **Ant**: Win v. No Reward.<br>**FD**: Reward Hit v. Reward Miss | Red = no reward squared; green = reward screen (no loss condition) |
| (Joseph et al., 2016) | 27 & 51 (78 total) | 11-14 & 18-25 | personality (impulsivity, avoidance, approach tendencies) | 66% | Contrasts are the demeaned versions of contrasts [1, 0.1, 0, .1, 1] and [− 1, 0.1, 0, 0.1, − 1] | Modified MID |
| (Martz et al., 2016) | 108 | 21-23 (3 fMRI scans) | Parental History SUD | 66%% | **Ant**: Big Win v. Small Win | modified MID - MLS |
| (van Hulst et al., 2015) | 18 | 9.5-14.5 | Pilot Child Friendly MID | NR | **Ant**: Big Win v. Smal Win<br>**Big Win v. Neutral** | Child Friendly MID |
| (Mori et al., 2016) | 30 | 18-19 | Depression | NR | **Ant:** Big Win v. No Gain, Large Loss v. No Loss | MID (40 gain, 40 loss, 10 neutral trils) |
| (Z. Li et al., 2015) | 26 | 18.7 (1.4) | DCM of MID | 66% | **Ant:** Win vs Neutral Loss v. Neautral,<br>**all vs neutral used in DCM)** | Modified MID 60 total trials (20, 20, 20) |
| (Chan et al., 2016) | 28 | 18.9 (1.8) | Social & Monetary Process, Anhedonia | 66% | **Ant:** Win v. Neutral, Lose v. Neutral.<br>**FB**: Win Hit v. Neutral Hit<br>Loss miss v. Neutral Miss. | Modified MID 60 total trials (20, 20, 20) |
| (Karoly et al., 2015) | 138 | 14-18 | Substance Use | 66% | **Ant:** Win v. Neutral<br>Lose v. Neutral | modified MID from Filbey et al. 2013 |

| | | | | | | |
|---|---|---|---|---|---|---|
| (Sauder et al., 2016) | 38 | 13-19 | Self-injury | NR | **Ant**: Reward v. Neutral - factorial design of reward magnitude x group. | MID |
| (von Rhein et al., 2015) | 350 | 17.8 | ADHD | 33% | **Ant:** Win v. Neutral **FB**: Win Hit v. Neutral Hit | modified MID 25 reward and 25 neutral experimental trials |
| (LeMoult et al., 2015) | 38 (21/17) | 11.2 (1.2) & 13.3 (1.4) | Menarche on diurnal cortisol production | 75% | **Ant**: Gain -- unclear | KID MID task- 100 trials |
| (Nees et al., 2015) | 530 | W1. 14.3 & W2. 16.2 | BDNF and reward in early substance use | 66% | **Ant & FB w/ subj specific regressors** | MID - IMAGEN study |
| (Boecker et al., 2014) | 162 | 24/4 | Early life adversity | NR | **Ant:** Win v. No Win | mod. MID |

*Note*. Median sample size (*N* = 91; min: 15 max: 1510).

Across 37 studies 61 modeled contrasts:

*Anticipation* (n = 43, 70%):

49% - All Win > Neutral

16% Big Win > Neutral

14% Big Win > Small Win

12% Loss > Neutral

9% others (Big Loss > Neutral; Small Win > Neutral; Win (or Loss) > Implicit Baseline)

*Feedback* (n = 8, 13%):

34% Reward Hit > Neutral Hit

25% Big Win Hit > Big Win Miss

38% others (Big Win Hit > Neutral Hit; Big Win Miss > Neutral Miss; Loss Miss > Neutral Miss)

*Others* (n = 10, 16%):

Demeaned contrasts, complex feedback contrast, linear model of anticipation cues, average of each trial, and other modulators.

Regions of interest: Below are the MNI coordinates for regions used in theses analyses, and a representation of regions on a glass brain representing the location (Figure C2).

*Table C.2* A prior MNI coordinates pulled from Neurosynth

| Region of Interest | Index | Glass Brain Index | MNI Coordinate (x, y, z) | | |
|---|---|---|---|---|---|
| Right Ventral Striatum | R_VS | Blue | 15 | 8 | -9 |
| Left Ventral Striatum | L_VS | | -12 | 8 | -8 |
| Medial Prefrontal Cortex | mPFC | Green | 2 | 40 | -8 |
| Anterior Cingulate Cortex | ACC | Pink | 3 | 29 | 21 |
| Left Orbitofrontal Cortex | L_OFC | Yellow | -22 | 34 | -14 |
| Right Orbitofrontal Cortex | R_OFC | | 32 | 33 | -14 |
| Right Insula | R_Insula | Red | 38 | 13 | -4 |
| Left Insula | L_Insula | | -38 | 12 | -9 |

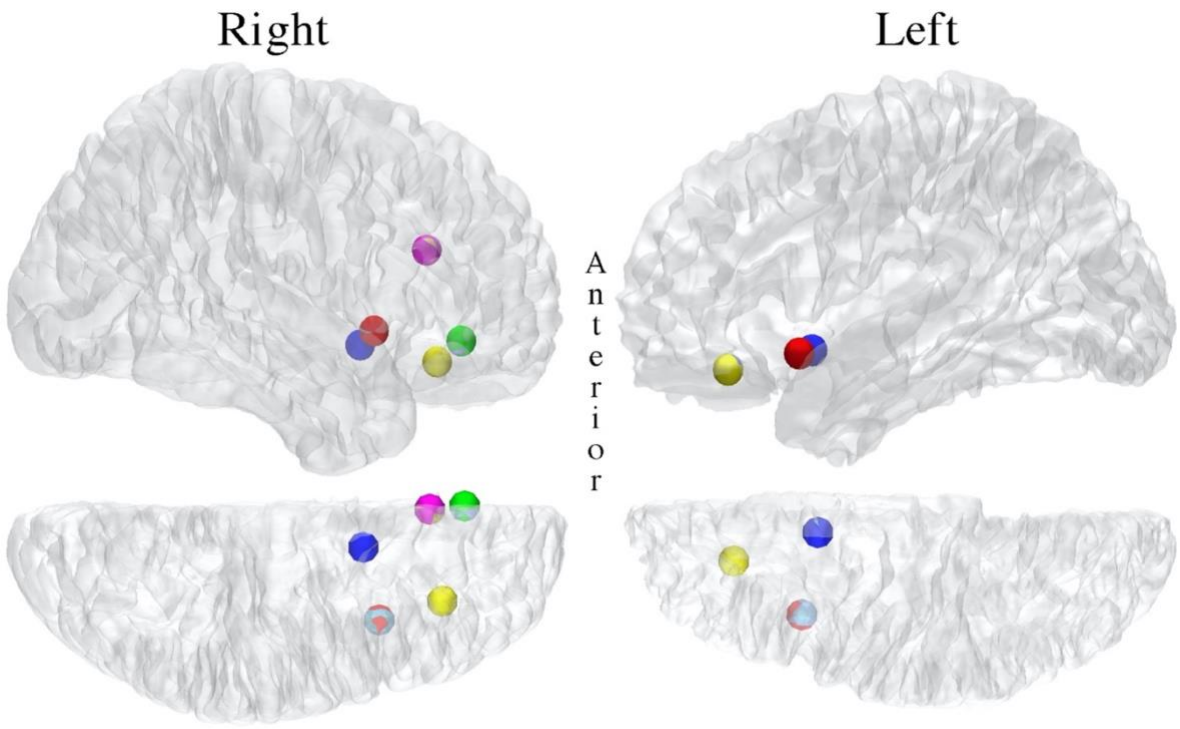


*Figure C.1* MNI Glass Brain Representing Location of Regions of Interest used in Analyses
Note: Index of colors in available in Table C2; Lateral and Axial Views of Left & Right Hemisphere

## Results

### *Similarity Matrices*

The percent overlap between any two activation maps is defined from a set theoretical point of view, where the overlap $J(A,B)$ is defined by the well-known relation as:

$$J(A,B) = \frac{A \cap B}{A + B - A \cap B}$$

The relation calculates the ratio of ***common pixels*** that are activated across two activation maps, to the total number of pixels present in the two maps. For example, the Anticipation Win > Neutral and Anticipation Big Win > Neutral have 38% of pixels that overlap in their thresholded statistical activation group level maps (see Table 1 in manuscript for description of contrasts).

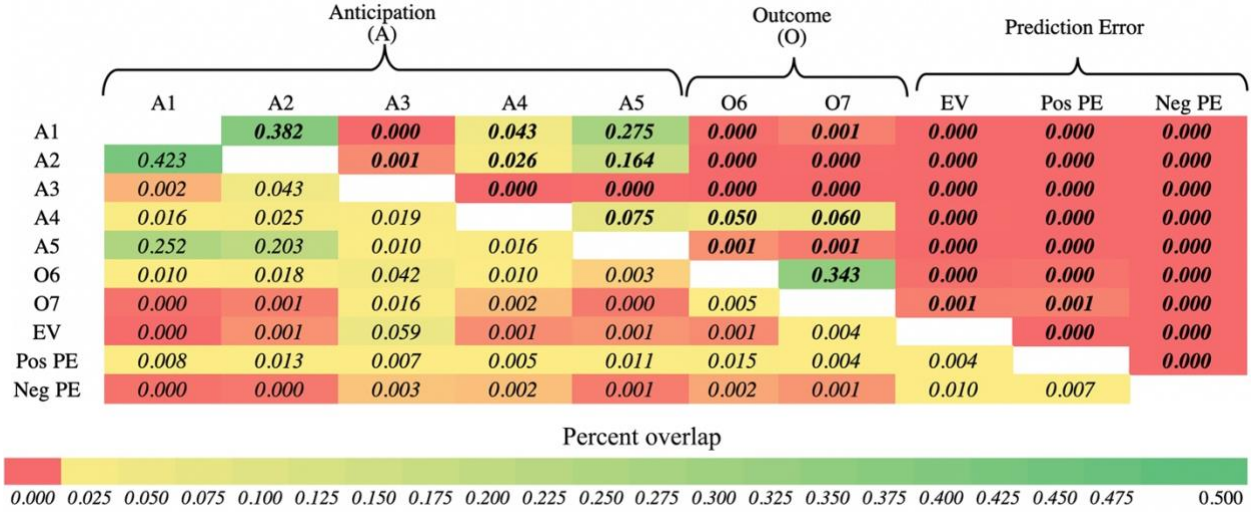


*Figure C.2* Similarity Matrix for thresholded individual and Group Level Maps
Note: Bolded values are group level similarity values and italicized are individual level similarities values from second level analysis

Correlations between Psychological Characteristics: Correlations among aggregated self-reported items (Wave 1 – Wave 3). BSSS = Brief Sensation Seeking Scale; BIS = Barratt Impulsivity Scale – Brief

*Table C.3* Correlations Between self-reported items (z-scored)

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 1. Internalizing | - | | | | |
| 2. Externalizing | .51 | - | | | |
| 3. Substance Use | .04 | .51 | - | | |
| 4. BIS | .30 | .57 | .23 | - | |
| 5. BSSS | .09 | .46 | .36 | .44 | - |

*Brain-behavior Estimates Across complete set of contrasts (10), regions (8) and behaviors (5)*

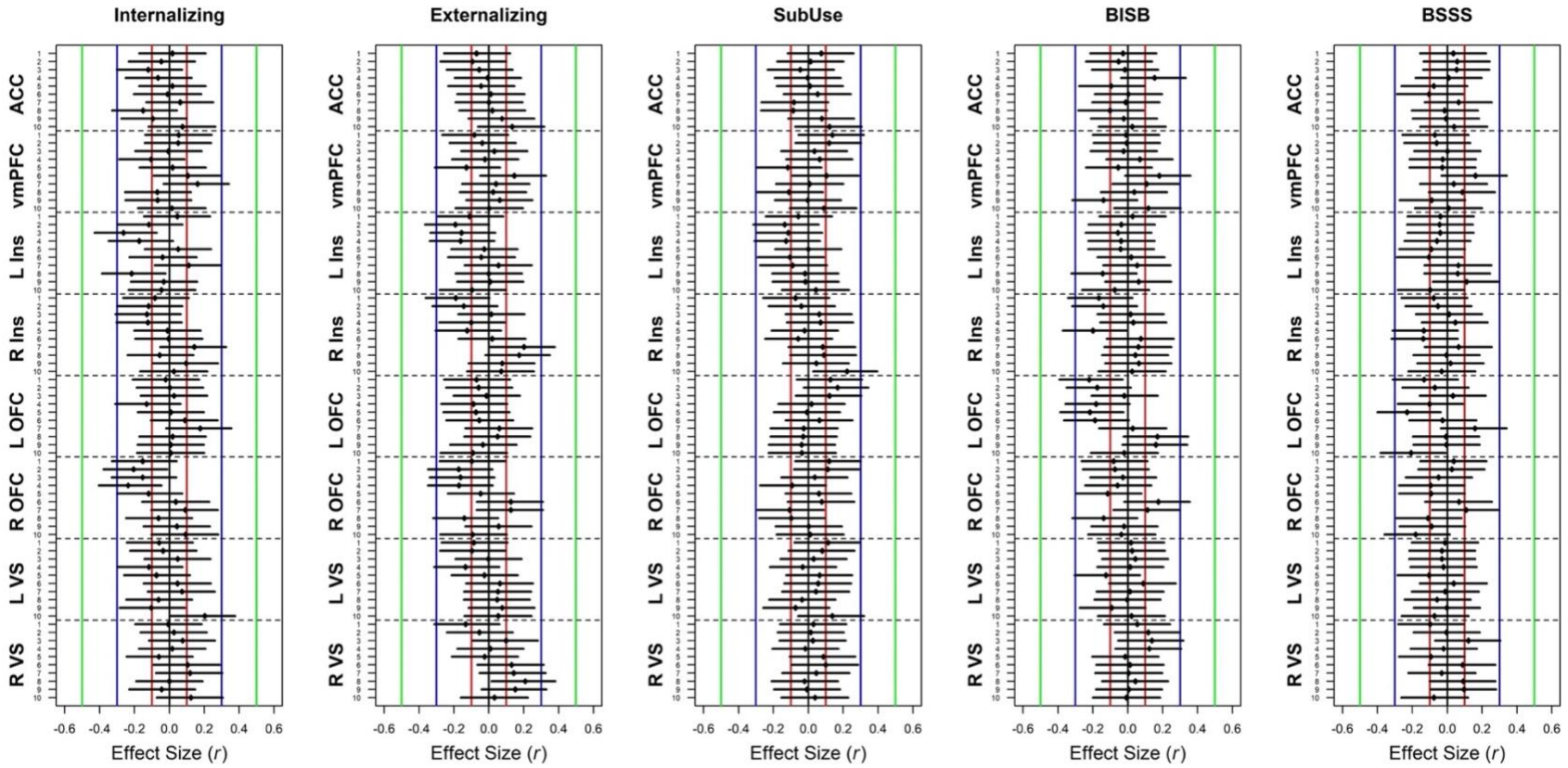


*Figure C.3 :* Forest plots displaying the most likely Pearson's r value (black diamonds) and 95% Bayesian credible interval (black lines) for correlational relationships between ROI activation estimates from each contrast and behavioral criterion measures.
Red, blue and green lines denote "small" (r=.10), "moderate" (r=.30) and "large" (r=.50) effect sizes. 1-10 = Ten contrasts listed in Table 4.1, Chapter 4; ACC = anterior cingulate cortex; mPFC = medial prefrontal cortex; Ins = insula; OFC = orbitofrontal cortex; VS = ventral striatum; L = left; R = right; SubUse = substance use composite measure; BISB = Barratt Impulsiveness Scale-Brief; BSSS = Brief Sensation Seeking Scale

*Interpretation of the BOLD plots:*

We expand here on the interpretation of the BOLD response. The nature of the anticipation signal bleeding into the feedback phase is apparent in the bilateral VS when the anticipation cues are locked to the feedback phase (Figure S8). There is significant separation for the first 4-5 TRs (or 3-4 sec) in the feedback phase in the Big Win as compared to the Neutral phase, until they reverse by TR 10. Since the signal is not appropriately deconvolved in the feedback phase, one approach is to model based on combinations of Hit/Miss trials. In our main feedback contrasts, F6 and F7, we modeled the Big Win versus Neutral Hit, which still demonstrates poor deconvolution in the VS regions (Figure S6), which likely stems from the between contrast spill-over HRF from the anticipatory phase (Figure S5). One alternative approach, which we did not model in the whole brain contrasts, is the contrast of Big Win/Loss Hit versus Big Win/Loss Miss. However, direct observation of the BOLD signal (Figure S7) demonstrates that for Big Win Hit and Big Win Miss, there is a higher signal for hit versus miss trials, however, these are nearly identical in the VS BOLD signal. However, whereas the mPFC demonstrates peak separation at TR 14 (~11 sec), this is occurring well into the subsequent trial, it is unclear what this change represents. Overall, we find appropriate peaks in direct BOLD signal after anticipation cue onset, but a complicated picture forms in the outcome phase with respect to bilateral VS and mPFC.

*Proportion of effect sizes across* 400 brain-behavior estimates

All values are absolute values of the reported effect sizes |*r*|

*Table C.4* Count/Proportion across Pearson r standard effect sizes, out of 400 observations (10 contrasts x 8 ROIs x 5 behaviors)

| | Count (n) | Proportion (%) |
|---|---|---|
| Small (*r:* .00 - .20) | 388 | 97% |
| Medium (*r:* .20 - .30) | 12 | 3% |
| Large (*r* < .30 - .50) | 0 | 0% |

*Table C.5* Count/Proportion across |.05| intervals in effect sizes, out of 400 observations (rounded, may not add up exactly to 100%)

| | Count (n) | Proportion (%) |
|---|---|---|
| *r* = 0.00 to 0.049 | 164 | 41% |
| *r* = 0.05 to 0.099 | 123 | 31% |
| *r* = 0.10 to 0.149 | 72 | 18% |
| *r* = 0.15 to 0.199 | 29 | 7% |
| *r* = 0.20 to 0.249 | 11 | 3% |
| *r* = 0.25 to 0.299 | 1 | < 1% |

*Signal-to-Noise Ratio for mPFC and bilateral VS*

SNR is calculated using the 3dTstat command below. mPFC here is the mPFC peak cluster from Neurosynth for "ventromedial prefrontal" search term. For references, the **nonbrain** of SNR table is for the ROI created in a non-brain region (will contain some smoothed signal) as our filter_func_data had bet extracted, so it was most reasonable for comparison. The signal to noise is calculated by run (two runs)

*$3dTstat -prefix <output_snr_file>  -cvarinv  <filter_func_data inputfile>*

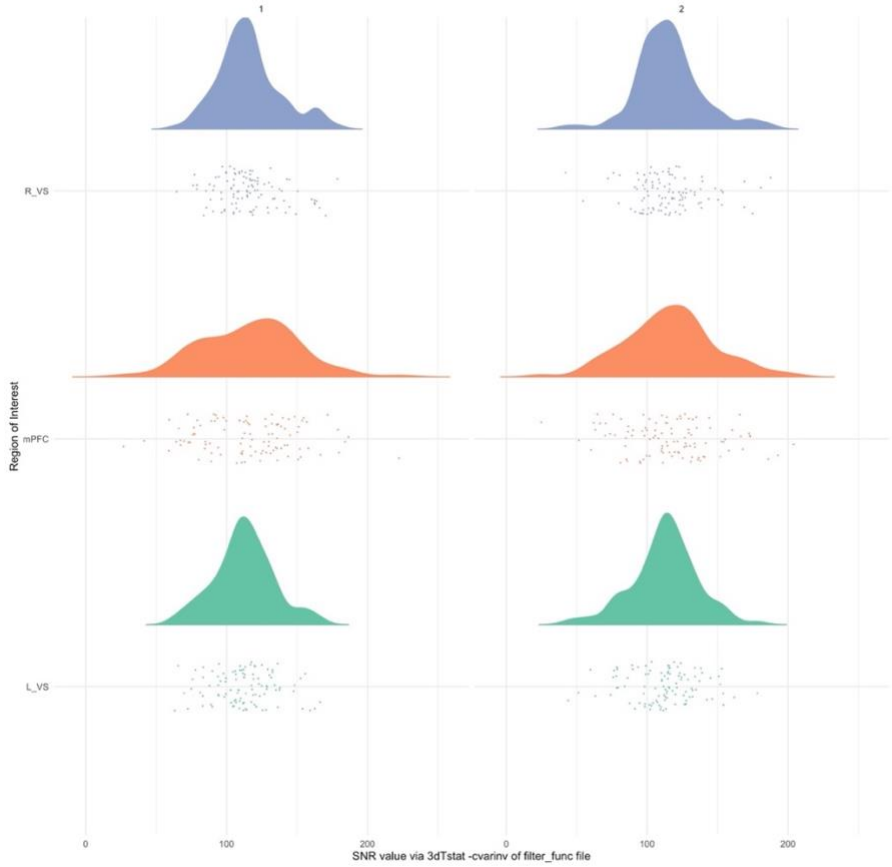


*Figure C.4* Comparison of signal-to-noise ratio for subcortical (VS) and cortical regions (mPFC)
R_VS = Right Ventral Striatum; L_VS = Left Ventral Striatum; mPFC = medial Prefrontal cortex

*Direct observation of the BOLD signal extracted for each cortical (mPFC) and subcortical (VS) regions.*

Several steps were taken to plot the peak BOLD signal for Anticipation/Feedback onset in the VS and mPFC. First, the mean signal was calculated of the preprocessed functional timeseries (t) using the calculation:

$$\%\ Signal\ Change_{\ t} = \frac{t\ -\ t_{\mu}}{t\ *\ 100}$$

using fslmaths (*fslmaths* <filtered_func_data> -sub <mean_func> -div <mean_func> -mul 100 <output_name>) for each run, extracting the timeseries percent signal change for the mPFC (10mm sphere) and bilateral VS (10mm sphere). Second, the behavioral onset files (100 trials) were expanded to match their occurrence in the 651.2 second length of the task across two runs (407 volumes per run = 814 total volumes. 814 * .8sec TR = 651.2 sec). Then, the TR matched behavioral files were merged with the extracted mean percent signal changed for each ROI, and from each locked onset, 15 subsequent TRs were extracted to reflect a BOLD signal change across 12 seconds (reflecting the delayed response). For each cue onset and subsequent TR, the ***mean*** **and** ***90% Confidence Interval*** was bootstrapped to get a robust estimate of the signal change across 104 subjects for phase (anticipation or feedback) and condition type (Big Win, Big Loss or Neutral).

First we present the anticipation phase compare Big Win (LgPun) and Big Loss (LgReward) conditions. Which demonstrate small differences between valence, Win and Loss cues.

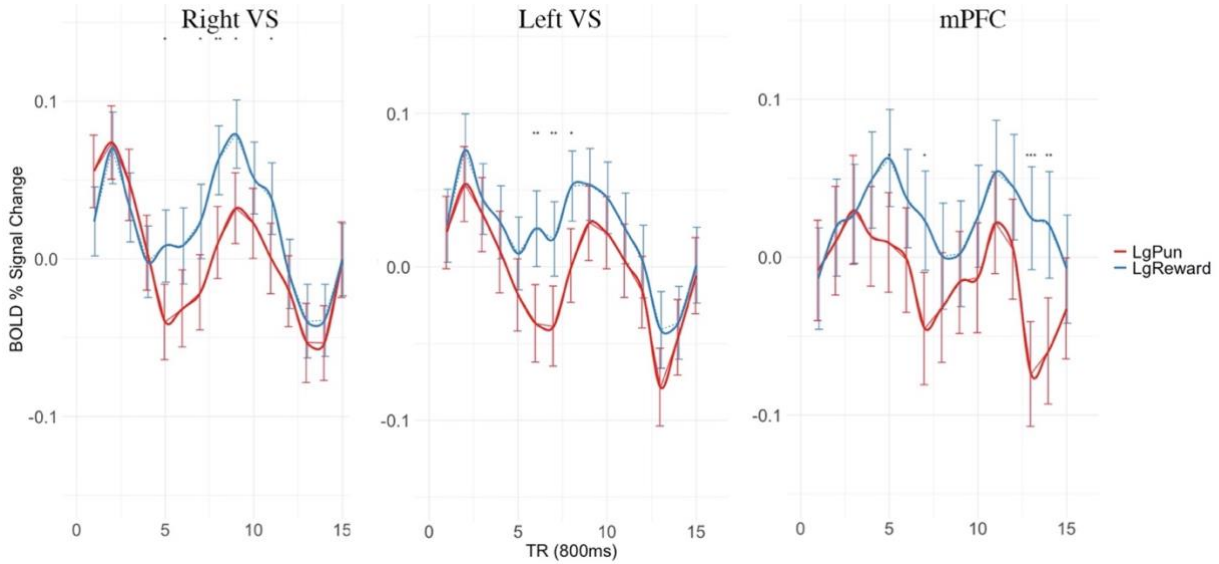


*Figure C.5* Anticipation Phase BOLD Signal change across 15 TRs.
LgPun = $5 Loss Cue; LgReward = $5 Win Cue; Error bars represent 90% Confidence Interval; p < .05 * ; p < .01**, p < .001***

Next, we plot the signal with respect to the feedback phase. We examine this at multiple levels: comparing Gain Hit Versus Neutral Hit (Figure S7); gain/loss Hit versus Miss (Figure S8); and general signal change for each Anticipation cue type to observe how much of the BOLD signal from the anticipation cue bleeds into the feedback phase (Figure S9).

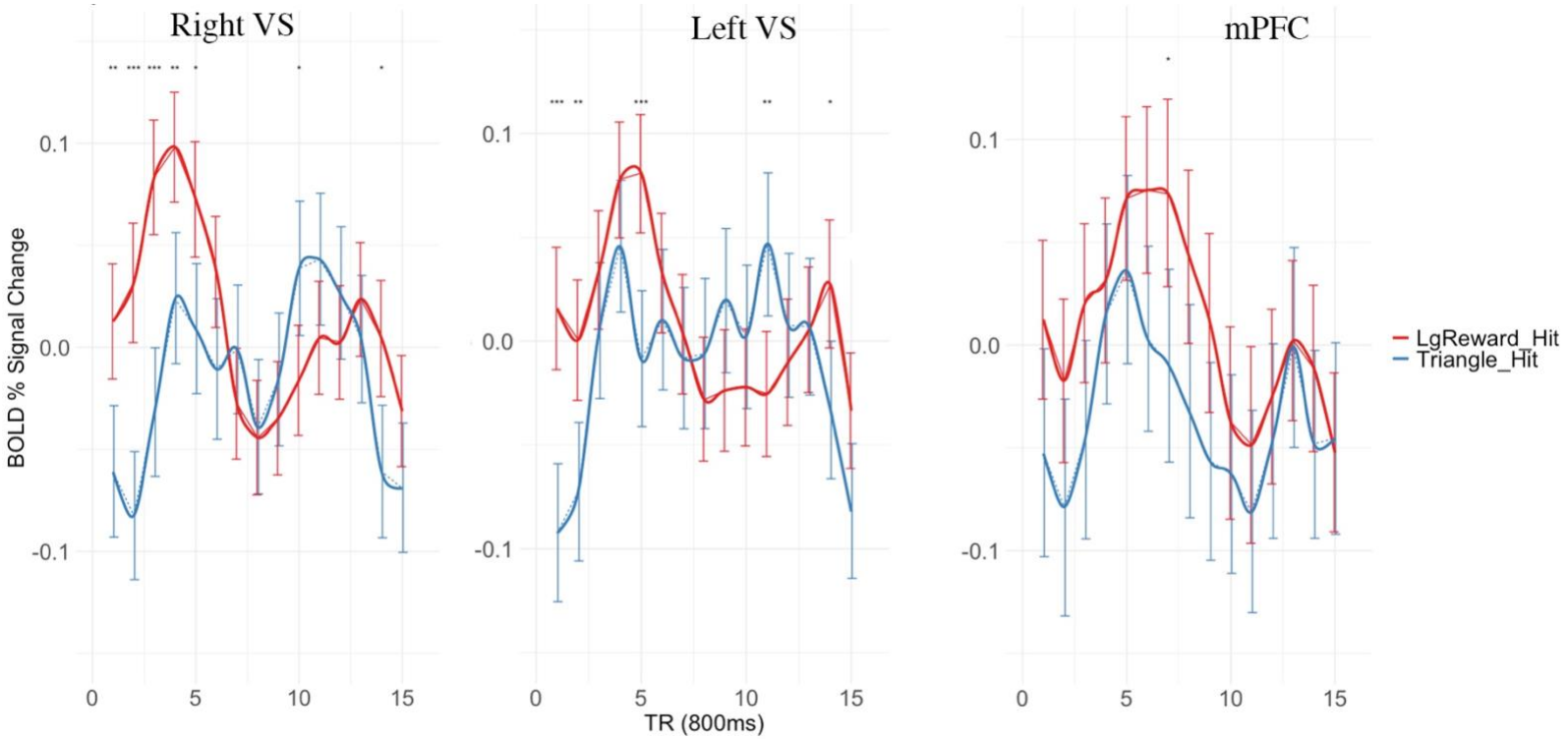


*Figure C.6* BOLD Signal Locked to Feedback onset and subsequent 15 TRs, Gain Hit versus Neutral Hit
LgReward Hit [Red] = Big Win Hit; Triangle_Hit [Blue] = Neutral Hit. VS = Ventral Striatum; mPFC = medial prefrontal cortex. Error bars represent 90% Confidence Interval; p < .05 * ; p < .01**, p < .001***

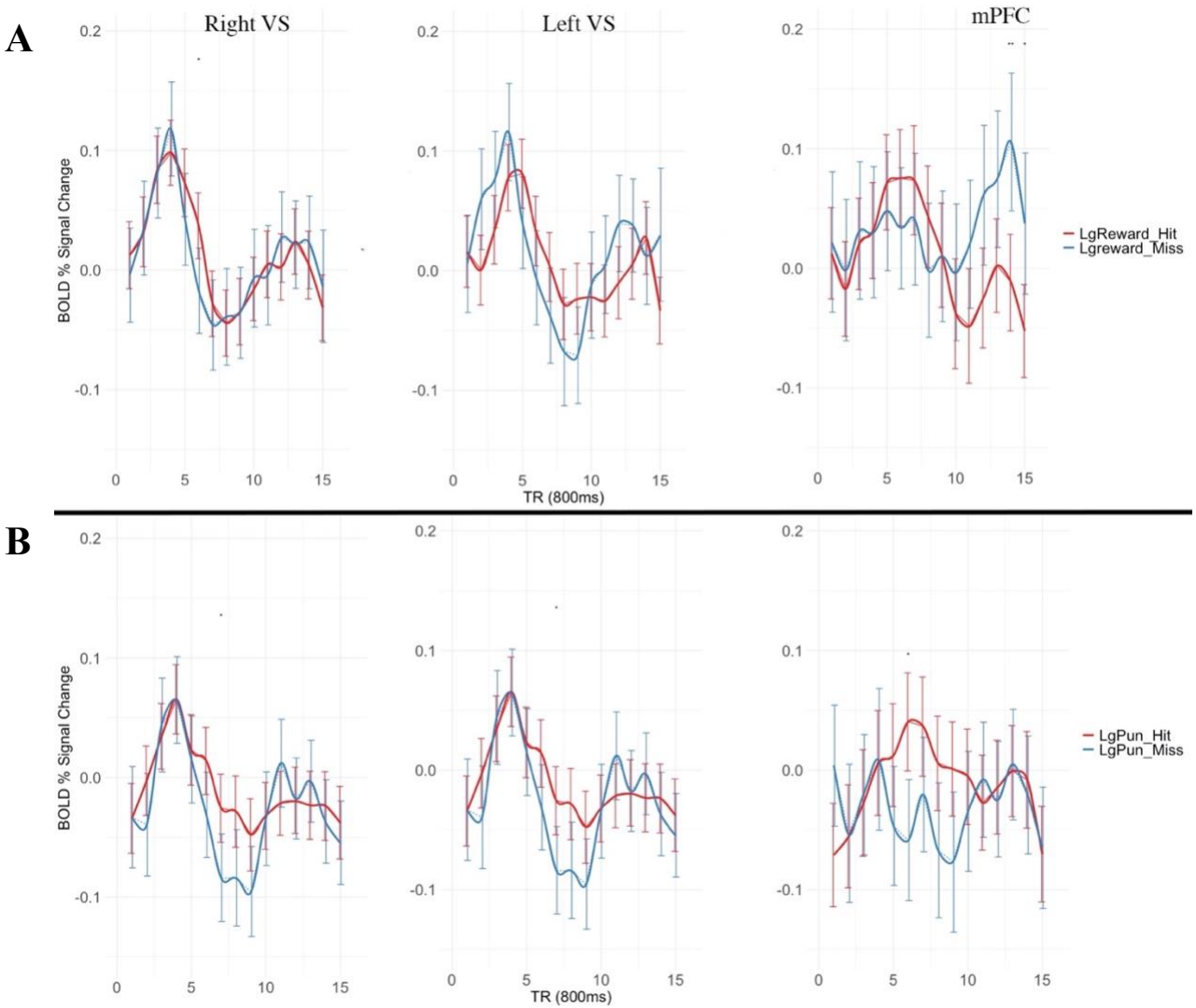


*Figure C.7* BOLD Signal Locked to Feedback onset and subsequent 15 TRs, Hit versus Miss
A: LgReward Hit [Red] = Big Win Hit; Lgreward_Miss [Blue] = Big Win Miss. B: LgPun Hit [Red] = Big Loss Hit; LgPun_Miss [Blue] = Big Loss Miss. VS = Ventral Striatum; mPFC = medial prefrontal cortex.
Error bars represent 90% Confidence Interval; $p < .05$ * ; $p < .01$**, $p < .001$***

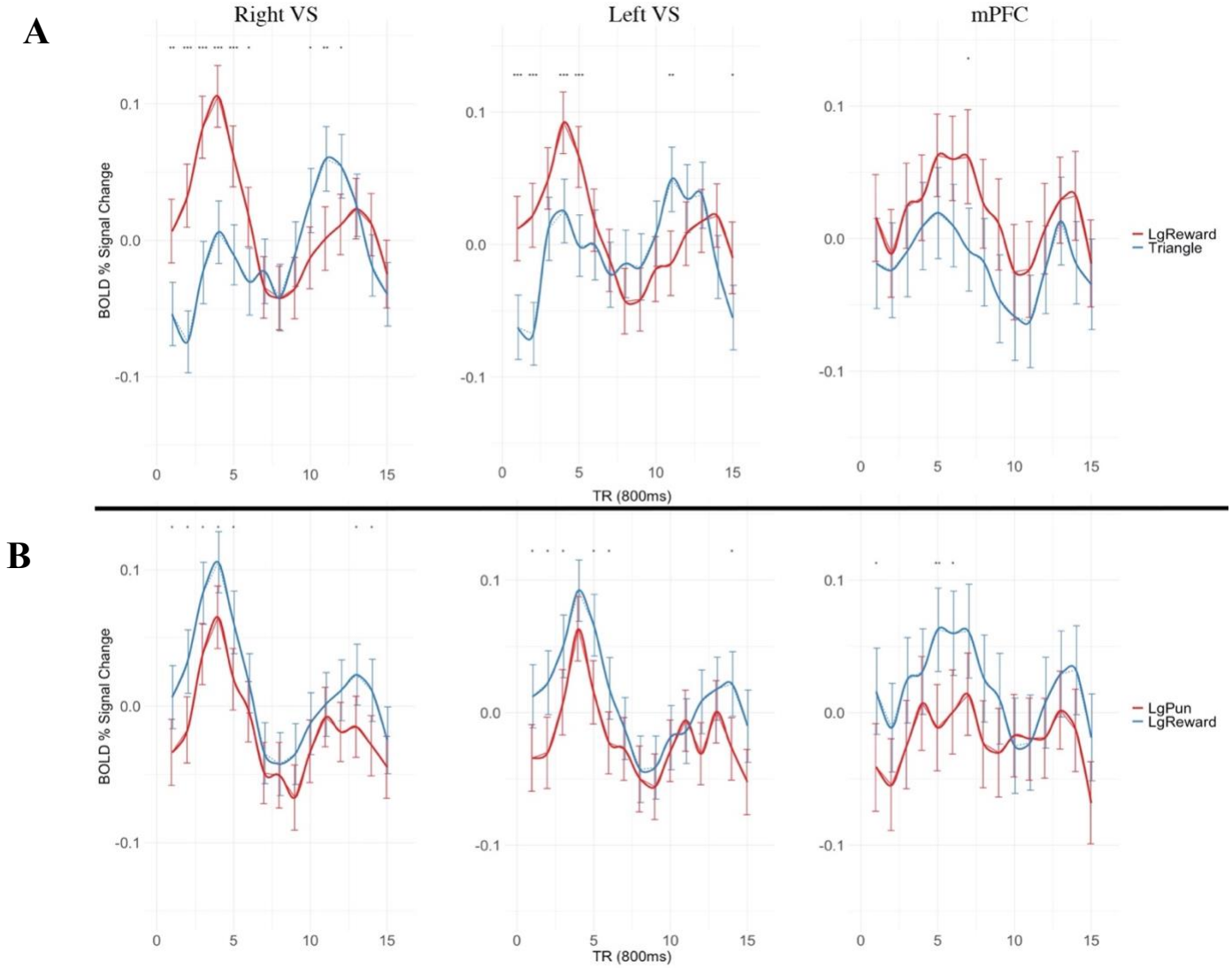


*Figure C.8* BOLD Signal Locked to Feedback onset and subsequent 15 TRs, by Anticipation Cue.
A: LgReward [Red] = Big Win ($5) Anticipation Cue Triangle [Blue] = Neutral Anticipation Cue. B: LgPun [Red] = Big Loss ($5) Anticipation Cue; LgReward [Blue] = Big Win ($5) Anticipation Cue. VS = Ventral Striatum; mPFC = medial prefrontal cortex. Error bars represent 90% Confidence Interval; $p < .05$ * ; $p < .01$**, $p < .001$***

## Appendix D : Supplemental Information for Study 3 (Chapter 5)

### Region of Interest Identification & Timeseries Extractions

ROIs were selected based on most common coordinates referenced in the literature (see supplemental table in Demidenko et al., 2020). in reviews (see Sherman et al 2018; Galvan, 2010) and overlapping referenced regions in imbalance models (Steinberg, 2008; Casey et al., 2008; Ernst, 2014). Each ROI uncovered in this review was entered into www.Neurosynth.org → Meta-analyses → Terms → <ROI>, then the ROI, such as ventral striatum, was selected and peak coordinate was defined.

*Table D.1* A priori MNI coordinates pulled from Neurosynth

| Region of Interest | Index | Index | MNI Coordinate (x, y, z) | | |
|---|---|---|---|---|---|
| Right Ventral Striatum | R_VS | Blue | 15 | 8 | -9 |
| Left Ventral Striatum | L_VS | | -12 | 8 | -8 |
| ventromedial Prefrontal Cortex | vmPFC | Green | 3 | 27 | -17 |
| Anterior Cingulate Cortex | ACC | Pink | 3 | 29 | 21 |
| Left Orbitofrontal Cortex | L_OFC | Yellow | -22 | 34 | -14 |
| Right Orbitofrontal Cortex | R_OFC | | 32 | 33 | -14 |
| Right Insula | R_Insula | Red | 38 | 13 | -4 |
| Left Insula | L_Insula | | -38 | 12 | -9 |
| Right Amygdala | R_Amyg | Cyan | 26 | -4 | -18 |
| Left Amygdala | L_Amyg | | -22 | -5 | -19 |
| Right Dorsolateral Prefrontal Cortex | R_DLPFC | Black | 43 | 37 | 29 |
| Left Dorsolateral Prefrontal Cortex | L_DLPFC | | -42 | 34 | 28 |

**Results**

Below are tables reporting information for demographics for the full sample overall and by run, and MID accuracy performance during the task. Then, by run, information regarding motion, GIMME fit statistics.

*Table D.2* Demographics Overall and By Run for Aim 1/Aim 2

| | *Overall* | *Run 01* | | *Run 02* | |
|---|---|---|---|---|---|
| | *n* = 104 | Subgrp01 *n* = 61 | Subgrp02 *n* = 43 | Subgrp01 *n* = 56 | Subgrp02 *n* = 48 |
| Age at Scan | 19.3 (1.3) | 19.2 (1.3) | 19.5 (1.3) | 19.4 (1.3) | 19.2 (1.4) |
| BSSS | 3.3 (0.4) | 3.2 (0.3) | 3.4 (0.4) | 3.3 (0.4) | 3.4 (0.5) |
| Sex, Female *n* (%) | 59 (56.7) | 36 (59.0) | 23 (53.4) | 36 (64.3) | 23 (47.9) |
| Race, *n* (%) | | | | | |
| White, non-Hispanic | 74 (71.2) | 47 (77.0) | 27 (62.8) | 41 (73.2) | 33 (68.8) |
| Black, non-Hispanic | 15 (14.4) | 8 (13.1) | 7 (16.3) | 8 (14.3) | 7 (14.6) |
| Hispanic/Latinx | 9 (8.7) | 2 (3.3) | 7 (16.3) | 5 (8.9) | 4 (8.3) |
| Other | 6 (5.8) | 4 (6.6) | 2 (4.7) | 2 (3.6) | 4 (8.3) |

BSSS = Brief Sensation Seeking

*Table D.3* MID Accuracy

| | *M (SD)* |
|---|---|
| Overall Acc. % | 56.9 (3.2) |
| Win Big | 62.7 (9.2) |
| Win Small | 57.8 (9.6) |
| Neutral | 47.7 (14.5) |
| Lose Small | 56.4 (8.8) |
| Lose Big | 59.9 (10.4) |

*Table D.4* Motion: Mean Framewise Displacement (FD) Pre/Post Preprocessing

| | *M (SD)* |
|---|---|
| Run 01 – Pre FD | .11 (.05) |
| Run 02 – Pre FD | .11 (.06) |
| Run 01 – Post FD | .02 (.01) |
| Run 02 – Post FD | .02 (.01) |

Person-specific Connectivity Differences Across Runs

Table D5 reports GIMME fit statistics Table S6 reports the crosstabulation of subgroups (2) across the runs (2). Table D7 reports differences in demographic characteristics for each group, summarized for Run 1 and Run 2.

*Table D.5* Four fit statistics from GIMME model

| | *M (SD)* | | | |
|---|---|---|---|---|
| | RMSEA | SRMR | NNFI | CFI |
| Run 01 | .05 (.01) | .05 (.01) | .93 (.01) | .96 (.01) |
| Run 02 | .05 (.01) | .05 (.00) | .93 (.01) | .96 (.01) |

*Table D.6* Crosstabs of subgrouping across runs (N = 104)

| | Subgroup 01 (Run 02) | Subgroup 02 (Run 02) | **Total** Run 01 |
|---|---|---|---|
| Subgroup 01 (Run 01) | 44 | 17 | 61 |
| Subgroup 02 (Run 01) | 12 | 31 | 43 |
| **Total** Run 02 | 56 | 48 | *104* |

$\chi$ (1) = 18.1, p < .001, $\Phi$ = .41

*Table D.7* Demographics Characteristics of participant's subgroup labels that are stable or changed across Run 01 and Run 02

| | **Stable** (N=75) | **Changed** (N=29) |
|---|---|---|
| | *M* (SD) | |
| **Age (Years)** | 19.4 (1.34) | 19.0 (1.17) |
| **Sensation Seeking** | 3.30 (0.41) | 3.33 (0.43) |
| | *N* (%) | |
| **Sex** | | |
| Female | 39 (52.0%) | 20 (69.0%) |
| Male | 36 (48.0%) | 9 (31.0%) |
| **Race/Ethnicity** | | |
| White, Non-Hispanic | 54 (72.0%) | 20 (69.0%) |
| Black, Non-Hispanic | 11 (14.7%) | 4 (13.8%) |
| Hispanic/Latinx | 6 (8.0%) | 3 (10.3%) |
| Other | 4 (5.3%) | 2 (6.9%) |

Below we present the connectivity paths that were fit at the group-level (for N subjects) and the subgroup level (for N subjects). We present thing information for both subgroups across each run. Beige colored rows represent connectivity paths that were not fit for both runs. Paths consistent across runs are represented by the binary column (1/0), and calculate the total overall between group and subgroup level paths

.

*Table D.8* Overlap in paths opened for Group, Subgroup02 and Subgroug02 across runs

| **Run 01 Group level connections** | | | N | **Run 02 Group level connections** | | | N | | Exist in both Runs? |
|---|---|---|---|---|---|---|---|---|---|
| **R_dlPFC** | ← | ACC | 104 | | | | | | 0 |
| **R_VS** | ← | ACC | 104 | **R_VS** | ← | ACC | 104 | | 1 |
| **R_Amygdala** | ← | L_Amygdala | 104 | | | | | | 0 |
| **L_Insula** | ← | L_dlPFC | 104 | **L_Insula** | ← | L_dlPFC | 104 | | 1 |
| **R_Insula** | ← | L_Insula | 104 | **R_Insula** | ← | L_Insula | 104 | | 1 |
| **L_dlPFC** | ← | R_dlPFC | 104 | **L_dlPFC** | ← | R_dlPFC | 104 | | 1 |
| **ACC** | ← | R_Insula | 104 | **ACC** | ← | R_Insula | 104 | | 1 |
| **L_OFC** | ← | R_OFC | 104 | | | | | | 0 |
| **L_VS** | ← | R_VS | 104 | **L_VS** | ← | R_VS | 104 | | 1 |
| | | | | **L_Amygdala** | ← | R_Amygdala | 104 | | 0 |
| | | | | **R_Amygdala** | ← | R_dlPFC | 104 | | 0 |
| | | | | | | | | **Overlap** | **55%** |
| **Run 01 Subgroup1 level connections** | | | | **Run 02 Subgroup1 level connections** | | | | | Exist in both? |
| **L_Amygdala** | ← | L_dlPFC | 61 | | | | | | 0 |
| **vmPFC** | ← | R_OFC | 61 | **vmPFC** | ← | R_OFC | 56 | | 1 |
| **ACC** | ← | vmPFC | 61 | **ACC** | ← | vmPFC | 56 | | 1 |
| | | | | **R_dlPFC** | ← | ACC | 56 | | 0 |
| | | | | | | | | **Overlap** | **50%** |
| **Run 01 Subgroup2 level connections** | | | | **Run 02 Subgroup2 level connections** | | | | | Exist in both? |
| **vmPFC** | ← | ACC | 43 | **vmPFC** | ← | ACC | 48 | | 1 |
| **ACC** | ← | L_Insula | 43 | **ACC** | ← | L_Insula | 48 | | 1 |
| **L_Amygdala** | ← | L_Insula | 43 | | | | | | 0 |
| **L_OFC** | ← | L_VS | 43 | **L_OFC** | ← | L_VS | 48 | | 1 |
| **L_Amygdala** | ← | R_dlPFC | 43 | | | | | | 0 |
| **R_dlPFC** | ← | R_Insula | 43 | **R_dlPFC** | ← | R_Insula | 48 | | 1 |
| **R_OFC** | ← | R_Insula | 43 | **R_OFC** | ← | R_Insula | 48 | | 1 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **R_VS** | ← | R_OFC | 43 | | | | | 0 |
| **R_OFC** | ← | vmPFC | 43 | **R_OFC** | ← | vmPFC | 48 | 1 |
| | | | | **L_OFC** | ← | R_OFC | 48 | 0 |
| | | | | **L_Amygdala** | ← | L_dlPFC | 48 | 0 |
| | | | | | | | **Overlap** | **55%** |

* Bold, Predicted by

Subgroup and connection strength associations with sensation seeking across runs

*Table D.9* Logistic Regression: Sensation seeking associated with GIMME-derived subgroup from MID task data, by run, without PostFD (N = 104)

| | *Run 01* | | | *Run 02* | | |
|---|---|---|---|---|---|---|
| | *b* | SE | *p* | *b* | SE | *P* |
| Age | - .18 | .16 | .25 | - .11 | .16 | .49 |
| Sex | .15 | .41 | .72 | .66 | .41 | .11 |
| BSSS | 1.1 | .53 | .03 | .55 | .50 | .29 |

*Table D.10* Logistic Regression: Moderating Effect of Motion on association between BSSS

| | Run 01 | | | Run 02 | | |
|---|---|---|---|---|---|---|
| | *b* | SE | *p* | *b* | SE | *p* |
| PostFD | -82.5 | 170.4 | 0.63 | 122.8 | 156.5 | 0.43 |
| BSSS | 1.1 | 0.54 | 0.04 | 0.59 | 0.5 | 0.24 |
| BSSS*PostFD | 39.3 | 51.2 | 0.44 | 0.58 | 46.7 | 0.54 |

PostFD: Post mean Framewise Displacement; BSSS: Brief Sensation Seeking Scale

*Table D.11* Multiple Regression: Individual traits of sensation seeking associated with GIMME FC Path strength in Subgroup 2 during MID task, by run

| **vmPFC → R OFC** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *Run 01* | | | | *Run 02* | | | |
| | *b* | β | *SE* | *p* | *b* | β | *SE* | *p* |
| Age | -.02 | -.12 | .02 | .40 | .02 | .11 | *.03* | .48 |
| Sex | -.04 | -.10 | .06 | .49 | -.02 | -.04 | *.07* | .81 |
| Post FD | -4.5 | -.29 | 2.2 | .05 | -.17 | .23 | *2.4* | .94 |
| BSSS | .21 | .36 | .08 | .02 | .02 | .02 | *.08* | .86 |
| **R OFC → R VS** | | | | | | | | |
| | *Run 01* | | | | *Run 02* | | | |
| | *B* | β | *SE* | *p* | *b* | β | *SE* | *p* |
| Age | -.00 | -.02 | .03 | .87 | | | | |
| Sex | .07 | .13 | .07 | .38 | *Algorithm did not open path for all subjects. See Table S8* | | | |
| Post FD | -.85 | -.05 | 2.69 | .75 | | | | |
| BSSS | -.27 | .40 | .10 | .01 | | | | |
| **L dlPFC → L Amyg** | | | | | | | | |
| | *Run 01* | | | | *Run 02* | | | |
| | *b* | β | *Se* | *p* | *b* | β | *SE* | |
| Age | | | | | -.05 | -.30 | *.02* | .01 |
| Sex | *Algorithm did not open path for all subjects. See Table S8* | | | | .01 | .02 | *.05* | .85 |
| Post FD | | | | | -6.4 | -.51 | *1.5* | .0001 |
| BSSS | | | | | .15 | .32 | *.05* | .009 |

Sex: 1 = Male, 0 = Female. BSSS = Brief Sensation Seeking; Post FD = mean Framewise displacement post-preprocessing

Beta weights from connectivity estimates from Run 01 and Run 2, and subgroup 2 associations with self-reported sensation seeking. For Run 02, Subgroup02, only the L dlPFC → L Amyg path was meaningfully associated with sensation seeking, b = .15, p = .009. R OFC → R VS path in Subgroup 2 Run 02 was not meaningful for everyone in the subgroup, therefore most subjects did not have this path estimated. Likewise, L DLPFC → L Amyg was not meaningful for Run 01, therefore most subjects did not have this path estimated (see Figure D3

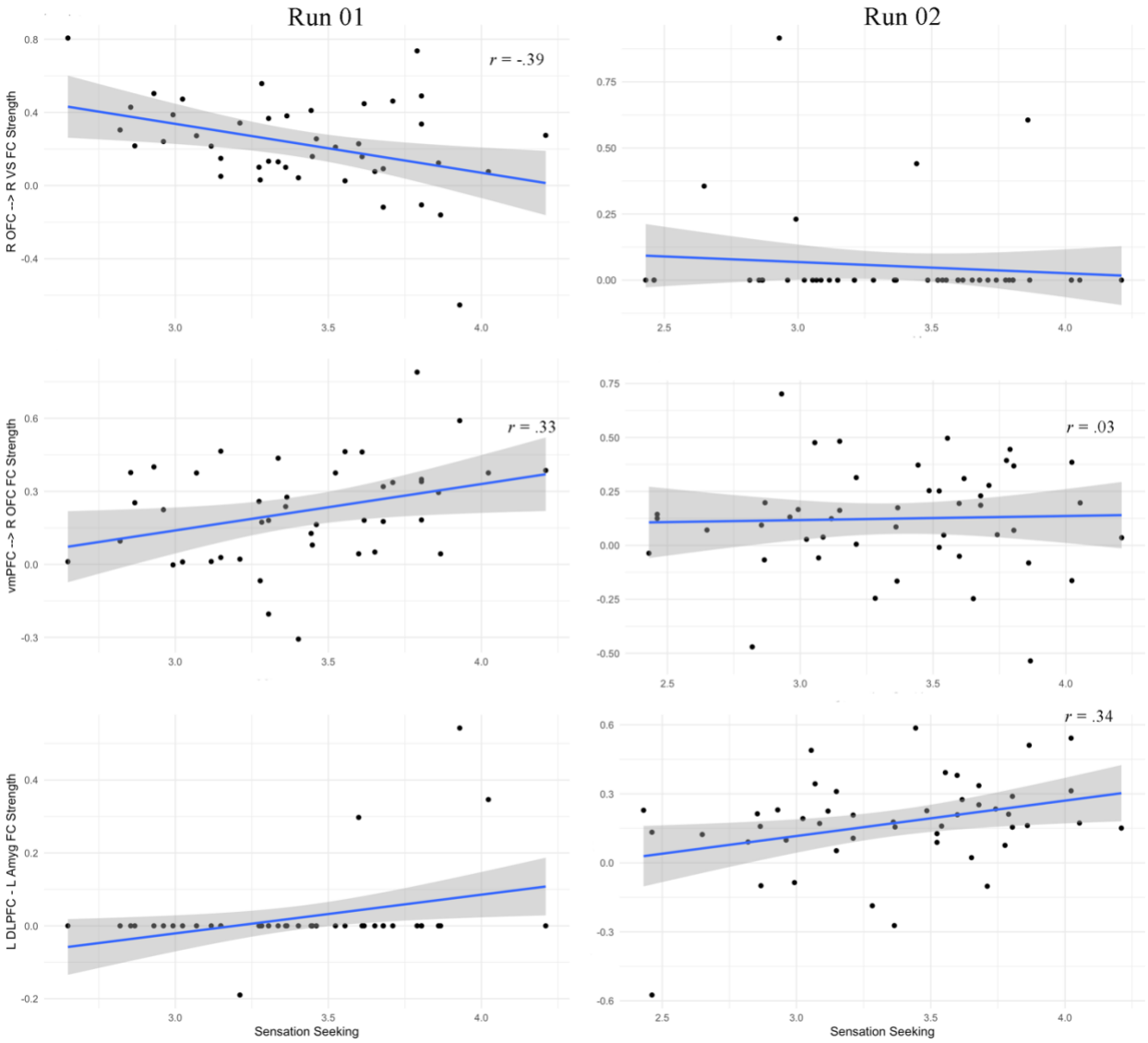


*Figure D.1* Connectivity Strength and Sensation Seeking raw plots for participants in Subgroup 2, by Run 01 (N = 43) and Run 02 (N = 48)

## Group-level Map for Combined Run Model

*Table D.12* Four fit statistics from GIMME model, Combined Runs

| | *M (SD)* | | | |
|---|---|---|---|---|
| | RMSEA | SRMR | NNFI | CFI |
| Combined | .09 (.01) | .04 (.01) | .93 (.01) | .96 (.01) |

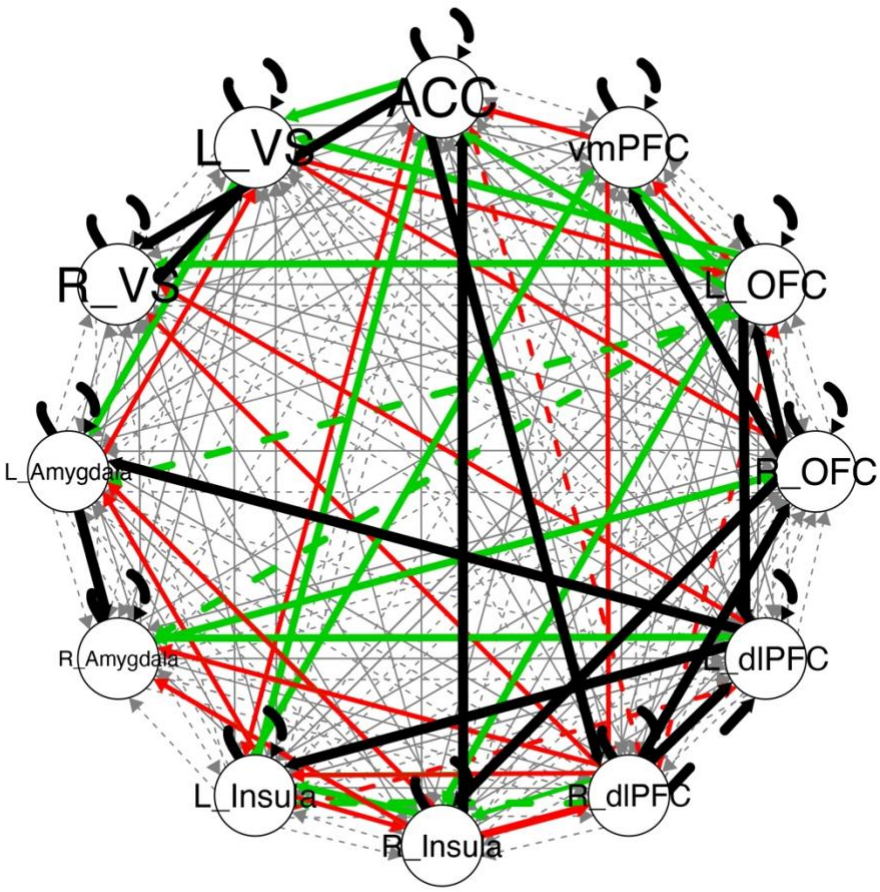


*Figure D.2* GIMME Full Model Connectivity Network, Combined MID Runs
Black = Group Paths; Red = Subgroup01 connections; Green = Subgroup02 connections; Grey = Individual Paths. Solid = Contemporaneous; Dashed = Lagged ($t - 1$). Weight is the proportion of subjects with the connection.

*Table D13* –

*Table D.13* Logistic Regression Model Predicting Subgroup Labels: Combined MID Runs and BSSS (N = 103)

| | *Combined* | |
|---|---|---|
| | *b* | *p* |
| Age | - .04 | .80 |
| Sex | .12 | .77 |
| Post FD | 1.02 | .95 |
| BSSS | -.51 | .34 |

## REFERENCES


Abler, B., Walter, H., Erk, S., Kammerer, H., & Spitzer, M. (2006). Prediction error as a linear function of reward probability is coded in human nucleus accumbens. *NeuroImage*, *31*(2), 790–795. https://doi.org/10.1016/j.neuroimage.2006.01.001

Achenbach, T. M., & Rescorla, L. (2001). *Manual for the ASEBA school-age forms & profiles: An integrated system of multi-informant assessment*. Burlington, VT : ASEBA. https://trove.nla.gov.au/version/11167240

Achenbach, T. M., & Rscorla, L. A. (2003). *Manual for the ASEBA Adult Forms & Profiles.* Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families.

Alfaro-Almagro, F., Jenkinson, M., Bangerter, N. K., Andersson, J. L. R., Griffanti, L., Douaud, G., Sotiropoulos, S. N., Jbabdi, S., Hernandez-Fernandez, M., Vallee, E., Vidaurre, D., Webster, M., McCarthy, P., Rorden, C., Daducci, A., Alexander, D. C., Zhang, H., Dragonu, I., Matthews, P. M., … Smith, S. M. (2018). Image processing and Quality Control for the first 10,000 brain imaging datasets from UK Biobank. *NeuroImage*, *166*, 400–424. https://doi.org/10.1016/j.neuroimage.2017.10.034

Aloi, J., Meffert, H., White, S. F., Blair, K. S., Hwang, S., Tyler, P. M., Thornton, L. C., Crum, K. I., Adams, K. O., Killanin, A. D., Filbey, F., Pope, K., & Blair, R. J. R. (2019). Differential dysfunctions related to alcohol and cannabis use disorder symptoms in reward and error-processing neuro-circuitries in adolescents. *Developmental Cognitive Neuroscience*, *36*, 100618. https://doi.org/10.1016/j.dcn.2019.100618

Apps, M. A. J., Rushworth, M. F. S., & Chang, S. W. C. (2016). The Anterior Cingulate Gyrus and Social Cognition: Tracking the Motivation of Others. *Neuron*, *90*(4), 692–707. https://doi.org/10.1016/j.neuron.2016.04.018

Arnett, J. J. (1994). Sensation seeking: A new conceptualization and a new scale. *Personality and Individual Differences*, *16*(2), 289–296. https://doi.org/10.1016/0191-8869(94)90165-1

Arnett, J. J. (2000). Emerging adulthood. A theory of development from the late teens through the twenties. *The American Psychologist*, *55*(5), 469–480.

Arnett, J. J. (2006). G. Stanley Hall's Adolescence: Brilliance and nonsense. *History of Psychology*, *9*(3), 186–197. https://doi.org/10.1037/1093-4510.9.3.186

Baker, A. E., Tashjian, S. M., Goldenberg, D., & Galván, A. (2020). Neural activity moderates the association between sleep and risky driving behaviors in adolescence. *Developmental Cognitive Neuroscience*, 100790. https://doi.org/10.1016/j.dcn.2020.100790

Baker, B., Lansdell, B., & Kording, K. (2021). A Philosophical Understanding of Representation for Neuroscience. *ArXiv:2102.06592 [q-Bio]*. http://arxiv.org/abs/2102.06592

Balleine, B. W., & O'Doherty, J. P. (2010). Human and Rodent Homologies in Action Control: Corticostriatal Determinants of Goal-Directed and Habitual Action. *Neuropsychopharmacology*, *35*(1), 48–69. https://doi.org/10.1038/npp.2009.131

Balodis, I. M., & Potenza, M. N. (2015). Anticipatory Reward Processing in Addicted Populations: A Focus on the Monetary Incentive Delay Task. *Biological Psychiatry*, *77*(5), 434–444. https://doi.org/10.1016/j.biopsych.2014.08.020

Baltes, P. B. (1987). Theoretical propositions of life-span developmental psychology: On the dynamics between growth and decline. *Developmental Psychology*, *23*(5), 611–626. https://doi.org/10.1037/0012-1649.23.5.611

Bandura, A. (1964). The stormy decade: Fact or fiction? *Psychology in the Schools*, *1*(3), 224–231.

Bartra, O., McGuire, J. T., & Kable, J. W. (2013). The valuation system: A coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. *NeuroImage*, *76*, 412–427. https://doi.org/10.1016/j.neuroimage.2013.02.063

Baumeister, R. F., Vohs, K. D., & Funder, D. C. (2007). Psychology as the Science of Self-Reports and Finger Movements: Whatever Happened to Actual Behavior? *Perspectives on Psychological Science*, *2*(4), 396–403. https://doi.org/10.1111/j.1745-6916.2007.00051.x

Becht, A. I., & Mills, K. L. (2020). Modeling Individual Differences in Brain Development. *Biological Psychiatry*. https://doi.org/10.1016/j.biopsych.2020.01.027

Beck, E. D., & Jackson, J. J. (2020). Consistency and change in idiographic personality: A longitudinal ESM network study. *Journal of Personality and Social Psychology*, *118*(5), 1080–1100. https://doi.org/10.1037/pspp0000249

Bell, C. C., & McBride, D. F. (2010). Affect regulation and prevention of risky behaviors. *JAMA*, *304*(5), 565–566. https://doi.org/10.1001/jama.2010.1058

Belsky, J. (2016). The Differential Susceptibility Hypothesis: Sensitivity to the Environment for Better and for Worse. *JAMA Pediatrics*, *170*(4), 321–322. https://doi.org/10.1001/jamapediatrics.2015.4263

Beltz, A. M. (2018). Connecting Theory and Methods in Adolescent Brain Research. *Journal of Research on Adolescence*, *28*(1), 10–25. https://doi.org/10.1111/jora.12366

Beltz, A. M., & Gates, K. M. (2017). Network Mapping with GIMME. *Multivariate Behavioral Research*, *52*(6), 789–804. https://doi.org/10.1080/00273171.2017.1373014

Beltz, A. M., Gates, K. M., Engels, A. S., Molenaar, P. C. M., Pulido, C., Turrisi, R., Berenbaum, S. A., Gilmore, R. O., & Wilson, S. J. (2013). Changes in Alcohol-Related Brain Networks Across the First Year of College: A Prospective Pilot Study Using fMRI Effective Connectivity Mapping. *Addictive Behaviors*, *38*(4), 2052–2059. https://doi.org/10.1016/j.addbeh.2012.12.023

Beltz, A. M., & Weigard, A. (2019). Methodological Advances in Leveraging Neuroimaging Datasets in Adolescent Substance Use Research. *Current Addiction Reports*, *6*(4), 495–503. https://doi.org/10.1007/s40429-019-00275-x

Beltz, A. M., Wright, A. G. C., Sprague, B. N., & Molenaar, P. C. M. (2016). Bridging the Nomothetic and Idiographic Approaches to the Analysis of Clinical Data. *Assessment*, *23*(4), 447–458. https://doi.org/10.1177/1073191116648209

Benjamini, Y., & Yekutieli, D. (2001). The control of the false discovery rate in multiple testing under dependency. *The Annals of Statistics*, *29*(4), 1165–1188. https://doi.org/10.1214/aos/1013699998

Benningfield, M. M., Blackford, J. U., Ellsworth, M. E., Samanez-Larkin, G. R., Martin, P. R., Cowan, R. L., & Zald, D. H. (2014). Caudate responses to reward anticipation associated with delay discounting behavior in healthy youth. *Developmental Cognitive Neuroscience*, *7*, 43–52. https://doi.org/10.1016/j.dcn.2013.10.009

Berridge, K. C. (2007). The debate over dopamine's role in reward: The case for incentive salience. *Psychopharmacology*, *191*(3), 391–431. https://doi.org/10.1007/s00213-006-0578-x

Berridge, K. C. (2019). Affective valence in the brain: Modules or modes? *Nature Reviews Neuroscience*, *20*(4), 225–234. https://doi.org/10.1038/s41583-019-0122-8

Berridge, K. C., Ho, C.-Y., Richard, J. M., & DiFeliceantonio, A. G. (2010). The tempted brain eats: Pleasure and desire circuits in obesity and eating disorders. *Brain Research*, *1350*, 43–64. https://doi.org/10.1016/j.brainres.2010.04.003

Berridge, K. C., & Kringelbach, M. L. (2015). Pleasure Systems in the Brain. *Neuron*, *86*(3), 646–664. https://doi.org/10.1016/j.neuron.2015.02.018

Berridge, K. C., & O'Doherty, J. P. (2014). Chapter 18—From Experienced Utility to Decision Utility. In P. W. Glimcher & E. Fehr (Eds.), *Neuroeconomics (Second Edition)* (pp. 335–351). Academic Press. https://doi.org/10.1016/B978-0-12-416008-8.00018-8

Berridge, K. C., & Robinson, T. E. (2003). Parsing reward. *Trends in Neurosciences*, *26*(9), 507–513. https://doi.org/10.1016/S0166-2236(03)00233-9

Bethlehem, R. a. I., Seidlitz, J., White, S. R., Vogel, J. W., Anderson, K. M., Adamson, C., Adler, S., Alexopoulos, G. S., Anagnostou, E., Areces-Gonzalez, A., Astle, D. E., Auyeung, B., Ayub, M., Ball, G., Baron-Cohen, S., Beare, R., Bedford, S. A., Benegal, V., Beyer, F., … Alexander-Bloch, A. F. (2021). *Brain charts for the human lifespan* (p. 2021.06.08.447489). https://doi.org/10.1101/2021.06.08.447489

Bjork, J. M. (2020). The Ups and Downs of Relating Nondrug Reward Activation to Substance Use Risk in Adolescents. *Current Addiction Reports*. https://doi.org/10.1007/s40429-020-00327-7

Bjork, J. M., Knutson, B., Fong, G. W., Caggiano, D. M., Bennett, S. M., & Hommer, D. W. (2004). Incentive-elicited brain activation in adolescents: Similarities and differences from young adults. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *24*(8), 1793–1802. https://doi.org/10.1523/JNEUROSCI.4862-03.2004

Bjork, J. M., Knutson, B., & Hommer, D. W. (2008a). Incentive-elicited striatal activation in adolescent children of alcoholics. *Addiction*, *103*(8), 1308–1319. https://doi.org/10.1111/j.1360-0443.2008.02250.x

Bjork, J. M., Knutson, B., & Hommer, D. W. (2008b). Incentive-elicited striatal activation in adolescent children of alcoholics. *Addiction (Abingdon, England)*, *103*(8), 1308–1319. https://doi.org/10.1111/j.1360-0443.2008.02250.x

Bjork, J. M., & Pardini, D. A. (2015). Who are those "risk-taking adolescents"? Individual differences in developmental neuroimaging research. *Developmental Cognitive Neuroscience*, *11*, 56–64. https://doi.org/10.1016/j.dcn.2014.07.008

Bjork, J. M., Smith, A. R., Chen, G., & Hommer, D. W. (2010). Adolescents, Adults and Rewards: Comparing Motivational Neurocircuitry Recruitment Using fMRI. *PLOS ONE*, *5*(7), e11440. https://doi.org/10.1371/journal.pone.0011440

Bjork, J. M., Smith, A. R., Chen, G., & Hommer, D. W. (2011a). Psychosocial problems and recruitment of incentive neurocircuitry: Exploring individual differences in healthy adolescents. *Developmental Cognitive Neuroscience*, *1*(4), 570–577. https://doi.org/10.1016/j.dcn.2011.07.005

Bjork, J. M., Smith, A. R., Chen, G., & Hommer, D. W. (2011b). Psychosocial problems and recruitment of incentive neurocircuitry: Exploring individual differences in healthy adolescents. *Developmental Cognitive Neuroscience*, *1*(4), 570–577. https://doi.org/10.1016/j.dcn.2011.07.005

Bloom, P. A., VanTieghem, M., Gabard-Durnam, L., Gee, D. G., Flannery, J., Caldera, C., Goff, B., Telzer, E. H., Humphreys, K. L., Fareri, D. S., Shapiro, M., Algharazi, S., Bolger, N., Aly, M., & Tottenham, N. (2021). *Age-related change in task-evoked amygdala-prefrontal circuitry: A multiverse approach with an accelerated longitudinal cohort aged 4-22 years* (p. 2021.10.08.463601). https://doi.org/10.1101/2021.10.08.463601

Blumstein, A. (2002). Youth, Guns, and Violent Crime. *The Future of Children*, *12*(2), 39–53. https://doi.org/10.2307/1602737

Boecker, R., Holz, N. E., Buchmann, A. F., Blomeyer, D., Plichta, M. M., Wolf, I., Baumeister, S., Meyer-Lindenberg, A., Banaschewski, T., Brandeis, D., & Laucht, M. (2014). Impact of early life adversity on reward processing in young adults: EEG-fMRI results from a prospective study over 25 years. *PloS One*, *9*(8), e104185. https://doi.org/10.1371/journal.pone.0104185

Botvinik-Nezer, R., Holzmeister, F., Camerer, C. F., Dreber, A., Huber, J., Johannesson, M., Kirchler, M., Iwanir, R., Mumford, J. A., Adcock, A., Avesani, P., Baczkowski, B., Bajracharya, A., Bakst, L., Ball, S., Barilari, M., Bault, N., Beaton, D., Beitner, J., … Schonberg, T. (2019). Variability in the analysis of a single neuroimaging dataset by many teams. *BioRxiv*, 843193. https://doi.org/10.1101/843193

Botvinik-Nezer, R., Holzmeister, F., Camerer, C. F., Dreber, A., Huber, J., Johannesson, M., Kirchler, M., Iwanir, R., Mumford, J. A., Adcock, R. A., Avesani, P., Baczkowski, B. M., Bajracharya, A., Bakst, L., Ball, S., Barilari, M., Bault, N., Beaton, D., Beitner, J., … Schonberg, T. (2020a). Variability in the analysis of a single neuroimaging dataset by many teams. *Nature*, 1–7. https://doi.org/10.1038/s41586-020-2314-9

Botvinik-Nezer, R., Holzmeister, F., Camerer, C. F., Dreber, A., Huber, J., Johannesson, M., Kirchler, M., Iwanir, R., Mumford, J. A., Adcock, R. A., Avesani, P., Baczkowski, B. M., Bajracharya, A., Bakst, L., Ball, S., Barilari, M., Bault, N., Beaton, D., Beitner, J., … Schonberg, T. (2020b). Variability in the analysis of a single neuroimaging dataset by many teams. *Nature*, *582*(7810), 84–88. https://doi.org/10.1038/s41586-020-2314-9

Bourque, J., Spechler, P. A., Potvin, S., Whelan, R., Banaschewski, T., Bokde, A. L. W., Bromberg, U., Büchel, C., Quinlan, E. B., Desrivières, S., Flor, H., Frouin, V., Gowland, P., Heinz, A., Ittermann, B., Martinot, J.-L., Paillère-Martinot, M.-L., McEwen, S. C., Nees, F., … IMAGEN Consortium. (2017). Functional Neuroimaging Predictors of Self-Reported Psychotic Symptoms in Adolescents. *The American Journal of Psychiatry*, *174*(6), 566–575. https://doi.org/10.1176/appi.ajp.2017.16080897

Braams, B. R., Peper, J. S., van der Heide, D., Peters, S., & Crone, E. A. (2016). Nucleus accumbens response to rewards and testosterone levels are related to alcohol use in adolescents and young adults. *Developmental Cognitive Neuroscience*, *17*, 83–93. https://doi.org/10.1016/j.dcn.2015.12.014

Braams, B. R., van Duijvenvoorde, A. C. K., Peper, J. S., & Crone, E. A. (2015). Longitudinal changes in adolescent risk-taking: A comprehensive study of neural responses to rewards, pubertal development, and risk-taking behavior. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *35*(18), 7226–7238. https://doi.org/10.1523/JNEUROSCI.4764-14.2015

Breckel, T. P. K., Giessing, C., & Thiel, C. M. (2011). Impact of brain networks involved in vigilance on processing irrelevant visual motion. *NeuroImage*, *55*(4), 1754–1762. https://doi.org/10.1016/j.neuroimage.2011.01.025

Breiter, H. C., Berke, J. D., Kennedy, W. A., Rosen, B. R., & Hyman, S. E. (1996). Activation of striatum and amygdala during reward conditioning: An FMRI study. *NeuroImage*, *3 Supplement*(3), S220. https://doi.org/10.1016/S1053-8119(96)80222-9

Briggs, D. (2021). *Historical and Conceptual Foundations of Measurement in the Human Sciences: Credos and Controversies*. https://doi.org/10.1201/9780429275326

Bringmann, W. G., Bringmann, M. W., & Early, C. E. (1992). G. Stanley Hall and the history of psychology. *American Psychologist*, *47*(2), 281–289. https://doi.org/10.1037/0003-066X.47.2.281

Bronfenbrenner, U., & Morris, P. A. (2007). The Bioecological Model of Human Development. In *Handbook of Child Psychology*. American Cancer Society. https://doi.org/10.1002/9780470147658.chpsy0114

Bryce, N. V., Flournoy, J. C., Guassi Moreira, J. F., Rosen, M. L., Sambook, K. A., Mair, P., & McLaughlin, K. A. (2021). Brain parcellation selection: An overlooked decision point with meaningful effects on individual differences in resting-state functional connectivity. *NeuroImage*, *243*, 118487. https://doi.org/10.1016/j.neuroimage.2021.118487

Buchel, C., Miedl, S., & Sprenger, C. (2018). Hedonic processing in humans is mediated by an opioidergic mechanism in a mesocorticolimbic system. *ELife*, *7*, e39648. https://doi.org/10.7554/eLife.39648

Büchel, C., Peters, J., Banaschewski, T., Bokde, A. L. W., Bromberg, U., Conrod, P. J., Flor, H., Papadopoulos, D., Garavan, H., Gowland, P., Heinz, A., Walter, H., Ittermann, B., Mann, K., Martinot, J.-L., Paillère-Martinot, M.-L., Nees, F., Paus, T., Pausova, Z., … Knutson, B. (2017). Blunted ventral striatal responses to anticipated rewards foreshadow problematic drug use in novelty-seeking adolescents. *Nature Communications*, *8*(1), 1–11. https://doi.org/10.1038/ncomms14140

Burt, M. R. (2002). Reasons to invest in adolescents. *Journal of Adolescent Health*, *31*(6, Supplement), 136–152. https://doi.org/10.1016/S1054-139X(02)00486-X

Button, K. S., Ioannidis, J. P. A., Mokrysz, C., Nosek, B. A., Flint, J., Robinson, E. S. J., & Munafò, M. R. (2013). Power failure: Why small sample size undermines the reliability of neuroscience. *Nature Reviews Neuroscience*, *14*(5), 365–376. https://doi.org/10.1038/nrn3475

Buxton, R. B. (2012). Dynamic Models of BOLD Contrast. *NeuroImage*, *62*(2), 953–961. https://doi.org/10.1016/j.neuroimage.2012.01.012

Cacioppo, J. T., Berntson, G. G., Lorig, T. S., Norris, C. J., Rickett, E., & Nusbaum, H. (2003). Just because you're imaging the brain doesn't mean you can stop using your head: A primer and set of first principles. *Journal of Personality and Social Psychology*, *85*(4), 650–661. https://doi.org/10.1037/0022-3514.85.4.650

Campbell, D. T., & Fiske, D. W. (1959). Convergent and discriminant validation by the multitrait-multimethod matrix. *Psychological Bulletin*, *56*(2), 81–105. https://doi.org/10.1037/h0046016

Cao, Z., Bennett, M., O'Halloran, L., Pragulbickaite, G., Flanagan, L., McHugh, L., & Whelan, R. (2020). Aberrant reward prediction errors in young adult at-risk alcohol users. *Addiction Biology*, *n/a*(n/a), e12873. https://doi.org/10.1111/adb.12873

Cao, Z., Bennett, M., Orr, C., Icke, I., Banaschewski, T., Barker, G. J., Bokde, A. L. W., Bromberg, U., Büchel, C., Quinlan, E. B., Desrivières, S., Flor, H., Frouin, V., Garavan, H., Gowland, P., Heinz, A., Ittermann, B., Martinot, J.-L., Nees, F., … Whelan, R. (2019). Mapping adolescent reward anticipation, receipt, and prediction error during the monetary incentive delay task. *Human Brain Mapping*, *40*(1), 262–283. https://doi.org/10.1002/hbm.24370

Caplan, D. (2007). Experimental design and interpretation of functional neuroimaging studies of cognitive processes. *Human Brain Mapping*, *30*(1), 59–77. https://doi.org/10.1002/hbm.20489

Carp, J. (2012). On the Plurality of (Methodological) Worlds: Estimating the Analytic Flexibility of fMRI Experiments. *Frontiers in Neuroscience*, *6*. https://doi.org/10.3389/fnins.2012.00149

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS Scales. *Journal of Personality and Social Psychology*, *67*(2), 319–333. https://doi.org/10.1037/0022-3514.67.2.319

Cascio, C. N., Carp, J., O'Donnell, M. B., Tinney, F. J., Bingham, C. R., Shope, J. T., Ouimet, M. C., Pradhan, A. K., Simons-Morton, B. G., & Falk, E. B. (2015). Buffering social influence: Neural correlates of response inhibition predict driving safety in the presence of a peer. *Journal of Cognitive Neuroscience*, *27*(1), 83–95. https://doi.org/10.1162/jocn_a_00693

Casey, B. J. (2015). Beyond simple models of self-control to circuit-based accounts of adolescent behavior. *Annual Review of Psychology*, *66*, 295–319. https://doi.org/10.1146/annurev-psych-010814-015156

Casey, B. J., Cannonier, T., Conley, M. I., Cohen, A. O., Barch, D. M., Heitzeg, M. M., Soules, M. E., Teslovich, T., Dellarco, D. V., Garavan, H., Orr, C. A., Wager, T. D., Banich, M. T., Speer, N. K., Sutherland, M. T., Riedel, M. C., Dick, A. S., Bjork, J. M., Thomas, K. M., … ABCD Imaging Acquisition Workgroup. (2018). The Adolescent Brain Cognitive Development (ABCD) study: Imaging acquisition across 21 sites. *Developmental Cognitive Neuroscience*, *32*, 43–54. https://doi.org/10.1016/j.dcn.2018.03.001

Casey, B. J., Getz, S., & Galvan, A. (2008). The adolescent brain. *Developmental Review : DR*, *28*(1), 62–77. https://doi.org/10.1016/j.dr.2007.08.003

Casey, B. J., Heller, A. S., Gee, D. G., & Cohen, A. O. (2019). Development of the emotional brain. *Neuroscience Letters*, *693*, 29–34. https://doi.org/10.1016/j.neulet.2017.11.055

Centers for Disease Control and Prevention. (2020, September 18). *Web-based Injury Statistics Query and Reporting System (WISQARS)*. https://www.cdc.gov/injury/wisqars/index.html

Chan, R. C. K., Li, Z., Li, K., Zeng, Y.-W., Xie, W.-Z., Yan, C., Cheung, E. F. C., & Jin, Z. (2016). Distinct processing of social and monetary rewards in late adolescents with trait anhedonia. *Neuropsychology*, *30*(3), 274–280. https://doi.org/10.1037/neu0000233

Chein, J., Albert, D., O'Brien, L., Uckert, K., & Steinberg, L. (2011). Peers increase adolescent risk taking by enhancing activity in the brain's reward circuitry. *Developmental Science*, *14*(2), F1–F10. https://doi.org/10.1111/j.1467-7687.2010.01035.x

Chronaki, G., Soltesz, F., Benikos, N., & Sonuga-Barke, E. J. S. (2017). An electrophysiological investigation of reinforcement effects in attention deficit/hyperactivity disorder: Dissociating cue sensitivity from down-stream effects on target engagement and performance. *Developmental Cognitive Neuroscience*, *28*, 12–20. https://doi.org/10.1016/j.dcn.2017.10.003

Chung, T., Paulsen, D. J., Geier, C. F., Luna, B., & Clark, D. B. (2015). Regional brain activation supporting cognitive control in the context of reward is associated with treated adolescents' marijuana problem severity at follow-up: A preliminary study. *Developmental Cognitive Neuroscience*, *16*, 93–100. https://doi.org/10.1016/j.dcn.2015.05.004

Claus, E. D., Feldstein Ewing, S. W., Magnan, R. E., Montanaro, E., Hutchison, K. E., & Bryan, A. D. (2018). Neural mechanisms of risky decision making in adolescents reporting frequent alcohol and/or marijuana use. *Brain Imaging and Behavior*, *12*(2), 564–576. https://doi.org/10.1007/s11682-017-9723-x

Cleophas, T. J., & Zwinderman, A. H. (2018). Bayesian Pearson Correlation Analysis. In T. J. Cleophas & A. H. Zwinderman (Eds.), *Modern Bayesian Statistics in Clinical Research* (pp. 111–118). Springer International Publishing. https://doi.org/10.1007/978-3-319-92747-3_11

Clifton, J. D. W. (2020). Managing validity versus reliability trade-offs in scale-building decisions. *Psychological Methods*, *25*(3), 259–270. https://doi.org/10.1037/met0000236

Cohen, J. (1994). The earth is round ($p < .05$). *American Psychologist*, *49*(12), 997–1003. https://doi.org/10.1037/0003-066X.49.12.997

Colich, N. L., Ho, T. C., Ellwood-Lowe, M. E., Foland-Ross, L. C., Sacchet, M. D., LeMoult, J. L., & Gotlib, I. H. (2017). Like mother like daughter: Putamen activation as a mechanism underlying intergenerational risk for depression. *Social Cognitive and Affective Neuroscience*, *12*(9), 1480–1489. https://doi.org/10.1093/scan/nsx073

Cook, T. D., & Campbell, D. T. (1979). *Quasi-Experimentation: Design and Analysis Issues for Field Settings*. https://www.scholars.northwestern.edu/en/publications/quasi-experimentation-design-and-analysis-issues-for-field-settin

Cope, L. M., Martz, M. E., Hardee, J. E., Zucker, R. A., & Heitzeg, M. M. (2019). Reward activation in childhood predicts adolescent substance use initiation in a high-risk sample. *Drug and Alcohol Dependence*, *194*, 318–325. https://doi.org/10.1016/j.drugalcdep.2018.11.003

Courtney, A. L., Casey, B. J., & Rapuano, K. M. (2020). A Neurobiological Model of Alcohol Marketing Effects on Underage Drinking. *Journal of Studies on Alcohol and Drugs. Supplement*, *Sup 19*, 68–80.

Cowles, M. (1989). *Statistics in psychology: An historical perspective*. Lawrence Erlbaum Associates, Inc.

Crane, N. A., Gorka, S. M., Phan, K. L., & Childs, E. (2018). Amygdala-orbitofrontal functional connectivity mediates the relationship between sensation seeking and alcohol use among binge-drinking adults. *Drug and Alcohol Dependence*, *192*, 208–214. https://doi.org/10.1016/j.drugalcdep.2018.07.044

Cremers, H. R., Wager, T. D., & Yarkoni, T. (2017). The relation between statistical power and inference in fMRI. *PLOS ONE*, *12*(11), e0184923. https://doi.org/10.1371/journal.pone.0184923

Cromer, B. A., & Stager, M. M. (2000). Research articles published in the Journal of Adolescent Health: A two-decade comparison. *The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine*, *27*(5), 306–313. https://doi.org/10.1016/s1054-139x(00)00147-6

Cronbach, L. J. (1957). The two disciplines of scientific psychology. *American Psychologist*, *12*(11), 671–684. https://doi.org/10.1037/h0043943

Cronbach, L. J., & Meehl, P. E. (1955). Construct validity in psychological tests. *Psychological Bulletin*, *52*(4), 281–302. https://doi.org/10.1037/h0040957

Crone, E. A., & Dahl, R. E. (2012). Understanding adolescence as a period of social–affective engagement and goal flexibility. *Nature Reviews Neuroscience*, *13*(9), 636–650. https://doi.org/10.1038/nrn3313

Crone, E. A., & van der Molen, M. W. (2004). Developmental changes in real life decision making: Performance on a gambling task previously shown to depend on the ventromedial prefrontal cortex. *Developmental Neuropsychology*, *25*(3), 251–279. https://doi.org/10.1207/s15326942dn2503_2

Cservenka, A., Herting, M. M., Seghete, K. L. M., Hudson, K. A., & Nagel, B. J. (2013). High and low sensation seeking adolescents show distinct patterns of brain activity during reward processing. *NeuroImage*, *66*, 184–193. https://doi.org/10.1016/j.neuroimage.2012.11.003

Cservenka, A., Jones, S. A., & Nagel, B. J. (2015). Reduced cerebellar brain activity during reward processing in adolescent binge drinkers. *Developmental Cognitive Neuroscience*, *16*, 110–120. https://doi.org/10.1016/j.dcn.2015.06.004

Curran, P., & Hancock, G. (n.d.). *Listen – quantitudethepodcast.org* (S2E33). Retrieved May 11, 2021, from https://quantitudepod.org/episodes/

Cyranowski, J. M., Frank, E., Young, E., & Shear, M. K. (2000). Adolescent onset of the gender difference in lifetime rates of major depression: A theoretical model. *Archives of General Psychiatry*, *57*(1), 21–27. https://doi.org/10.1001/archpsyc.57.1.21

Dahl, R. E. (2004). Adolescent brain development: A period of vulnerabilities and opportunities. Keynote address. *Annals of the New York Academy of Sciences*, *1021*, 1–22. https://doi.org/10.1196/annals.1308.001

Dahl, R. E., Allen, N. B., Wilbrecht, L., & Suleiman, A. B. (2018). Importance of investing in adolescence from a developmental science perspective. *Nature*, *554*(7693), 441–450. https://doi.org/10.1038/nature25770

Dang, J., King, K. M., & Inzlicht, M. (2020). Why Are Self-Report and Behavioral Measures Weakly Correlated? *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2020.01.007

Davis-Stober, C. P., & Regenwetter, M. (2019). The 'paradox' of converging evidence. *Psychological Review*, *126*(6), 865–879. https://doi.org/10.1037/rev0000156

Defoe, I. N., Dubas, J. S., Figner, B., & van Aken, M. A. G. (2015). A meta-analysis on age differences in risky decision making: Adolescents versus children and adults. *Psychological Bulletin*, *141*(1), 48–84. https://doi.org/10.1037/a0038088

Del Giacco, A. C., Jones, S. A., Morales, A. M., Kliamovich, D., & Nagel, B. J. (2021). Adolescent novelty seeking is associated with greater ventral striatal and prefrontal brain

response during evaluation of risk and reward. *Cognitive, Affective, & Behavioral Neuroscience*. https://doi.org/10.3758/s13415-021-00937-2

Demidenko, M. I., Huntley, E. D., Jahn, A., Thomason, M. E., Monk, C. S., & Keating, D. P. (2020). Cortical and subcortical response to the anticipation of reward in high and average/low risk-taking adolescents. *Developmental Cognitive Neuroscience*, *44*, 100798. https://doi.org/10.1016/j.dcn.2020.100798

Demidenko, M. I., Huntley, E. D., Martz, M. E., & Keating, D. P. (2019). Adolescent Health Risk Behaviors: Convergent, Discriminant and Predictive Validity of Self-Report and Cognitive Measures. *Journal of Youth and Adolescence*, *48*(9), 1765–1783. https://doi.org/10.1007/s10964-019-01057-4

Demidenko, M. I., Huntley, E. D., Weigard, A. S., Keating, D. P., & Beltz, A. M. (2022). Neural heterogeneity underlying late adolescent motivational processing is linked to individual differences in behavioral sensation seeking. *Journal of Neuroscience Research*, *n/a*(n/a). https://doi.org/10.1002/jnr.25005

Demidenko, M. I., Weigard, A. S., Ganesan, K., Jang, H., Jahn, A., Huntley, E. D., & Keating, D. P. (2021a). Interactions between methodological and interindividual variability: How Monetary Incentive Delay (MID) task contrast maps vary and impact associations with behavior. *Brain and Behavior*, *11*(5), e02093. https://doi.org/10.1002/brb3.2093

Demidenko, M. I., Weigard, A. S., Ganesan, K., Jang, H., Jahn, A., Huntley, E. D., & Keating, D. P. (2021b). Interactions between methodological and interindividual variability: How Monetary Incentive Delay (MID) task contrast maps vary and impact associations with behavior. *Brain and Behavior*, *11*(5), e02093. https://doi.org/10.1002/brb3.2093

Demos, J., & Demos, V. (1969). Adolescence in Historical Perspective. *Journal of Marriage and Family*, *31*(4), 632–638. https://doi.org/10.2307/349302

Dhingra, I., Zhang, S., Zhornitsky, S., Le, T. M., Wang, W., Chao, H. H., Levy, I., & Li, C.-S. R. (2019). The effects of age on reward magnitude processing in the monetary incentive delay task. *NeuroImage*, 116368. https://doi.org/10.1016/j.neuroimage.2019.116368

Di, X., & Biswal, B. B. (2017). Psychophysiological Interactions in a Visual Checkerboard Task: Reproducibility, Reliability, and the Effects of Deconvolution. *Frontiers in Neuroscience*, *11*, 573. https://doi.org/10.3389/fnins.2017.00573

DiCiccio, T. J., & Efron, B. (1996). Bootstrap confidence intervals. *Statistical Science*, *11*(3), 189–228. https://doi.org/10.1214/ss/1032280214

Dick, A. S., Watts, A. L., Heeringa, S., Lopez, D. A., Bartsch, H., Fan, C. C., Palmer, C., Reuter, C., Marshall, A., Haist, F., Hawes, S., Nichols, T. E., Barch, D. M., Jernigan, T. L., Garavan, H., Grant, S., Pariyadath, V., Hoffman, E., Neale, M., … Thompson, W. K. (2020). Meaningful Effects in the Adolescent Brain Cognitive Development Study. *BioRxiv*, 2020.09.01.276451. https://doi.org/10.1101/2020.09.01.276451

Diekhof, E. K., Kaps, L., Falkai, P., & Gruber, O. (2012). The role of the human ventral striatum and the medial orbitofrontal cortex in the representation of reward magnitude—An activation likelihood estimation meta-analysis of neuroimaging studies of passive reward expectancy and outcome processing. *Neuropsychologia*, *50*(7), 1252–1266. https://doi.org/10.1016/j.neuropsychologia.2012.02.007

Duell, N., & Steinberg, L. (2020). Differential Correlates of Positive and Negative Risk Taking in Adolescence. *Journal of Youth and Adolescence*. https://doi.org/10.1007/s10964-020-01237-7

Duffy, K. A., Fisher, Z. F., Arizmendi, C. A., Molenaar, P. C. M., Hopfinger, J., Cohen, J. R., Beltz, A. M., Lindquist, M. A., Hallquist, M. N., & Gates, K. M. (2021). Detecting Task-Dependent Functional Connectivity in Group Iterative Multiple Model Estimation with Person-Specific Hemodynamic Response Functions. *Brain Connectivity*, *11*(6), 418–429. https://doi.org/10.1089/brain.2020.0864

Dugré, J. R., Dumais, A., Bitar, N., & Potvin, S. (2018). Loss anticipation and outcome during the Monetary Incentive Delay Task: A neuroimaging systematic review and meta-analysis. *PeerJ*, *6*, e4749. https://doi.org/10.7717/peerj.4749

Duka, T., Nikolaou, K., King, S. L., Banaschewski, T., Bokde, A. L. W., Büchel, C., Carvalho, F. M., Conrod, P. J., Flor, H., Gallinat, J., Garavan, H., Heinz, A., Jia, T., Gowland, P., Martinot, J.-L., Paus, T., Rietschel, M., Robbins, T. W., Smolka, M., … Stephens, D. N. (2017). GABRB1 Single Nucleotide Polymorphism Associated with Altered Brain Responses (but not Performance) during Measures of Impulsivity and Reward Sensitivity in Human Adolescents. *Frontiers in Behavioral Neuroscience*, *11*, 24. https://doi.org/10.3389/fnbeh.2017.00024

Edwards, J. R., & Bagozzi, R. P. (2000). On the nature and direction of relationships between constructs and measures. *Psychological Methods*, *5*(2), 155–174. https://doi.org/10.1037/1082-989x.5.2.155

Eisenberg, I. W., Bissett, P. G., Zeynep Enkavi, A., Li, J., MacKinnon, D. P., Marsch, L. A., & Poldrack, R. A. (2019). Uncovering the structure of self-regulation through data-driven ontology discovery. *Nature Communications*, *10*(1), 1–13. https://doi.org/10.1038/s41467-019-10301-1

Ekhtiari, H., Kuplicki, R., Aupperle, R. P., & Paulus, M. P. (2020). It is Never as Good the Second Time Around: Brain Areas Involved in Salience Processing Habituate During Repeated Drug Cue Exposure in Methamphetamine and Opioid Users. *BioRxiv*, 2020.04.18.036368. https://doi.org/10.1101/2020.04.18.036368

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences of the United States of America*, *113*(28), 7900–7905. https://doi.org/10.1073/pnas.1602413113

Elliott, M. L., Knodt, A. R., Caspi, A., Moffitt, T. E., & Hariri, A. R. (2021). Need for Psychometric Theory in Neuroscience Research and Training: Reply to Kragel et al. (2021). *Psychological Science*, 956797621996665. https://doi.org/10.1177/0956797621996665

Elliott, M. L., Knodt, A. R., & Hariri, A. R. (2021). Striving toward translation: Strategies for reliable fMRI measurement. *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2021.05.008

Elliott, M. L., Knodt, A. R., Ireland, D., Morris, M. L., Poulton, R., Ramrakha, S., Sison, M. L., Moffitt, T. E., Caspi, A., & Hariri, A. R. (2019). Poor test-retest reliability of task-fMRI: New empirical evidence and a meta-analysis. *BioRxiv*, 681700. https://doi.org/10.1101/681700

Elliott, M. L., Knodt, A. R., Ireland, D., Morris, M. L., Poulton, R., Ramrakha, S., Sison, M. L., Moffitt, T. E., Caspi, A., & Hariri, A. R. (2020). What Is the Test-Retest Reliability of Common Task-Functional MRI Measures? New Empirical Evidence and a Meta-Analysis: *Psychological Science*. https://doi.org/10.1177/0956797620916786

Erikson, E. H. (1968). *Identity: Youth and Crisis*. W. W. Norton & Company.

Ernst, M. (2014). The triadic model perspective for the study of adolescent motivated behavior. *Brain and Cognition*, *89*, 104–111. https://doi.org/10.1016/j.bandc.2014.01.006

Ernst, M., Gowin, J., & Gaillard, C. (2022). The Triadic Neural Systems Model through a Machine-Learning Mill. In G. Borst & O. Houdé (Eds.), *The Cambridge Handbook of Cognitive Development* (pp. 516–534). Cambridge University Press. https://doi.org/10.1017/9781108399838.028

Ernst, M., & Luciana, M. (2015). Neuroimaging of the dopamine/reward system in adolescent drug use. *CNS Spectrums*, *20*(4), 427–441. https://doi.org/10.1017/S1092852915000395

Ernst, M., Nelson, E. E., Jazbec, S., McClure, E. B., Monk, C. S., Leibenluft, E., Blair, J., & Pine, D. S. (2005). Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. *NeuroImage*, *25*(4), 1279–1291. https://doi.org/10.1016/j.neuroimage.2004.12.038

Ernst, M., Pine, D. S., & Hardin, M. (2006). Triadic model of the neurobiology of motivated behavior in adolescence. *Psychological Medicine*, *36*(3), 299–312. https://doi.org/10.1017/S0033291705005891

Ernst, M., & Spear, L. P. (2009). Reward systems. In *Handbook of developmental social neuroscience* (pp. 324–341). The Guilford Press.

Eronen, M. I., & Bringmann, L. F. (2021). The Theory Crisis in Psychology: How to Move Forward. *Perspectives on Psychological Science*, 1745691620970586. https://doi.org/10.1177/1745691620970586

Eshel, N., Nelson, E. E., Blair, J., Pine, D. S., & Ernst, M. (2007). Neural substrates of choice selection in adults and adolescents: Development of the ventrolateral prefrontal and anterior cingulate cortices. *Neuropsychologia*, *45*(6), 1270–1279. https://doi.org/10.1016/j.neuropsychologia.2006.10.004

Eshel, N., & Steinberg, E. E. (2018). Learning what to approach. *PLoS Biology*, *16*(10), e3000043. https://doi.org/10.1371/journal.pbio.3000043

Failing, M., & Theeuwes, J. (2018). Selection history: How reward modulates selectivity of visual attention. *Psychonomic Bulletin & Review*, *25*(2), 514–538. https://doi.org/10.3758/s13423-017-1380-y

Ferdinand, A. O., Menachemi, N., Blackburn, J. L., Sen, B., Nelson, L., & Morrisey, M. (2015). The impact of texting bans on motor vehicle crash-related hospitalizations. *American Journal of Public Health*, *105*(5), 859–865. https://doi.org/10.2105/AJPH.2014.302537

Ferster, C. B., & Skinner, B. F. (1957). *Schedules of Reinforcement*. Prentice-Hall, Inc.

Finn, E. S., Scheinost, D., Finn, D. M., Shen, X., Papademetris, X., & Constable, R. T. (2017). Can brain state be manipulated to emphasize individual differences in functional connectivity? *NeuroImage*, *160*, 140–151. https://doi.org/10.1016/j.neuroimage.2017.03.064

Fiske, D. W., & Campbell, D. T. (1992). Citations do not solve problems. *Psychological Bulletin*, *112*(3), 393–395. https://doi.org/10.1037/0033-2909.112.3.393

Flake, J. K., & Fried, E. I. (2020). Measurement Schmeasurement: Questionable Measurement Practices and How to Avoid Them. *Advances in Methods and Practices in Psychological Science*, *3*(4), 456–465. https://doi.org/10.1177/2515245920952393

Flake, J. K., Pek, J., & Hehman, E. (2017). Construct Validation in Social and Personality Research: Current Practice and Recommendations. *Social Psychological and Personality Science*, *8*(4), 370–378. https://doi.org/10.1177/1948550617693063

Flake, J. K., Shaw, M., & Luong, R. (2021). *Addressing a Crisis of Generalizability with Large-Scale Construct Validation*. PsyArXiv. https://doi.org/10.31234/osf.io/c45t9

Flannery, J. S., Riedel, M. C., Bottenhorn, K. L., Poudel, R., Salo, T., Hill-Bowen, L. D., Laird, A. R., & Sutherland, M. T. (2020). Meta-analytic clustering dissociates brain activity and behavior profiles across reward processing paradigms. *Cognitive, Affective, & Behavioral Neuroscience*, *20*(2), 215–235. https://doi.org/10.3758/s13415-019-00763-7

Floresco, S. B. (2015). The nucleus accumbens: An interface between cognition, emotion, and action. *Annual Review of Psychology*, *66*, 25–52. https://doi.org/10.1146/annurev-psych-010213-115159

Fong, A. H. C., Yoo, K., Rosenberg, M. D., Zhang, S., Li, C.-S. R., Scheinost, D., Constable, R. T., & Chun, M. M. (2019). Dynamic functional connectivity during task performance and rest predicts individual differences in attention across studies. *NeuroImage*, *188*, 14–25. https://doi.org/10.1016/j.neuroimage.2018.11.057

Forbes, E. E., & Dahl, R. E. (2010). Pubertal development and behavior: Hormonal activation of social and motivational tendencies. *Brain and Cognition*, *72*(1), 66–72. https://doi.org/10.1016/j.bandc.2009.10.007

Fried, E. I. (2020). Lack of Theory Building and Testing Impedes Progress in The Factor and Network Literature. *Psychological Inquiry*, *31*(4), 271–288. https://doi.org/10.1080/1047840X.2020.1853461

Friston, K., Moran, R., & Seth, A. K. (2013). Analysing connectivity with Granger causality and dynamic causal modelling. *Current Opinion in Neurobiology*, *23*(2), 172–178. https://doi.org/10.1016/j.conb.2012.11.010

Frith, U. (2019). Fast Lane to Slow Science. *Trends in Cognitive Sciences*, *0*(0). https://doi.org/10.1016/j.tics.2019.10.007

Funder, D. C., & Ozer, D. J. (2019). Evaluating Effect Size in Psychological Research: Sense and Nonsense. *Advances in Methods and Practices in Psychological Science*, *2*(2), 156–168. https://doi.org/10.1177/2515245919847202

Galván, A. (2010). Adolescent development of the reward system. *Frontiers in Human Neuroscience*, *4*. https://doi.org/10.3389/neuro.09.006.2010

Galvan, A. (2010). Adolescent development of the reward system. *Frontiers in Human Neuroscience*, *4*, 6. https://doi.org/10.3389/neuro.09.006.2010

Galván, A. (2013). The Teenage Brain: Sensitivity to Rewards. *Current Directions in Psychological Science*, *22*(2), 88–93. https://doi.org/10.1177/0963721413480859

Galvan, A., Hare, T. A., Parra, C. E., Penn, J., Voss, H., Glover, G., & Casey, B. J. (2006). Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *26*(25), 6885–6892. https://doi.org/10.1523/JNEUROSCI.1062-06.2006

Galvan, A., Hare, T., Voss, H., Glover, G., & Casey, B. J. (2007). Risk-taking and the adolescent brain: Who is at risk? *Developmental Science*, *10*(2), F8–F14. https://doi.org/10.1111/j.1467-7687.2006.00579.x

Galván, A., & McGlennen, K. M. (2012). Enhanced Striatal Sensitivity to Aversive Reinforcement in Adolescents versus Adults. *Journal of Cognitive Neuroscience*, *25*(2), 284–296. https://doi.org/10.1162/jocn_a_00326

Garrison, K. A., Yip, S. W., Balodis, I. M., Carroll, K. M., Potenza, M. N., & Krishnan-Sarin, S. (2017). Reward-related frontostriatal activity and smoking behavior among adolescents in

treatment for smoking cessation. *Drug and Alcohol Dependence*, *177*, 268–276. https://doi.org/10.1016/j.drugalcdep.2017.03.035

Gates, K. M., Henry, T., Steinley, D., & Fair, D. A. (2016). A Monte Carlo Evaluation of Weighted Community Detection Algorithms. *Frontiers in Neuroinformatics*, *10*, 45. https://doi.org/10.3389/fninf.2016.00045

Gates, K. M., Lane, S. T., Varangis, E., Giovanello, K., & Guiskewicz, K. (2017). Unsupervised Classification During Time-Series Model Building. *Multivariate Behavioral Research*, *52*(2), 129–148. https://doi.org/10.1080/00273171.2016.1256187

Gates, K. M., & Molenaar, P. C. M. (2012). Group search algorithm recovers effective connectivity maps for individuals in homogeneous and heterogeneous samples. *NeuroImage*, *63*(1), 310–319. https://doi.org/10.1016/j.neuroimage.2012.06.026

Gates, K. M., Molenaar, P. C. M., Hillary, F. G., & Slobounov, S. (2011). Extended unified SEM approach for modeling event-related fMRI data. *NeuroImage*, *54*(2), 1151–1158. https://doi.org/10.1016/j.neuroimage.2010.08.051

Gelman, A., & Loken, E. (2014). The statistical crisis in science: Data-dependent analysis—A" garden of forking paths"—Explains why many statistically significant comparisons don't hold up. *American Scientist*, *102*(6), 460–466.

Glover, G. H., Li, T. Q., & Ress, D. (2000). Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. *Magnetic Resonance in Medicine*, *44*(1), 162–167. https://doi.org/10.1002/1522-2594(200007)44:1<162::aid-mrm23>3.0.co;2-e

Goetschius, L. G., Hein, T. C., McLanahan, S. S., Brooks-Gunn, J., McLoyd, V. C., Dotterer, H. L., Lopez-Duran, N., Mitchell, C., Hyde, L. W., Monk, C. S., & Beltz, A. M. (2020). Association of Childhood Violence Exposure With Adolescent Neural Network Density. *JAMA Network Open*, *3*(9). https://doi.org/10.1001/jamanetworkopen.2020.17850

Gonzalez, M. Z., Allen, J. P., & Coan, J. A. (2016). Lower neighborhood quality in adolescence predicts higher mesolimbic sensitivity to reward anticipation in adulthood. *Developmental Cognitive Neuroscience*, *22*, 48–57. https://doi.org/10.1016/j.dcn.2016.10.003

Gordon, E. M., Laumann, T. O., Gilmore, A. W., Newbold, D. J., Greene, D. J., Berg, J. J., Ortega, M., Hoyt-Drazen, C., Gratton, C., Sun, H., Hampton, J. M., Coalson, R. S., Nguyen, A. L., McDermott, K. B., Shimony, J. S., Snyder, A. Z., Schlaggar, B. L., Petersen, S. E., Nelson, S. M., & Dosenbach, N. U. F. (2017). Precision Functional Mapping of Individual Human Brains. *Neuron*, *95*(4), 791-807.e7. https://doi.org/10.1016/j.neuron.2017.07.011

Grady, C. L., Rieck, J. R., Nichol, D., Rodrigue, K. M., & Kennedy, K. M. (2020). Influence of sample size and analytic approach on stability and interpretation of brain-behavior correlations in task-related fMRI data. *Human Brain Mapping*. https://doi.org/10.1002/hbm.25217

Grahek, I., Schaller, M., & Tackett, J. L. (2021). Anatomy of a Psychological Theory: Integrating Construct-Validation and Computational-Modeling Methods to Advance Theorizing. *Perspectives on Psychological Science*, *16*(4), 803–815. https://doi.org/10.1177/1745691620966794

Greene, A. S., Gao, S., Scheinost, D., & Constable, R. T. (2018). Task-induced brain state manipulation improves prediction of individual traits. *Nature Communications*, *9*(1), 1–13. https://doi.org/10.1038/s41467-018-04920-3

Group for the Advancement of Psychiatry Committee on Adolescence. (1968). *Normal Adolescence: Its Dynamics and Impact*. Scribner.

Haber, S. N., & Behrens, T. E. J. (2014). The Neural Network Underlying Incentive-Based Learning: Implications for Interpreting Circuit Disruptions in Psychiatric Disorders. *Neuron, 83*(5), 1019–1039. https://doi.org/10.1016/j.neuron.2014.08.031

Haber, S. N., & Knutson, B. (2010). The Reward Circuit: Linking Primate Anatomy and Human Imaging. *Neuropsychopharmacology*, *35*(1), 4–26. https://doi.org/10.1038/npp.2009.129

Hagler, D. J., Hatton, S., Cornejo, M. D., Makowski, C., Fair, D. A., Dick, A. S., Sutherland, M. T., Casey, B. J., Barch, D. M., Harms, M. P., Watts, R., Bjork, J. M., Garavan, H. P., Hilmer, L., Pung, C. J., Sicat, C. S., Kuperman, J., Bartsch, H., Xue, F., … Dale, A. M. (2019). Image processing and analysis methods for the Adolescent Brain Cognitive Development Study. *NeuroImage*, *202*, 116091. https://doi.org/10.1016/j.neuroimage.2019.116091

Hale, D. R., Fitzgerald-Yau, N., & Viner, R. M. (2014). A Systematic Review of Effective Interventions for Reducing Multiple Health Risk Behaviors in Adolescence. *American Journal of Public Health, 104*(5), e19–e41. https://doi.org/10.2105/AJPH.2014.301874

Hall, G. S. (1882). The Moral and Religious Training of Children. *The Princeton Review*, *58*(1), 26–48.

Hall, G. S. (1891). The Moral and Religious Training of Children and Adolescents. *The Pedagogical Seminary*, *1*(2), 196–210. https://doi.org/10.1080/08919402.1891.10533932

Hall, G. S. (1904a). *Adolescence: Its psychology and its relations to physiology, anthropology, sociology, sex, crime, religion, and education.* (Vol. 1). D. Appleton & Company.

Hall, G. S. (1904b). *Adolescence: Its psychology and its relations to physiology, anthropology, sociology, sex, crime, religion, and education.* (Vol. 2). D. Appleton & Company.

Hall, G. S. (1924). Can the Masses Rule the World? *The Scientific Monthly*, *18*(5), 456–466.

Hardee, J. E., Cope, L. M., Martz, M. E., & Heitzeg, M. M. (2018). Review of Neurobiological Influences on Externalizing and Internalizing Pathways to Alcohol Use Disorder. *Current Behavioral Neuroscience Reports*, *5*(4), 249–262. https://doi.org/10.1007/s40473-018-0166-5

Harden, K. P., & Tucker-Drob, E. M. (2011). Individual differences in the development of sensation seeking and impulsivity during adolescence: Further evidence for a dual systems model. *Developmental Psychology*, *47*(3), 739–746. https://doi.org/10.1037/a0023279

Hawes, S. W., Chahal, R., Hallquist, M. N., Paulsen, D. J., Geier, C. F., & Luna, B. (2017). Modulation of reward-related neural activation on sensation seeking across development. *NeuroImage, 147*, 763–771. https://doi.org/10.1016/j.neuroimage.2016.12.020

Haxby, J. V., Guntupalli, J. S., Connolly, A. C., Halchenko, Y. O., Conroy, B. R., Gobbini, M. I., Hanke, M., & Ramadge, P. J. (2011). A Common, High-Dimensional Model of the Representational Space in Human Ventral Temporal Cortex. *Neuron, 72*(2), 404–416. https://doi.org/10.1016/j.neuron.2011.08.026

Hedge, C., Powell, G., & Sumner, P. (2018). The reliability paradox: Why robust cognitive tasks do not produce reliable individual differences. *Behavior Research Methods*, *50*(3), 1166–1186. https://doi.org/10.3758/s13428-017-0935-1

Heitzeg, M. M., Villafuerte, S., Weiland, B. J., Enoch, M.-A., Burmeister, M., Zubieta, J.-K., & Zucker, R. A. (2014). Effect of GABRA2 Genotype on Development of Incentive-

Motivation Circuitry in a Sample Enriched for Alcoholism Risk. *Neuropsychopharmacology*, *39*(13), 3077–3086. https://doi.org/10.1038/npp.2014.161
Henry, T. R., Feczko, E., Cordova, M., Earl, E., Williams, S., Nigg, J. T., Fair, D. A., & Gates, K. M. (2019). Comparing directed functional connectivity between groups with confirmatory subgrouping GIMME. *NeuroImage*, *188*, 642–653. https://doi.org/10.1016/j.neuroimage.2018.12.040
Higgins, S. T., & Bickel, W. K. (2000). Celebrating the decade of behavior: Introduction to special issue. *Experimental and Clinical Psychopharmacology*, *8*(3), 261–263. https://doi.org/10.1037/1064-1297.8.3.261
Hillary, F. G., Medaglia, J. D., Gates, K. M., Molenaar, P. C., & Good, D. C. (2014). Examining network dynamics after traumatic brain injury using the extended unified SEM approach. *Brain Imaging and Behavior*, *8*(3), 435–445. https://doi.org/10.1007/s11682-012-9205-0
Hinrichs, H., Scholz, M., Tempelmann, C., Woldorff, M. G., Dale, A. M., & Heinze, H.-J. (2000). Deconvolution of Event-Related fMRI Responses in Fast-Rate Experimental Designs: Tracking Amplitude Variations. *Journal of Cognitive Neuroscience*, *12*(Supplement 2), 76–89. https://doi.org/10.1162/089892900564082
Hong, Y.-W., Yoo, Y., Han, J., Wager, T. D., & Woo, C.-W. (2019). False-positive neuroimaging: Undisclosed flexibility in testing spatial hypotheses allows presenting anything as a replicated finding. *NeuroImage*, *195*, 384–395. https://doi.org/10.1016/j.neuroimage.2019.03.070
Horvath, P., & Zuckerman, M. (1993). Sensation seeking, risk appraisal, and risky behavior. *Personality and Individual Differences*, *14*(1), 41–52. https://doi.org/10.1016/0191-8869(93)90173-Z
Hoyle, R. H., Stephenson, M. T., Palmgreen, P., Lorch, E. P., & Donohew, R. L. (2002). Reliability and validity of a brief measure of sensation seeking. *Personality and Individual Differences*, *32*(3), 401–414. https://doi.org/10.1016/S0191-8869(01)00032-0
Hull, C. L. (1952). *A behavior system; an introduction to behavior theory concerning the individual organism*. Yale University Press.
Hussey, I., & Hughes, S. (2020). Hidden Invalidity Among 15 Commonly Used Measures in Social and Personality Psychology. *Advances in Methods and Practices in Psychological Science*, *3*(2), 166–184. https://doi.org/10.1177/2515245919882903
Inzlicht, M., Shenhav, A., & Olivola, C. Y. (2018). The Effort Paradox: Effort Is Both Costly and Valued. *Trends in Cognitive Sciences*, *22*(4), 337–349. https://doi.org/10.1016/j.tics.2018.01.007
JASP Team. (2019). *ASP (version 0.10. 2)[computer software]*. https://jasp-stats.org
Jenkinson, M., Bannister, P., Brady, M., & Smith, S. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage*, *17*(2), 825–841.
Jenkinson, M., & Smith, S. (2001). A global optimisation method for robust affine registration of brain images. *Medical Image Analysis*, *5*(2), 143–156.
Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. E., & Patrick, M. E. (2020). Monitoring the Future National Survey Results on Drug Use, 1975-2019: Overview, Key Findings on Adolescent Drug Use. In *Institute for Social Research*. Institute for Social Research. https://eric.ed.gov/?id=ED604018
Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Patrick, M. E. (2019). Monitoring the Future National Survey Results on Drug Use, 1975-2018:

Overview, Key Findings on Adolescent Drug Use. In *Institute for Social Research*. Institute for Social Research. https://eric.ed.gov/?id=ED594190

Joseph, J. E., Zhu, X., Lynam, D., & Kelly, T. H. (2016). Modulation of meso-limbic reward processing by motivational tendencies in young adolescents and adults. *NeuroImage*, *129*, 40–54. https://doi.org/10.1016/j.neuroimage.2015.12.005

Juavinett, A. L. (2022). The next generation of neuroscientists needs to learn how to code, and we need new ways to teach them. *Neuron*. https://doi.org/10.1016/j.neuron.2021.12.001

Kahn, L. E., Peake, S. J., Dishion, T. J., Stormshak, E. A., & Pfeifer, J. H. (2015). Learning to play it safe (or not): Stable and evolving neural responses during adolescent risky decision-making. *Journal of Cognitive Neuroscience*, *27*(1), 13–25. https://doi.org/10.1162/jocn_a_00694

Kann, L., McManus, T., Harris, W. A., Shanklin, S. L., Flint, K. H., Queen, B., Lowry, R., Chyen, D., Whittle, L., Thornton, J., Lim, C., Bradford, D., Yamakawa, Y., Leon, M., Brener, N., & Ethier, K. A. (2018). Youth Risk Behavior Surveillance—United States, 2017. *Morbidity and Mortality Weekly Report. Surveillance Summaries (Washington, D.C.: 2002)*, *67*(8), 1–114. https://doi.org/10.15585/mmwr.ss6708a1

Karoly, H. C., Bryan, A. D., Weiland, B. J., Mayer, A., Dodd, A., & Feldstein Ewing, S. W. (2015). Does incentive-elicited nucleus accumbens activation differ by substance of abuse? An examination with adolescents. *Developmental Cognitive Neuroscience*, *16*, 5–15. https://doi.org/10.1016/j.dcn.2015.05.005

Keating, D. P., Demidenko, M. I., & Kelly, D. (2023). Cognition in Adolescence and the Transition to Adulthood. In L. Crockett, Carlo, G., & J. Schulenberg (Eds.), *APA Handbook of Adolescent and Young Adult Development.* American Psychological Association. https://doi.org/10.1037/0000298-005

Keating, D. P., List, J. A., & Merriman, W. E. (1985). Cognitive processing and cognitive ability: A multivariate validity investigation. *Intelligence*, *9*(2), 149–170. https://doi.org/10.1016/0160-2896(85)90014-5

Kelley, T. L. (1927). *Interpretation of educational measurements*. World Book Co.

Knutson, B., & Greer, S. (2008). Anticipatory affect: Neural correlates and consequences for choice. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *363*(1511), 3771–3786. https://doi.org/10.1098/rstb.2008.0155

Knutson, B., & Heinz, A. (2015). Probing Psychiatric Symptoms with the Monetary Incentive Delay Task. *Biological Psychiatry*, *77*(5), 418–420. https://doi.org/10.1016/j.biopsych.2014.12.022

Knutson, B., Katovich, K., & Suri, G. (2014). Inferring affect from fMRI data. *Trends in Cognitive Sciences*, *18*(8), 422–428. https://doi.org/10.1016/j.tics.2014.04.006

Knutson, B., Westdorp, A., Kaiser, E., & Hommer, D. (2000). FMRI visualization of brain activity during a monetary incentive delay task. *NeuroImage*, *12*(1), 20–27. https://doi.org/10.1006/nimg.2000.0593

Korb, S., Götzendorfer, S. J., Massaccesi, C., Sezen, P., Graf, I., Willeit, M., Eisenegger, C., & Silani, G. (2020). Dopaminergic and opioidergic regulation during anticipation and consumption of social and nonsocial rewards. *ELife*, *9*, e55797. https://doi.org/10.7554/eLife.55797

Kragel, P. A., Han, X., Kraynak, T. E., Gianaros, P. J., & Wager, T. D. (2021). Functional MRI Can Be Highly Reliable, but It Depends on What You Measure: A Commentary on

Elliott et al. (2020). *Psychological Science*, 0956797621989730. https://doi.org/10.1177/0956797621989730

Krebs, R. M., Boehler, C. N., Roberts, K. C., Song, A. W., & Woldorff, M. G. (2012). The Involvement of the Dopaminergic Midbrain and Cortico-Striatal-Thalamic Circuits in the Integration of Reward Prospect and Attentional Task Demands. *Cerebral Cortex*, *22*(3), 607–615. https://doi.org/10.1093/cercor/bhr134

Kruschke, J. K., & Liddell, T. M. (2018). Bayesian data analysis for newcomers. *Psychonomic Bulletin & Review*, *25*(1), 155–177. https://doi.org/10.3758/s13423-017-1272-1

Lamm, C., Benson, B. E., Guyer, A. E., Perez-Edgar, K., Fox, N. A., Pine, D. S., & Ernst, M. (2014). Longitudinal study of striatal activation to reward and loss anticipation from mid-adolescence into late adolescence/early adulthood. *Brain and Cognition*, *89*, 51–60. https://doi.org/10.1016/j.bandc.2013.12.003

Lancaster, T. M., Linden, D. E., Tansey, K. E., Banaschewski, T., Bokde, A. L. W., Bromberg, U., Büchel, C., Cattrell, A., Conrod, P. J., Flor, H., Frouin, V., Gallinat, J., Garavan, H., Gowland, P., Heinz, A., Ittermann, B., Martinot, J.-L., Paillère Martinot, M.-L., Artiges, E., … IMAGEN Consortium. (2016). Polygenic Risk of Psychosis and Ventral Striatal Activation During Reward Processing in Healthy Adolescents. *JAMA Psychiatry*, *73*(8), 852–861. https://doi.org/10.1001/jamapsychiatry.2016.1135

Landes, I., Bakos, S., Kohls, G., Bartling, J., Schulte-Körne, G., & Greimel, E. (2018). Altered neural processing of reward and punishment in adolescents with Major Depressive Disorder. *Journal of Affective Disorders*, *232*, 23–33. https://doi.org/10.1016/j.jad.2018.01.017

Lane, S. T., Gates, K. M., Pike, H. K., Beltz, A. M., & Wright, A. G. C. (2019). Uncovering general, shared, and unique temporal patterns in ambulatory assessment data. *Psychological Methods*, *24*(1), 54–69. https://doi.org/10.1037/met0000192

Ledford, H. (2018). Who exactly counts as an adolescent? *Nature*, *554*(7693), 429–431. https://doi.org/10.1038/d41586-018-02169-w

Lejuez, C. W., Aklin, W. M., Zvolensky, M. J., & Pedulla, C. M. (2003). Evaluation of the Balloon Analogue Risk Task (BART) as a predictor of adolescent real-world risk-taking behaviours. *Journal of Adolescence*, *26*(4), 475–479. https://doi.org/10.1016/S0140-1971(03)00036-8

Lejuez, C. W., Read, J. P., Kahler, C. W., Richards, J. B., Ramsey, S. E., Stuart, G. L., Strong, D. R., & Brown, R. A. (2002). Evaluation of a behavioral measure of risk taking: The Balloon Analogue Risk Task (BART). *Journal of Experimental Psychology. Applied*, *8*(2), 75–84. https://doi.org/10.1037//1076-898x.8.2.75

LeMoult, J., Colich, N. L., Sherdell, L., Hamilton, J. P., & Gotlib, I. H. (2015). Influence of menarche on the relation between diurnal cortisol production and ventral striatum activity during reward anticipation. *Social Cognitive and Affective Neuroscience*, *10*(9), 1244–1250. https://doi.org/10.1093/scan/nsv016

Lerner, R. M. (2006). Developmental Science, Developmental Systems, and Contemporary Theories of Human Development. In *Handbook of child psychology: Theoretical models of human development, Vol. 1, 6th ed* (pp. 1–17). John Wiley & Sons Inc.

Li, X., Ai, L., Giavasis, S., Jin, H., Feczko, E., Xu, T., Clucas, J., Franco, A., Heinsfeld, A. S., Adebimpe, A., Vogelstein, J. T., Yan, C.-G., Esteban, O., Poldrack, R. A., Craddock, C., Fair, D., Satterthwaite, T., Kiar, G., & Milham, M. P. (2021). *Moving Beyond Processing*

*and Analysis-Related Variation in Neuroscience* (p. 2021.12.01.470790). https://doi.org/10.1101/2021.12.01.470790

Li, Z., Yan, C., Xie, W.-Z., Li, K., Zeng, Y.-W., Jin, Z., Cheung, E. F. C., & Chan, R. C. K. (2015). Anticipatory pleasure predicts effective connectivity in the mesolimbic system. *Frontiers in Behavioral Neuroscience*, *9*, 217. https://doi.org/10.3389/fnbeh.2015.00217

Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E., & Barrett, L. F. (2012). The brain basis of emotion: A meta-analytic review. *The Behavioral and Brain Sciences*, *35*(3), 121–143. https://doi.org/10.1017/S0140525X11000446

Luciana, M., & Collins, P. F. (2012). Incentive Motivation, Cognitive Control, and the Adolescent Brain: Is It Time for a Paradigm Shift? *Child Development Perspectives*, *6*(4), 392–399. https://doi.org/10.1111/j.1750-8606.2012.00252.x

Luna, B., & Wright, C. (2016). Adolescent brain development: Implications for the juvenile criminal justice system. In *APA handbook of psychology and juvenile justice* (pp. 91–116). American Psychological Association. https://doi.org/10.1037/14643-005

Lutz, K., & Widmer, M. (2014). What can the monetary incentive delay task tell us about the neural processing of reward and punishment? *Neuroscience and Neuroeconomics*, *3*, 33–45. https://doi.org/10.2147/NAN.S38864

Ly, A., Marsman, M., & Wagenmakers, E.-J. (2018). Analytic posteriors for Pearson's correlation coefficient. *Statistica Neerlandica*, *72*(1), 4–13. https://doi.org/10.1111/stan.12111

Lydon-Staley, D. M., & Bassett, D. S. (2018). The Promise and Challenges of Intensive Longitudinal Designs for Imbalance Models of Adolescent Substance Use. *Frontiers in Psychology*, *9*. https://doi.org/10.3389/fpsyg.2018.01576

Lynch, M., & Cicchetti, D. (1998). An ecological-transactional analysis of children and contexts: The longitudinal interplay among child maltreatment, community violence, and children's symptomatology. *Development and Psychopathology*, *10*(2), 235–257.

Maitra, R. (2010). A re-defined and generalized percent-overlap-of-activation measure for studies of fMRI reproducibility and its use in identifying outlier activation maps. *NeuroImage*, *50*(1), 124–135. https://doi.org/10.1016/j.neuroimage.2009.11.070

Marek, S., Hwang, K., Foran, W., Hallquist, M. N., & Luna, B. (2015). The Contribution of Network Organization and Integration to the Development of Cognitive Control. *PLoS Biology*, *13*(12), e1002328. https://doi.org/10.1371/journal.pbio.1002328

Marek, S., Tervo-Clemmens, B., Calabro, F. J., Montez, D. F., Kay, B. P., Hatoum, A. S., Donohue, M. R., Foran, W., Miller, R. L., Feczko, E., Miranda-Dominguez, O., Graham, A. M., Earl, E. A., Perrone, A. J., Cordova, M., Doyle, O., Moore, L. A., Conan, G., Uriarte, J., … Dosenbach, N. U. F. (2020). Towards Reproducible Brain-Wide Association Studies. *BioRxiv*, 2020.08.21.257758. https://doi.org/10.1101/2020.08.21.257758

Marek, S., Tervo-Clemmens, B., Calabro, F. J., Montez, D. F., Kay, B. P., Hatoum, A. S., Donohue, M. R., Foran, W., Miller, R. L., Hendrickson, T. J., Malone, S. M., Kandala, S., Feczko, E., Miranda-Dominguez, O., Graham, A. M., Earl, E. A., Perrone, A. J., Cordova, M., Doyle, O., … Dosenbach, N. U. F. (2022). Reproducible brain-wide association studies require thousands of individuals. *Nature*, 1–7. https://doi.org/10.1038/s41586-022-04492-9

Maresh, E. L., Stim, J. J., Van Voorhis, A. C., Kang, S. S., Luciana, M., Sponheim, S. R., & Urošević, S. (2019). Neurophysiological correlates of cognitive control and approach

motivation abnormalities in adolescent bipolar disorders. *Cognitive, Affective & Behavioral Neuroscience*, *19*(3), 677–691. https://doi.org/10.3758/s13415-019-00719-x

Martz, M. E., Trucco, E. M., Cope, L. M., Hardee, J. E., Jester, J. M., Zucker, R. A., & Heitzeg, M. M. (2016). Association of Marijuana Use With Blunted Nucleus Accumbens Response to Reward Anticipation. *JAMA Psychiatry*, *73*(8), 838–844. https://doi.org/10.1001/jamapsychiatry.2016.1161

Martz, M. E., Zucker, R. A., Schulenberg, J. E., & Heitzeg, M. M. (2018). Psychosocial and neural indicators of resilience among youth with a family history of substance use disorder. *Drug and Alcohol Dependence*, *185*, 198–206. https://doi.org/10.1016/j.drugalcdep.2017.12.015

May, J. C., Delgado, M. R., Dahl, R. E., Stenger, V. A., Ryan, N. D., Fiez, J. A., & Carter, C. S. (2004). Event-related functional magnetic resonance imaging of reward-related brain circuitry in children and adolescents. *Biological Psychiatry*, *55*(4), 359–366. https://doi.org/10.1016/j.biopsych.2003.11.008

McCormick, E. M., & Telzer, E. H. (2017). Failure to retreat: Blunted sensitivity to negative feedback supports risky behavior in adolescents. *NeuroImage*, *147*, 381–389. https://doi.org/10.1016/j.neuroimage.2016.12.041

McGaugh, J. L. (1990). The "Decade of the Brain." *APS Observer*, *3*(1). https://www.psychologicalscience.org/observer/the-decade-of-the-brain

McLaren, D. G., Ries, M. L., Xu, G., & Johnson, S. C. (2012). A generalized form of context-dependent psychophysiological interactions (gPPI): A comparison to standard approaches. *NeuroImage*, *61*(4), 1277–1286. https://doi.org/10.1016/j.neuroimage.2012.03.068

McNeish, D. (2018). Thanks coefficient alpha, we'll take it from here. *Psychological Methods*, *23*(3), 412–433. https://doi.org/10.1037/met0000144

Medaglia, J. D., Lynall, M.-E., & Bassett, D. S. (2015). Cognitive network neuroscience. *Journal of Cognitive Neuroscience*, *27*(8), 1471–1491. https://doi.org/10.1162/jocn_a_00810

Meehl, P. E. (1967). Theory-Testing in Psychology and Physics: A Methodological Paradox. *Philosophy of Science*, *34*(2), 103–115. JSTOR.

Meehl, P. E. (1978). Theoretical risks and tabular asterisks: Sir Karl, Sir Ronald, and the slow progress of soft psychology. *Journal of Consulting and Clinical Psychology*, *46*(4), 806–834. https://doi.org/10.1037/0022-006X.46.4.806

Meehl, P. E. (1990). Why Summaries of Research on Psychological Theories are Often Uninterpretable. *Psychological Reports*, *66*(1), 195–244. https://doi.org/10.2466/pr0.1990.66.1.195

Meisel, S. N., Fosco, W. D., Hawk, L. W., & Colder, C. R. (2019). Mind the gap: A review and recommendations for statistically evaluating Dual Systems models of adolescent risk behavior. *Developmental Cognitive Neuroscience*, *39*, 100681. https://doi.org/10.1016/j.dcn.2019.100681

Mikita, N., Simonoff, E., Pine, D. S., Goodman, R., Artiges, E., Banaschewski, T., Bokde, A. L., Bromberg, U., Büchel, C., Cattrell, A., Conrod, P. J., Desrivières, S., Flor, H., Frouin, V., Gallinat, J., Garavan, H., Heinz, A., Ittermann, B., Jurk, S., … Stringaris, A. (2016). Disentangling the autism-anxiety overlap: FMRI of reward processing in a community-based longitudinal study. *Translational Psychiatry*, *6*(6), e845. https://doi.org/10.1038/tp.2016.107

Miller, P. H. (2009). *Theories of Developmental Psychology* (Fifth edition). Worth Publishers.

Mischel, W. (2008). The Toothbrush Problem. *APS Observer*, *21*(11). https://www.psychologicalscience.org/observer/the-toothbrush-problem

Modak, P., Hutslar, C., Polk, R., Atkinson, E., Fisher, L., Macy, J., Chassin, L., Presson, C., Finn, P. R., & Brown, J. W. (2021). Neural bases of risky decisions involving nicotine vapor versus monetary reward. *BioRxiv*, 2021.04.14.439907. https://doi.org/10.1101/2021.04.14.439907

Moffitt, T. E. (1993). Adolescence-limited and life-course-persistent antisocial behavior: A developmental taxonomy. *Psychological Review*, *100*(4), 674–701.

Mori, A., Okamoto, Y., Okada, G., Takagaki, K., Jinnin, R., Takamura, M., Kobayakawa, M., & Yamawaki, S. (2016). Behavioral activation can normalize neural hypoactivation in subthreshold depression during a monetary incentive delay task. *Journal of Affective Disorders*, *189*, 254–262. https://doi.org/10.1016/j.jad.2015.09.036

*Mplus User's Guide.* (2012). Muthén & Muthén. https://www.statmodel.com/

Mumford, J. A., & Ramsey, J. D. (2014). Bayesian networks for fMRI: A primer. *NeuroImage*, *86*, 573–582. https://doi.org/10.1016/j.neuroimage.2013.10.020

Munn, B. R., Müller, E. J., Wainstein, G., & Shine, J. M. (2021). The ascending arousal system shapes neural dynamics to mediate awareness of cognitive states. *Nature Communications*, *12*(1), 6016. https://doi.org/10.1038/s41467-021-26268-x

Murray, L., Lopez-Duran, N. L., Mitchell, C., Monk, C. S., & Hyde, L. W. (2020). Neural Mechanisms of Reward and Loss Processing in a Low-Income Sample of At-Risk Adolescents. *Social Cognitive and Affective Neuroscience*. https://doi.org/10.1093/scan/nsaa157

Muthukrishna, M., & Henrich, J. (2019). A problem in theory. *Nature Human Behaviour*, *3*(3), 221–229. https://doi.org/10.1038/s41562-018-0522-1

Navas, J. F., Barrós-Loscertales, A., Costumero-Ramos, V., Verdejo-Román, J., Vilar-López, R., & Verdejo-García, A. (2018). Excessive body fat linked to blunted somatosensory cortex response to general reward in adolescents. *International Journal of Obesity (2005)*, *42*(1), 88–94. https://doi.org/10.1038/ijo.2017.207

Nees, F., Tzschoppe, J., Patrick, C. J., Vollstädt-Klein, S., Steiner, S., Poustka, L., Banaschewski, T., Barker, G. J., Büchel, C., Conrod, P. J., Garavan, H., Heinz, A., Gallinat, J., Lathrop, M., Mann, K., Artiges, E., Paus, T., Poline, J.-B., Robbins, T. W., … IMAGEN Consortium. (2012). Determinants of early alcohol use in healthy adolescents: The differential contribution of neuroimaging and psychological factors. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*, *37*(4), 986–995. https://doi.org/10.1038/npp.2011.282

Nees, F., Witt, S. H., Dinu-Biringer, R., Lourdusamy, A., Tzschoppe, J., Vollstädt-Klein, S., Millenet, S., Bach, C., Poustka, L., Banaschewski, T., Barker, G. J., Bokde, A. L. W., Bromberg, U., Büchel, C., Conrod, P. J., Frank, J., Frouin, V., Gallinat, J., Garavan, H., … IMAGEN consortium. (2015). BDNF Val66Met and reward-related brain function in adolescents: Role for early alcohol consumption. *Alcohol (Fayetteville, N.Y.)*, *49*(2), 103–110. https://doi.org/10.1016/j.alcohol.2014.12.004

Nestor, L. J., Behan, B., Suckling, J., & Garavan, H. (2019). Cannabis-dependent adolescents show differences in global reward-associated network topology: A functional connectomics approach. *Addiction Biology*, e12752. https://doi.org/10.1111/adb.12752

Newell, A. (1973). You can ’t play 20 questions with nature and win: Projective comments on the papers of this symposium. In *Visual Information Processing* (pp. 283–308). Elsevier. https://doi.org/10.1016/B978-0-12-170150-5.50012-3

Noble, S., Scheinost, D., & Constable, R. T. (2019). A decade of test-retest reliability of functional connectivity: A systematic review and meta-analysis. *NeuroImage*, *203*, 116157. https://doi.org/10.1016/j.neuroimage.2019.116157

Noble, W. S. (2009). How does multiple testing correction work? *Nature Biotechnology*, *27*(12), 1135–1137. https://doi.org/10.1038/nbt1209-1135

Oberauer, K., & Lewandowsky, S. (2019). Addressing the theory crisis in psychology. *Psychonomic Bulletin & Review*, *26*(5), 1596–1618. https://doi.org/10.3758/s13423-019-01645-2

Oldham, S., & Fornito, A. (2019). The development of brain network hubs. *Developmental Cognitive Neuroscience*, *36*. https://doi.org/10.1016/j.dcn.2018.12.005

Oldham, S., Murawski, C., Fornito, A., Youssef, G., Yücel, M., & Lorenzetti, V. (2018). The anticipation and outcome phases of reward and loss processing: A neuroimaging meta-analysis of the monetary incentive delay task. *Human Brain Mapping*, *39*(8), 3398–3418. https://doi.org/10.1002/hbm.24184

Op de Macks, Z. A., Bunge, S. A., Bell, O. N., Wilbrecht, L., Kriegsfeld, L. J., Kayser, A. S., & Dahl, R. E. (2016). Risky decision-making in adolescent girls: The role of pubertal hormones and reward circuitry. *Psychoneuroendocrinology*, *74*, 77–91. https://doi.org/10.1016/j.psyneuen.2016.08.013

Orman, G. K., & Labatut, V. (2009). A Comparison of Community Detection Algorithms on Artificial Networks. In J. Gama, V. S. Costa, A. M. Jorge, & P. B. Brazdil (Eds.), *Discovery Science* (pp. 242–256). Springer. https://doi.org/10.1007/978-3-642-04747-3_20

Padoa-Schioppa, C., & Conen, K. E. (2017). Orbitofrontal Cortex: A Neural Circuit for Economic Decisions. *Neuron*, *96*(4), 736–754. https://doi.org/10.1016/j.neuron.2017.09.031

Papanastasiou, E., Mouchlianitis, E., Joyce, D. W., McGuire, P., Banaschewski, T., Bokde, A. L. W., Bromberg, U., Büchel, C., Quinlan, E. B., Desrivières, S., Flor, H., Frouin, V., Garavan, H., Spechler, P., Gowland, P., Heinz, A., Ittermann, B., Martinot, J.-L., Paillère Martinot, M.-L., … IMAGEN Consortium. (2018). Examination of the Neural Basis of Psychoticlike Experiences in Adolescence During Reward Processing. *JAMA Psychiatry*, *75*(10), 1043–1051. https://doi.org/10.1001/jamapsychiatry.2018.1973

Park, H. R. P., Kostandyan, M., Boehler, C. N., & Krebs, R. M. (2018). Smiling faces and cash bonuses: Exploring common affective coding across positive and negative emotional and motivational stimuli using fMRI. *Cognitive, Affective, & Behavioral Neuroscience*, *18*(3), 550–563. https://doi.org/10.3758/s13415-018-0587-3

Parkes, L., Fulcher, B., Yücel, M., & Fornito, A. (2018). An evaluation of the efficacy, reliability, and sensitivity of motion correction strategies for resting-state functional MRI. *NeuroImage*, *171*, 415–436. https://doi.org/10.1016/j.neuroimage.2017.12.073

Paulus, M. P., Squeglia, L. M., Bagot, K., Jacobus, J., Kuplicki, R., Breslin, F. J., Bodurka, J., Morris, A. S., Thompson, W. K., Bartsch, H., & Tapert, S. F. (2019). Screen media activity and brain structure in youth: Evidence for diverse structural correlation networks from the ABCD study. *NeuroImage*, *185*, 140–153. https://doi.org/10.1016/j.neuroimage.2018.10.040

Paulus, M. P., & Thompson, W. K. (2019). The Challenges and Opportunities of Small Effects: The New Normal in Academic Psychiatry. *JAMA Psychiatry*, *76*(4), 353–354. https://doi.org/10.1001/jamapsychiatry.2018.4540

Pavlov, I. P. (1927). *Conditioned reflexes: An investigation of the physiological activity of the cerebral cortex* (pp. xv, 430). Oxford Univ. Press.

Payne, M. A. (2011). "All Gas and No Brakes!": Helpful Metaphor or Harmful Stereotype? *Journal of Adolescent Research*. https://doi.org/10.1177/0743558411412956

Peper, J. S., Koolschijn, P. C. M. P., & Crone, E. A. (2013). Development of Risk Taking: Contributions from Adolescent Testosterone and the Orbito-frontal Cortex. *Journal of Cognitive Neuroscience*, *25*(12), 2141–2150. https://doi.org/10.1162/jocn_a_00445

Pessoa, L. (2017). A Network Model of the Emotional Brain. *Trends in Cognitive Sciences*, *21*(5), 357–371. https://doi.org/10.1016/j.tics.2017.03.002

Pessoa, L. (2021). *Complex Systems: The Science of Interacting Parts*. OSF Preprints. https://doi.org/10.31219/osf.io/635tq

Pessoa, L., Medina, L., & Desfilis, E. (2022). Refocusing neuroscience: Moving away from mental categories and towards complex behaviours. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *377*(1844), 20200534. https://doi.org/10.1098/rstb.2020.0534

Peters, M. S., Demeter, E., Lustig, C., Bruno, J. P., & Sarter, M. (2011). Enhanced Control of Attention by Stimulating Mesolimbic–Corticopetal Cholinergic Circuitry. *Journal of Neuroscience*, *31*(26), 9760–9771. https://doi.org/10.1523/JNEUROSCI.1902-11.2011

Pfeifer, J. H., & Allen, N. B. (2012). Arrested development? Reconsidering dual-systems models of brain function in adolescence and disorders. *Trends in Cognitive Sciences*, *16*(6), 322–329. https://doi.org/10.1016/j.tics.2012.04.011

Pfeifer, J. H., & Allen, N. B. (2016). The audacity of specificity: Moving adolescent developmental neuroscience towards more powerful scientific paradigms and translatable models. *Developmental Cognitive Neuroscience*, *17*, 131–137. https://doi.org/10.1016/j.dcn.2015.12.012

Pfeifer, J. H., Flournoy, J., Cheng, T., Cosme, D., Flannery, J., Vijayakumar, N., Chavez, S., Jankowski, K., Byrne, M. L., & Macks, Z. O. (2019). *Improving Practices and Inferences in DCN*. https://osf.io/y9h8z/

Pfeifer, J. H., Masten, C. L., Moore, W. E., Oswald, T. M., Mazziotta, J. C., Iacoboni, M., & Dapretto, M. (2011). Entering Adolescence: Resistance to Peer Influence, Risky Behavior, and Neural Changes in Emotion Reactivity. *Neuron*, *69*(5). https://doi.org/10.1016/j.neuron.2011.02.019

Pinti, P., Scholkmann, F., Hamilton, A., Burgess, P., & Tachtsidis, I. (2019). Current Status and Issues Regarding Pre-processing of fNIRS Neuroimaging Data: An Investigation of Diverse Signal Filtering Methods Within a General Linear Model Framework. *Frontiers in Human Neuroscience*, *12*. https://doi.org/10.3389/fnhum.2018.00505

Plichta, M. M., Schwarz, A. J., Grimm, O., Morgen, K., Mier, D., Haddad, L., Gerdes, A. B. M., Sauer, C., Tost, H., Esslinger, C., Colman, P., Wilson, F., Kirsch, P., & Meyer-Lindenberg, A. (2012). Test–retest reliability of evoked BOLD signals from a cognitive–emotive fMRI test battery. *NeuroImage*, *60*(3), 1746–1758. https://doi.org/10.1016/j.neuroimage.2012.01.129

Poldrack, R. A. (2010). Mapping mental function to brain structure: How can cognitive neuroimaging succeed? *Perspectives on Psychological Science : A Journal of the*

*Association for Psychological Science*, *5*(5), 753–761. https://doi.org/10.1177/1745691610388777

Poldrack, R. A. (2017). Precision Neuroscience: Dense Sampling of Individual Brains. *Neuron*, *95*(4), 727–729. https://doi.org/10.1016/j.neuron.2017.08.002

Poldrack, R. A. (2019). The Costs of Reproducibility. *Neuron*, *101*(1), 11–14. https://doi.org/10.1016/j.neuron.2018.11.030

Poldrack, R. A., Laumann, T. O., Koyejo, O., Gregory, B., Hover, A., Chen, M.-Y., Gorgolewski, K. J., Luci, J., Joo, S. J., Boyd, R. L., Hunicke-Smith, S., Simpson, Z. B., Caven, T., Sochat, V., Shine, J. M., Gordon, E., Snyder, A. Z., Adeyemo, B., Petersen, S. E., … Mumford, J. A. (2015). Long-term neural and physiological phenotyping of a single human. *Nature Communications*, *6*(1), 8885. https://doi.org/10.1038/ncomms9885

Poldrack, R. A., & Yarkoni, T. (2016). From Brain Maps to Cognitive Ontologies: Informatics and the Search for Mental Structure. *Annual Review of Psychology*, *67*(1), 587–612. https://doi.org/10.1146/annurev-psych-122414-033729

Pons, P., & Latapy, M. (2005). Computing Communities in Large Networks Using Random Walks. In pInar Yolum, T. Güngör, F. Gürgen, & C. Özturan (Eds.), *Computer and Information Sciences—ISCIS 2005* (pp. 284–293). Springer. https://doi.org/10.1007/11569596_31

Posner, J., Russell, J. A., & Peterson, B. S. (2005). The circumplex model of affect: An integrative approach to affective neuroscience, cognitive development, and psychopathology. *Development and Psychopathology*, *17*(3), 715–734. https://doi.org/10.1017/S0954579405050340

Power, J. D., Mitra, A., Laumann, T. O., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2014). Methods to detect, characterize, and remove motion artifact in resting state fMRI. *NeuroImage*, *84*, 320–341. https://doi.org/10.1016/j.neuroimage.2013.08.048

Price, C. J., & Friston, K. J. (1997). Cognitive conjunction: A new approach to brain activation experiments. *NeuroImage*, *5*(4 Pt 1), 261–270. https://doi.org/10.1006/nimg.1997.0269

Price, C. J., & Friston, K. J. (2005). Functional ontologies for cognition: The systematic definition of structure and function. *Cognitive Neuropsychology*, *22*(3), 262–275. https://doi.org/10.1080/02643290442000095

Price, R. B., Beltz, A. M., Woody, M. L., Cummings, L., Gilchrist, D., & Siegle, G. J. (2020). Neural Connectivity Subtypes Predict Discrete Attentional-Bias Profiles Among Heterogeneous Anxiety Patients. *Clinical Psychological Science*, *8*(3), 491–505. https://doi.org/10.1177/2167702620906149

Proulx, T., & Morey, R. D. (2021). Beyond Statistical Ritual: Theory in Psychological Science. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science*, *16*(4), 671–681. https://doi.org/10.1177/17456916211017098

Puzzanchera, C. (2021). *Juvenile Arrests, 2019* (Juvenile Justice Statistics: National Report Series Bulletin, pp. 1–13). National Center for Juvenile Justice. https://ojjdp.ojp.gov/publications/juvenile-arrests-2019.pdf

Qu, Y., Fuligni, A. J., Galvan, A., & Telzer, E. H. (2015). Buffering effect of positive parent-child relationships on adolescent risk taking: A longitudinal neuroimaging investigation. *Developmental Cognitive Neuroscience*, *15*, 26–34. https://doi.org/10.1016/j.dcn.2015.08.005

R Core Team. (2019). *R: A language and environment for statistical computing.* R Foundation for Statistical Computing. https://www.R-project.org/

R Core Team. (2020). *R: A language and environment for statistical computing.* R Foundation for Statistical Computing. https://www.R-project.org/

Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., & Fusar-Poli, P. (2015). Ventral Striatal Activation During Reward Processing in Psychosis: A Neurofunctional Meta-Analysis. *JAMA Psychiatry*, *72*(12), 1243–1251. https://doi.org/10.1001/jamapsychiatry.2015.2196

Ram, N., & Grimm, K. J. (2009). Growth Mixture Modeling: A Method for Identifying Differences in Longitudinal Change Among Unobserved Groups. *International Journal of Behavioral Development*, *33*(6), 565–576. https://doi.org/10.1177/0165025409343765

Rangel, A., & Hare, T. (2010). Neural computations associated with goal-directed choice. *Current Opinion in Neurobiology*, *20*(2), 262–270. https://doi.org/10.1016/j.conb.2010.03.001

Rescorla, R. A., & Wagner, A. R. (1972). A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and non reinforcement. In *In AH. Black & W.F. Prokasy (eds.), Classical conditioning II: current research and theory* (pp. 64–99). Appleton-Century-Crofts.

Richards, J. M., Plate, R. C., & Ernst, M. (2013). A systematic review of fMRI reward paradigms used in studies of adolescents vs. adults: The impact of task design and implications for understanding neurodevelopment. *Neuroscience & Biobehavioral Reviews*, *37*(5), 976–991. https://doi.org/10.1016/j.neubiorev.2013.03.004

Richards, J. S., Arias Vásquez, A., von Rhein, D., van der Meer, D., Franke, B., Hoekstra, P. J., Heslenfeld, D. J., Oosterlaan, J., Faraone, S. V., Buitelaar, J. K., & Hartman, C. A. (2016). Adolescent behavioral and neural reward sensitivity: A test of the differential susceptibility theory. *Translational Psychiatry*, *6*, e771. https://doi.org/10.1038/tp.2016.37

Risk, B. B., Kociuba, M. C., & Rowe, D. B. (2018). Impacts of simultaneous multislice acquisition on sensitivity and specificity in fMRI. *NeuroImage*, *172*, 538–553. https://doi.org/10.1016/j.neuroimage.2018.01.078

Rogers, D. (1969). *Issues in Adolescent Psychology*. Appleton-Century-Crofts.

Rolls, E. T. (2014). Emotion and decision-making explained: A précis. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *59*, 185–193. https://doi.org/10.1016/j.cortex.2014.01.020

Romer, D. (2010). Adolescent Risk Taking, Impulsivity, and Brain Development: Implications for Prevention. *Developmental Psychobiology*, *52*(3), 263–276. https://doi.org/10.1002/dev.20442

Romer, D., Reyna, V. F., & Satterthwaite, T. D. (2017). Beyond stereotypes of adolescent risk taking: Placing the adolescent brain in developmental context. *Developmental Cognitive Neuroscience*, *27*, 19–34. https://doi.org/10.1016/j.dcn.2017.07.007

Roy, M., Shohamy, D., & Wager, T. D. (2012). Ventromedial prefrontal-subcortical systems and the generation of affective meaning. *Trends in Cognitive Sciences*, *16*(3), 147–156. https://doi.org/10.1016/j.tics.2012.01.005

Rubin, D. B. (1976). Inference and missing data. *Biometrika*, *63*(3), 581–592. https://doi.org/10.1093/biomet/63.3.581

Rubin, M. (2021). When to adjust alpha during multiple testing: A consideration of disjunction, conjunction, and individual testing. *Synthese*. https://doi.org/10.1007/s11229-021-03276-4

Ruck, M. D., Keating, D. P., Saewyc, E. M., Earls, F., & Ben-Arieh, A. (2016). The United Nations Convention on the Rights of the Child: Its Relevance for Adolescents. *Journal of Research on Adolescence*, *26*(1), 16–29. https://doi.org/10.1111/jora.12172

Russell, J. A., & Bullock, M. (1985). Multidimensional scaling of emotional facial expressions: Similarity from preschoolers to adults. *Journal of Personality and Social Psychology*, *48*(5), 1290–1298. https://doi.org/10.1037/0022-3514.48.5.1290

Samaha, A.-N., Khoo, S. Y.-S., Ferrario, C. R., & Robinson, T. E. (2021). Dopamine 'ups and downs' in addiction revisited. *Trends in Neurosciences*, *0*(0). https://doi.org/10.1016/j.tins.2021.03.003

Sameroff, A. (2010). A Unified Theory of Development: A Dialectic Integration of Nature and Nurture. *Child Development*, *81*(1), 6–22. https://doi.org/10.1111/j.1467-8624.2009.01378.x

Sauder, C. L., Derbidge, C. M., & Beauchaine, T. P. (2016). Neural responses to monetary incentives among self-injuring adolescent girls. *Development and Psychopathology*, *28*(1), 277–291. https://doi.org/10.1017/S0954579415000449

Sawyer, S. M., Azzopardi, P. S., Wickremarathne, D., & Patton, G. C. (2018). The age of adolescence. *The Lancet. Child & Adolescent Health*, *2*(3), 223–228. https://doi.org/10.1016/S2352-4642(18)30022-1

Saxbe, D., Piero, L. D., Immordino-Yang, M. H., Kaplan, J., & Margolin, G. (2015). Neural correlates of adolescents' viewing of parents' and peers' emotions: Associations with risk-taking behavior and risky peer affiliations. *Social Neuroscience*, *10*(6), 592–604. https://doi.org/10.1080/17470919.2015.1022216

Schäfer, T., & Schwarz, M. A. (2019). The Meaningfulness of Effect Sizes in Psychological Research: Differences Between Sub-Disciplines and the Impact of Potential Biases. *Frontiers in Psychology*, *10*. https://doi.org/10.3389/fpsyg.2019.00813

Schouppe, N., Demanet, J., Boehler, C. N., Ridderinkhof, K. R., & Notebaert, W. (2014). The role of the striatum in effort-based decision-making in the absence of reward. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *34*(6), 2148–2154. https://doi.org/10.1523/JNEUROSCI.1214-13.2014

Schultz, W. (1998). Predictive reward signal of dopamine neurons. *Journal of Neurophysiology*, *80*(1), 1–27. https://doi.org/10.1152/jn.1998.80.1.1

Schultz, W. (2015). Neuronal Reward and Decision Signals: From Theories to Data. *Physiological Reviews*, *95*(3), 853–951. https://doi.org/10.1152/physrev.00023.2014

Schumann, G., Loth, E., Banaschewski, T., Barbot, A., Barker, G., Büchel, C., Conrod, P. J., Dalley, J. W., Flor, H., Gallinat, J., Garavan, H., Heinz, A., Itterman, B., Lathrop, M., Mallik, C., Mann, K., Martinot, J.-L., Paus, T., Poline, J.-B., … IMAGEN consortium. (2010). The IMAGEN study: Reinforcement-related behaviour in normal brain function and psychopathology. *Molecular Psychiatry*, *15*(12), 1128–1139. https://doi.org/10.1038/mp.2010.4

Schwartz, K. T. G., Kryza-Lacombe, M., Liuzzi, M. T., Weersing, V. R., & Wiggins, J. L. (2019). Social and Non-social Reward: A Preliminary Examination of Clinical Improvement and Neural Reactivity in Adolescents Treated With Behavioral Therapy for Anxiety and Depression. *Frontiers in Behavioral Neuroscience*, *13*. https://doi.org/10.3389/fnbeh.2019.00177

Science, A. A. for the A. of. (1998). Next, the Decade of Behavior? *Science*, *279*(5349), 311–311. https://doi.org/10.1126/science.279.5349.311d

Serlin, R. C., & Lapsley, D. K. (1985). Rationality in psychological research: The good-enough principle. *American Psychologist*, *40*(1), 73–83. https://doi.org/10.1037/0003-066X.40.1.73

Shadish, W. R., Cook, T. D., & Campbell, D. T. (2002). *Experimental and quasi-experimental designs for generalized causal inference* (pp. xxi, 623). Houghton, Mifflin and Company.

Sheehan, P., Sweeny, K., Rasmussen, B., Wils, A., Friedman, H. S., Mahon, J., Patton, G. C., Sawyer, S. M., Howard, E., Symons, J., Stenberg, K., Chalasani, S., Maharaj, N., Reavley, N., Shi, H., Fridman, M., Welsh, A., Nsofor, E., & Laski, L. (2017). Building the foundations for sustainable development: A case for global investment in the capabilities of adolescents. *The Lancet*, *390*(10104), 1792–1806. https://doi.org/10.1016/S0140-6736(17)30872-3

Sherman, L., Steinberg, L., & Chein, J. (2018). Connecting brain responsivity and real-world risk taking: Strengths and limitations of current methodological approaches. *Developmental Cognitive Neuroscience*, *33*, 27–41. https://doi.org/10.1016/j.dcn.2017.05.007

Shulman, E. P., Smith, A. R., Silva, K., Icenogle, G., Duell, N., Chein, J., & Steinberg, L. (2016). The dual systems model: Review, reappraisal, and reaffirmation. *Developmental Cognitive Neuroscience*, *17*, 103–117. https://doi.org/10.1016/j.dcn.2015.12.010

Siegel, J. S., Power, J. D., Dubis, J. W., Vogel, A. C., Church, J. A., Schlaggar, B. L., & Petersen, S. E. (2014). Statistical improvements in functional magnetic resonance imaging analyses produced by censoring high-motion data points. *Human Brain Mapping*, *35*(5), 1981–1996. https://doi.org/10.1002/hbm.22307

Silverman, M. H., Jedd, K., & Luciana, M. (2015). Neural networks involved in adolescent reward processing: An activation likelihood estimation meta-analysis of functional neuroimaging studies. *NeuroImage*, *122*, 427–439. https://doi.org/v

Simmons, J. P., Nelson, L. D., & Simonsohn, U. (2011). False-positive psychology: Undisclosed flexibility in data collection and analysis allows presenting anything as significant. *Psychological Science*, *22*(11), 1359–1366. https://doi.org/10.1177/0956797611417632

Smith, K. E., & Pollak, S. D. (2020). Rethinking Concepts and Categories for Understanding the Neurodevelopmental Effects of Childhood Adversity. *Perspectives on Psychological Science*, 1745691620920725. https://doi.org/10.1177/1745691620920725

Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping*, *17*(3), 143–155. https://doi.org/10.1002/hbm.10062

Smith, S. M., Miller, K. L., Salimi-Khorshidi, G., Webster, M., Beckmann, C. F., Nichols, T. E., Ramsey, J. D., & Woolrich, M. W. (2011). Network modelling methods for FMRI. *NeuroImage*, *54*(2), 875–891. https://doi.org/10.1016/j.neuroimage.2010.08.063

Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage*, *44*(1), 83–98. https://doi.org/10.1016/j.neuroimage.2008.03.061

Snow, J. C., & Culham, J. C. (2021). The Treachery of Images: How Realism Influences Brain and Behavior. *Trends in Cognitive Sciences*, *25*(6), 506–519. https://doi.org/10.1016/j.tics.2021.02.008

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Il Shin, J., Kirkbride, J. B., Jones, P., Kim, J. H., Kim, J. Y., Carvalho, A. F., Seeman, M. V., Correll, C. U., & Fusar-Poli, P. (2021). Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry*, 1–15. https://doi.org/10.1038/s41380-021-01161-7

Spear, L. P. (2000). The adolescent brain and age-related behavioral manifestations. *Neuroscience and Biobehavioral Reviews*, *24*(4), 417–463.
Spear, L. P. (2011). Rewards, aversions and affect in adolescence: Emerging convergences across laboratory animal and human data. *Developmental Cognitive Neuroscience*, *1*(4), 390–403. https://doi.org/10.1016/j.dcn.2011.08.001
Steegen, S., Tuerlinckx, F., Gelman, A., & Vanpaemel, W. (2016). Increasing Transparency Through a Multiverse Analysis: *Perspectives on Psychological Science*. https://doi.org/10.1177/1745691616658637
Steinberg, L. (2008). A Social Neuroscience Perspective on Adolescent Risk-Taking. *Developmental Review: DR*, *28*(1), 78–106. https://doi.org/10.1016/j.dr.2007.08.002
Steinberg, L. (2010). A dual systems model of adolescent risk-taking. *Developmental Psychobiology*, *52*(3), 216–224. https://doi.org/10.1002/dev.20445
Steinberg, L. (2013). The influence of neuroscience on US Supreme Court decisions about adolescents' criminal culpability. *Nature Reviews Neuroscience*, *14*(7), 513–518. https://doi.org/10.1038/nrn3509
Steinberg, L. (2017). Adolescent brain science and juvenile justice policymaking. *Psychology, Public Policy, and Law*, *23*(4), 410–420. https://doi.org/10.1037/law0000128
Steinberg, L., & Cauffman, E. (1996). Maturity of judgment in adolescence: Psychosocial factors in adolescent decision making. *Law and Human Behavior*, *20*(3), 249–272. https://doi.org/10.1007/BF01499023
Steinberg, L., & Icenogle, G. (2019). Using Developmental Science to Distinguish Adolescents and Adults Under the Law. *Annual Review of Developmental Psychology*, *1*(1), 21–40. https://doi.org/10.1146/annurev-devpsych-121318-085105
Steinberg, L., Icenogle, G., Shulman, E. P., Breiner, K., Chein, J., Bacchini, D., Chang, L., Chaudhary, N., Giunta, L. D., Dodge, K. A., Fanti, K. A., Lansford, J. E., Malone, P. S., Oburu, P., Pastorelli, C., Skinner, A. T., Sorbring, E., Tapanya, S., Tirado, L. M. U., … Takash, H. M. S. (2018). Around the world, adolescence is a time of heightened sensation seeking and immature self-regulation. *Developmental Science*, *21*(2). https://doi.org/10.1111/desc.12532
Steinberg, L., Sharp, C., Stanford, M. S., & Tharp, A. T. (2013). New tricks for an old measure: The development of the Barratt Impulsiveness Scale-Brief (BIS-Brief). *Psychological Assessment*, *25*(1), 216–226. https://doi.org/10.1037/a0030550
Stevens, M. C., Pearlson, G. D., Calhoun, V. D., & Bessette, K. L. (2018). Functional Neuroimaging Evidence for Distinct Neurobiological Pathways in Attention-Deficit/Hyperactivity Disorder. *Biological Psychiatry. Cognitive Neuroscience and Neuroimaging*, *3*(8), 675–685. https://doi.org/10.1016/j.bpsc.2017.09.005
Stevenson, R. A., Mikels, J. A., & James, T. W. (2007). Characterization of the Affective Norms for English Words by discrete emotional categories. *Behavior Research Methods*, *39*(4), 1020–1024. https://doi.org/10.3758/BF03192999
Strauss, M. E., & Smith, G. T. (2009). Construct validity: Advances in theory and methodology. *Annual Review of Clinical Psychology*, *5*, 1–25. https://doi.org/10.1146/annurev.clinpsy.032408.153639
Substance Abuse and Mental Health Services Administration. (2020). *Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health* ((HHS Publication No. PEP20-07-01-001, NSDUH Series H-55)).

Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/

Suzuki, S., Lawlor, V. M., Cooper, J. A., Arulpragasam, A. R., & Treadway, M. T. (2020). Distinct regions of the striatum underlying effort, movement initiation and effort discounting. *Nature Human Behaviour*, 1–11. https://doi.org/10.1038/s41562-020-00972-y

Swartz, J. R., Weissman, D. G., Ferrer, E., Beard, S. J., Fassbender, C., Robins, R. W., Hastings, P. D., & Guyer, A. E. (2019). Reward-Related Brain Activity Prospectively Predicts Increases in Alcohol Use in Adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*. https://doi.org/10.1016/j.jaac.2019.05.022

Szczepanski, S. M., & Knight, R. T. (2014). Insights into human behavior from lesions to the prefrontal cortex. *Neuron*, *83*(5), 1002–1018. https://doi.org/10.1016/j.neuron.2014.08.011

Szucs, D., & Ioannidis, J. P. A. (2017). Empirical assessment of published effect sizes and power in the recent cognitive neuroscience and psychology literature. *PLOS Biology*, *15*(3), e2000797. https://doi.org/10.1371/journal.pbio.2000797

Szucs, D., & Ioannidis, J. PA. (2020). Sample size evolution in neuroimaging research: An evaluation of highly-cited studies (1990–2012) and of latest practices (2017–2018) in high-impact journals. *NeuroImage*, *221*, 117164. https://doi.org/10.1016/j.neuroimage.2020.117164

Tapia León, I., Kruse, O., Stark, R., & Klucken, T. (2019). Relationship of sensation seeking with the neural correlates of appetitive conditioning. *Social Cognitive and Affective Neuroscience*, *14*(7), 769–775. https://doi.org/10.1093/scan/nsz046

Telzer, E. H., Fuligni, A. J., Lieberman, M. D., Miernicki, M. E., & Galván, A. (2015). The quality of adolescents' peer relationships modulates neural sensitivity to risk taking. *Social Cognitive and Affective Neuroscience*, *10*(3), 389–398. https://doi.org/10.1093/scan/nsu064

Tervo-Clemmens, B., Quach, A., Calabro, F. J., Foran, W., & Luna, B. (2020). Meta-analysis and review of functional neuroimaging differences underlying adolescent vulnerability to substance use. *NeuroImage*, *209*, 116476. https://doi.org/10.1016/j.neuroimage.2019.116476

Thompson, W. H., Wright, J., & Bissett, P. G. (2020). Open exploration. *ELife*, *9*, e52157. https://doi.org/10.7554/eLife.52157

Urošević, S., Luciana, M., Jensen, J. B., Youngstrom, E. A., & Thomas, K. M. (2016). Age associations with neural processing of reward anticipation in adolescents with bipolar disorders. *NeuroImage. Clinical*, *11*, 476–485. https://doi.org/10.1016/j.nicl.2016.03.013

U.S. Census Bureau. (2019). *American Community Survey Data: 5-Year Estimates Data Profiles*. Census.Gov. https://www.census.gov/programs-surveys/acs/data.html

van den Bergh, D., Haaf, J. M., Ly, A., Rouder, J. N., & Wagenmakers, E. (2019). *A Cautionary Note on Estimating Effect Size.* https://doi.org/10.31234/osf.io/h6pr8

van Hulst, B. M., de Zeeuw, P., Lupas, K., Bos, D. J., Neggers, S. F. W., & Durston, S. (2015). Reward Anticipation in Ventral Striatum and Individual Sensitivity to Reward: A Pilot Study of a Child-Friendly fMRI Task. *PloS One*, *10*(11), e0142413. https://doi.org/10.1371/journal.pone.0142413

Van Leijenhorst, L., Gunther Moor, B., Op de Macks, Z. A., Rombouts, S. A. R. B., Westenberg, P. M., & Crone, E. A. (2010). Adolescent risky decision-making: Neurocognitive

development of reward and control regions. *NeuroImage*, *51*(1), 345–355. https://doi.org/10.1016/j.neuroimage.2010.02.038

Van Leijenhorst, L., Zanolie, K., Van Meel, C. S., Westenberg, P. M., Rombouts, S. A. R. B., & Crone, E. A. (2010). What motivates the adolescent? Brain regions mediating reward sensitivity across adolescence. *Cerebral Cortex (New York, N.Y.: 1991)*, *20*(1), 61–69. https://doi.org/10.1093/cercor/bhp078

Varoquaux, G. (2018). Cross-validation failure: Small sample sizes lead to large error bars. *NeuroImage*, *180*, 68–77. https://doi.org/10.1016/j.neuroimage.2017.06.061

Vasishth, S., Mertzen, D., Jäger, L. A., & Gelman, A. (2018). The statistical significance filter leads to overoptimistic expectations of replicability. *Journal of Memory and Language*, *103*, 151–175. https://doi.org/10.1016/j.jml.2018.07.004

Vassena, E., Deraeve, J., & Alexander, W. H. (2020). Surprise, value and control in anterior cingulate cortex during speeded decision-making. *Nature Human Behaviour*, 1–11. https://doi.org/10.1038/s41562-019-0801-5

Veroude, K., von Rhein, D., Chauvin, R. J. M., van Dongen, E. V., Mennes, M. J. J., Franke, B., Heslenfeld, D. J., Oosterlaan, J., Hartman, C. A., Hoekstra, P. J., Glennon, J. C., & Buitelaar, J. K. (2016). The link between callous-unemotional traits and neural mechanisms of reward processing: An fMRI study. *Psychiatry Research. Neuroimaging*, *255*, 75–80. https://doi.org/10.1016/j.pscychresns.2016.08.005

Volkow, N. D., Koob, G. F., Croyle, R. T., Bianchi, D. W., Gordon, J. A., Koroshetz, W. J., Pérez-Stable, E. J., Riley, W. T., Bloch, M. H., Conway, K., Deeds, B. G., Dowling, G. J., Grant, S., Howlett, K. D., Matochik, J. A., Morgan, G. D., Murray, M. M., Noronha, A., Spong, C. Y., … Weiss, S. R. B. (2018). The conception of the ABCD study: From substance use to a broad NIH collaboration. *Developmental Cognitive Neuroscience*, *32*, 4–7. https://doi.org/10.1016/j.dcn.2017.10.002

Volkow, N. D., Wang, G.-J., Fowler, J. S., Tomasi, D., Telang, F., & Baler, R. (2010). Addiction: Decreased reward sensitivity and increased expectation sensitivity conspire to overwhelm the brain's control circuit. *BioEssays : News and Reviews in Molecular, Cellular and Developmental Biology*, *32*(9), 748–755. https://doi.org/10.1002/bies.201000042

von Rhein, D., Cools, R., Zwiers, M. P., van der Schaaf, M., Franke, B., Luman, M., Oosterlaan, J., Heslenfeld, D. J., Hoekstra, P. J., Hartman, C. A., Faraone, S. V., van Rooij, D., van Dongen, E. V., Lojowska, M., Mennes, M., & Buitelaar, J. (2015). Increased neural responses to reward in adolescents and young adults with attention-deficit/hyperactivity disorder and their unaffected siblings. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(5), 394–402. https://doi.org/10.1016/j.jaac.2015.02.012

Vul, E., Harris, C., Winkielman, P., & Pashler, H. (2009). Puzzlingly High Correlations in fMRI Studies of Emotion, Personality, and Social Cognition. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science*, *4*(3), 274–290. https://doi.org/10.1111/j.1745-6924.2009.01125.x

Wan, Z., Rolls, E. T., Cheng, W., & Feng, J. (2020). Sensation-seeking is related to functional connectivities of the medial orbitofrontal cortex with the anterior cingulate cortex. *NeuroImage*, 116845. https://doi.org/10.1016/j.neuroimage.2020.116845

Weigard, A., Beltz, A., Reddy, S. N., & Wilson, S. J. (2018). Characterizing the role of the pre-SMA in the control of speed/accuracy trade-off with directed functional connectivity

mapping and multiple solution reduction. *Human Brain Mapping*, *40*(6), 1829–1843. https://doi.org/10.1002/hbm.24493

Weiland, B. J., Welsh, R. C., Yau, W.-Y. W., Zucker, R. A., Zubieta, J.-K., & Heitzeg, M. M. (2013). Accumbens functional connectivity during reward mediates sensation-seeking and alcohol use in high-risk youth. *Drug and Alcohol Dependence*, *128*(1), 130–139. https://doi.org/10.1016/j.drugalcdep.2012.08.019

Westbrook, A., & Braver, T. S. (2016). Dopamine Does Double Duty in Motivating Cognitive Effort. *Neuron*, *89*(4), 695–710. https://doi.org/10.1016/j.neuron.2015.12.029

White, J. L., Moffitt, T. E., Caspi, A., Bartusch, D. J., Needles, D. J., & Stouthamer-Loeber, M. (1994). Measuring impulsivity and examining its relationship to delinquency. *Journal of Abnormal Psychology*, *103*(2), 192–205. https://doi.org/10.1037//0021-843x.103.2.192

Willoughby, T., Good, M., Adachi, P. J. C., Hamza, C., & Tavernier, R. (2013). Examining the link between adolescent brain development and risk taking from a social-developmental perspective. *Brain and Cognition*, *83*(3), 315–323. https://doi.org/10.1016/j.bandc.2013.09.008

Wilson, R. P., Colizzi, M., Bossong, M. G., Allen, P., Kempton, M., Abe, N., Barros-Loscertales, A. R., Bayer, J., Beck, A., Bjork, J., Boecker, R., Bustamante, J. C., Choi, J. S., Delmonte, S., Dillon, D., Figee, M., Garavan, H., Hagele, C., Hermans, E. J., … MTAC. (2018). The Neural Substrate of Reward Anticipation in Health: A Meta-Analysis of fMRI Findings in the Monetary Incentive Delay Task. *Neuropsychology Review*, *28*(4), 496–506. https://doi.org/10.1007/s11065-018-9385-5

Winkler, A. M., Ridgway, G. R., Webster, M. A., Smith, S. M., & Nichols, T. E. (2014). Permutation inference for the general linear model. *NeuroImage*, *92*, 381–397. https://doi.org/10.1016/j.neuroimage.2014.01.060

Witte, J. S. (2010). Genome-Wide Association Studies and Beyond. *Annual Review of Public Health*, *31*, 9–20. https://doi.org/10.1146/annurev.publhealth.012809.103723

Woo, C.-W., Chang, L. J., Lindquist, M. A., & Wager, T. D. (2017). Building better biomarkers: Brain models in translational neuroimaging. *Nature Neuroscience*, *20*(3), 365–377. https://doi.org/10.1038/nn.4478

Woolrich, M. W., Ripley, B. D., Brady, M., & Smith, S. M. (2001). Temporal autocorrelation in univariate linear modeling of FMRI data. *NeuroImage*, *14*(6), 1370–1386. https://doi.org/10.1006/nimg.2001.0931

Wu, C. C., Samanez-Larkin, G. R., Katovich, K., & Knutson, B. (2014). Affective traits link to reliable neural markers of incentive anticipation. *NeuroImage*, *84*, 279–289. https://doi.org/10.1016/j.neuroimage.2013.08.055

Xu, B., Jia, T., Macare, C., Banaschewski, T., Bokde, A. L. W., Bromberg, U., Büchel, C., Cattrell, A., Conrod, P. J., Flor, H., Frouin, V., Gallinat, J., Garavan, H., Gowland, P., Heinz, A., Ittermann, B., Martinot, J.-L., Paillère Martinot, M.-L., Nees, F., … IMAGEN Consortium. (2017). Impact of a Common Genetic Variation Associated With Putamen Volume on Neural Mechanisms of Attention-Deficit/Hyperactivity Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *56*(5), 436-444.e4. https://doi.org/10.1016/j.jaac.2017.02.009

Yarkoni, T. (2009). Big Correlations in Little Studies: Inflated fMRI Correlations Reflect Low Statistical Power-Commentary on Vul et al. (2009). *Perspectives on Psychological Science: A Journal of the Association for Psychological Science*, *4*(3), 294–298. https://doi.org/10.1111/j.1745-6924.2009.01127.x

Yarkoni, T. (2020). The generalizability crisis. *Behavioral and Brain Sciences*, 1–37. https://doi.org/10.1017/S0140525X20001685

Yip, S. W., Kiluk, B., & Scheinost, D. (2019). Toward Addiction Prediction: An Overview of Cross-Validated Predictive Modeling Findings and Considerations for Future Neuroimaging Research. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. https://doi.org/10.1016/j.bpsc.2019.11.001

Zhang, Y., Padmanabhan, A., Gross, J. J., & Menon, V. (2019). Development of Human Emotion Circuits Investigated Using a Big-Data Analytic Approach: Stability, Reliability, and Robustness. *Journal of Neuroscience*, *39*(36), 7155–7172. https://doi.org/10.1523/JNEUROSCI.0220-19.2019

Zucker, R. A., Fitzgerald, H. E., Refior, S. K., Puttler, L. I., Pallas, D. M., & Ellis, D. A. (2000). In H. E. Fitzgerald, B. M. Lester, & B. S. Zuckerman (Eds.), *Children of Addiction: Research, Health, and Public Policy Issues* (pp. 109–141). Taylor & Francis.

Zuckerman, M. (1979). Sensation Seeking and Risk Taking. In C. E. Izard (Ed.), *Emotions in Personality and Psychopathology* (pp. 161–197). Springer US. https://doi.org/10.1007/978-1-4613-2892-6_7

Zuckerman, M. S., Eysenck, S. B. G., & Eysenck, H. J. (1978). Sensation seeking in England and America: Cross-cultural, age, and sex comparisons. *Journal of Consulting and Clinical Psychology*, *46*(1), 139–149. https://doi.org/10.1037/0022-006x.46.1.139