Neuroeconomic Predictors of Adolescent Risky Decision-Making

Nina Lauharatanahirun

Dissertation submitted to the faculty of the Virginia Polytechnic Institute and State University in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Psychology

Brooks King-Casas, Chair

Sheryl B. Ball

Pearl Chiu

Jungmeen Kim-Spoon

November 21, 2017

Blacksburg, VA

Keywords: adolescence; risky decision-making; fMRI; individual differences; longitudinal

Neuroeconomic Predictors of Adolescent Risky Decision-Making

Nina Lauharatanahirun

ABSTRACT

Adolescence is a critical developmental period characterized by neurobiological changes and exposure to novel experiences. According to the Center for Disease Control, approximately 70% of adolescent deaths in the United States are due to risky behaviors such as reckless driving and risky sexual behavior (Kann et al., 2016). In order to better understand what drives adolescent risk-taking, the current studies utilized an interdisciplinary approach, which combined behavioral economic models and functional magnetic resonance imaging (fMRI) to understand neurobehavioral mechanisms of risky choice. The focus of the current studies is to investigate the extent to which neurobehavioral mechanisms of risky choice change across adolescence, and to identify individual differences that explain real-world risky behavior. In Study 1, we show that behavioral sensitivity to risk and neural correlates of risk processing change across a critical period of adolescence. Importantly, our results indicate that individual differences in neural, not behavioral risk sensitivity are predictive of future engagement in health risk behaviors. In Study 2, we examined the relation between inter-individual differences in adolescent expectations of valued rewards and self-reported risky behavior using an adapted behavioral economic model. Implications and future directions for adolescent risky decision-making are discussed.

Neuroeconomic Predictors of Adolescent Risky Decision-Making

Nina Lauharatanahirun

GENERAL AUDIENCE ABSTRACT

According to the Center for Disease Control, approximately 70% of adolescent deaths in the United States are due to risky behaviors such as reckless driving and risky sexual behavior (Kann et al., 2016). In order to prevent and reduce such risk-taking behavior during adolescence, it is essential to improve our current understanding of the mechanisms contributing to risky decision-making. One promising mechanism that may be critical in guiding adolescents either toward or away from risky behavior is the extent to which adolescents are sensitive to the *risk* or likelihood of receiving potential rewarding outcomes. To this end, the current work leveraged the used of a longitudinal design with an interdisciplinary approach that combined the use of behavioral economic models, functional magnetic resonance imaging (fMRI), and developmental psychological theory to better understand how adolescents develop risk sensitivity at both the behavioral and neural levels. Importantly, our results in Study 1 indicated that individual differences in neural, not behavioral risk sensitivity are predictive of future engagement in health risk behaviors. In Study 2, we used an adapted behavioral economic model to identify individual differences in adolescent expectations of valued rewards, and assess the relation of these differences to self-reported risky behavior. This research illuminates the critical role that neurobehavioral risk sensitivity might play during risky decision-making, which may have implications for the prevention and amelioration of adverse health risk behaviors.

Dedication

For my Mom and brother, Timmy

Acknowledgements

First, I would like to thank my advisor, Dr. Brooks King-Casas, for initially taking me on as a research assistant at BCM and then as his first graduate student at VT. He challenged me to think and reach beyond what I thought I was capable of, always made himself available to discuss research (even when there was a grant due), and has generously supported my research ideas, which always seemed to end with a motivational mantra of "Go Team!" I would also like to express my deepest gratitude to my committee members, Dr. Pearl Chiu, Dr. Sheryl Ball, and Dr. Jungmeen Kim-Spoon, for providing me with mentorship, research and professional guidance, help with statistical analyses, stimulating discussions, and motivating me to push forward even when it felt impossible. Thank you also to the adolescents and parents who participated in these studies and made this research possible.

Thank you to my lab, especially Katie McCurry, for always brightening up our work buddy sessions with Starbucks, candy, and providing reminders that it's okay to take breaks. To my BCM lab mates and friends, Jessica, Kat, Dharol, and LaRaun, thank you for cheering me on from afar. I am very fortunate to have found lifelong friends in my graduate school cohort at VT. To Caitlin Conner and Amber Turner, thank you for providing never ending support and encouragement, immediately answering my g-chat messages, and helping me get through all of the work by sending me texts, memes, reminders to eat, and lots of laughs. Graduate school would not have been the same without you two, and I am grateful for your friendship.

There are many people, who have served as cheerleaders and mentors throughout this process. To my IMSD family, especially Dr. Anne McNabb and Dr. Ed Smith, thank you for your constant support, homemade lunches, and never forgetting to check in with me. Thank you to all those at VTCRI who have felt more like family over the years rather than colleagues, I feel

so lucky to be supported by so many. To my California family (Michelle, Lani, Harmony, Steve, Kyle, Cody, Christian, Amanda, Grandma Jean, Nolan, Natalie) who have always dropped everything that they have going on to make an effort to see me when I visit, thank you for unconditionally loving and supporting me despite my aspirations of becoming a scientist taking me far away from home.

Last but certainly not least, thank you to my family and friends who had absolutely no doubt and wholehearted belief that I could do this. To my Mom, and brother, Timmy, thank you for your immeasurable and unending love and support. To Derek, thank you for being my loyal partner, reading over anything I write, answering my statistics questions, and enjoying food as much as I do. Thank you to Cari and Lauren, for your surprise visits, phone calls, daily check-ins, shopping trips, and texts, which have been immensely helpful during this process.

Table of Contents

Introduction

Adolescence is a transformative period during which significant neurobiological changes occur. It is also a time when propensity for increases with highest levels of risky behavior occurring between the ages of 13 and 16 (Burnett, Bault, Coricelli, & Blakemore, 2010; Steinberg, 2008). Risk-taking during adolescence, including substance use, risky sexual behavior, and delinquency, dramatically increase vulnerability to current and future psychopathology. It has been theorized that consequences of risk-taking produce cascading effects that accumulate over time producing long-lasting alterations on health and development (Masten & Ciccheti, 2010).

Given the potential impact of risk-taking during adolescence and subsequently adulthood, it is critical to develop effective prevention and intervention strategies to help adolescents make better decisions. To create such strategies, it is essential to first improve our current understanding of the psychological and neural processes driving adolescent risk-taking behavior while also identifying individual differences that may emerge. Previous research indicates that although adolescence is a critical transitional period for all, there are some adolescents who may be more vulnerable to risk-taking than others (Bjork & Pardini, 2015; Willoughby, Good, Adachi, Hamza, & Tavernier, 2013). Discovery of the behavioral and neural correlates of risky decision-making in adults has been advanced by the use of model-based approaches allowing for the explicit specification of elements contributing to risky choice (Chistopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009; Huettel, 2006; Tobler, O'Doherty, Dolan, & Schultz,, 2007; for review see Weber & Johnson, 2008). Decomposing decision-making processes permits identification of the specific processes that might be altered.

More recently, developmental researchers have taken advantage of methodology used in economics and decision sciences to uncover decision-making processes during adolescence (Blankenstein, Crone, van den Bos, & van Duijvenvoorde, 2016; 2017; Tymula et al., 2012; van Duijvenvoorde& Crone, 2013), but these studies have primarily been cross-sectional limiting inferences regarding intra-individual change over time. Furthermore, extant literature focuses on adolescents' neurobehavioral sensitivity to reward values rather than sensitivity to risk (Barkley-Levenson & Galvan, 2014; Braams, van Duijvenvoorde, Peper, & Crone, 2015; Galvan et al., 2006; Silverman, Jedd, & Luciana, 2015; van Leijenhorst et al., 2010), even though it is well-known that both sensitivity to reward values and the risks associated with such rewards contribute to individual differences in risky choice (d'Acremont & Bossaerts, 2008; Huettel, 2006; Tobler, O'Doherty, Dolan, & Schultz, 2007).

To address this gap, the present study aims to examine inter-individual differences and intra-individual change in both behavioral risk sensitivity and neural correlates of risk processing during adolescence. Specific aims can be summarized as the following: (i) to identify how behavioral and neural risk sensitivity change during adolescence; (ii) to determine whether either behavioral or neural markers of risk can be used to predict future risk-taking; and (iii) to test an adapted model of risky decision-making to identify potential individual differences that may be related to real-world risky behavior.

Background

Defining Adolescence

Defining the age range that represents adolescence has been debated in the literature especially given the vast societal and cultural differences that exist. However, in Western societies, there is a consensus that adolescence approximately spans 10 to 22 years of age

(Blakemore & Robbins, 2012; Crone & Dahl, 2012). The onset of adolescence begins with the inception of puberty, a process during which physiological and neurobiological changes occur resulting in the capacity to reproduce (Dahl, 2004). However, physical changes associated with puberty do not solely encapsulate the period adolescence. Adolescence is representative of a critical transition period from childhood to adulthood, in which social roles evolve from being reliant on caretakers to becoming independent and responsible for one's behaviors (Crone & Dahl, 2012; Dahl, 2004). In Western societies, the period of adolescence typically includes the transition from middle school to high school and from high school into college (Crone & Dahl, 2012; Shulman et al., 2016).

The rapid increase of gonadal hormones during puberty has also been shown to produce significant neurobiological changes on both brain structure and function (Peper & Dahl, 2013; Raznahan et al., 2010). In particular, adolescence is associated with a decrease in the formation of new synapses, increased myelination, and an increase in white matter suggesting the strengthening of existing synaptic connections (Benes, 1989; Casey, Giedd, & Thomas, 2000; Huttenlocher, 1990). Not surprisingly, the prefrontal cortex, a brain area implicated in the support of complex cognitive functions, is one of the last brain regions to mature (Giedd, 2004). Concurrent with the maturation of brain structures, increased capacity for both cognitive (e.g., attention, memory) and social cognitive (e.g., processing emotions) functioning increases throughout adolescence and into early adulthood (Casey, Giedd, & Thomas, 2000; Paus, 2005).

Developmental Theories of Adolescent Risk-taking

Over the last decade, a number of developmental theories have been posited to explain the surge in risk-taking observed during adolescence. Perhaps, the most prominent of these theories is the "dual-systems" model, stemming from the two-system model of willpower by

Metcalf & Mischel (1999). The idea being that control over behavior is a balance between a "cool" calculating and emotionally neutral system and a "hot" reflexive and emotionally reactive system (Metcalf & Mischel, 1999). Drawing on this conceptualization, Steinberg (2008) proposed that puberty triggers activation of a "socio-emotional system" that develops earlier in adolescence, which manifest in intensifying urges to seek out rewarding and novel experiences, while an underdeveloped "cognitive control" system has not yet developed capacity for regulating reactive and reflexive impulses. Early maturation of a "socio-emotional system" that increases sensitivity to rewarding stimuli is produced by neurobiological changes involving dopaminergic pathways, while the "cognitive control system" represents protracted development of prefrontal cortices that are implicated in self-regulation abilities (Steinberg, 2008). Under this model, adolescents' vulnerability to risk-taking may be explained by an inverted-U shape trajectory of the socio-emotional system and a linear developmental trajectory of the cognitive control system (Steinberg, 2008; Shulman et al., 2016).

Paralleling this line of thought, Casey (2008) proposed the neurobiological "imbalance" model of adolescent risk-taking, which is very similar to the "dual systems" model. The imbalance model is based on the development of brain circuitry at the neurochemical, structural, and functional level (Casey, 2015). Examination of the developmental transition from childhood to adolescence and into adulthood shows that subcortical brain areas (e.g., ventral striatum) mature at an earlier rate compared to later developing cortical regions (e.g., prefrontal cortex). Maturation of sensorimotor and subcortical brain areas are evidenced by an increase in cortical thickness (Gogtay et al., 2004), an increase in dopamine receptor density (Brenhouse, Sonntag, & Andersen, 2008), and dendritic pruning of synaptic connections (Huttenlocher, 1990).

However, unlike the "dual systems" model, the "imbalance model" predicts that the

motivational system (similar to the socioemotional system) develops until mid-adolescence and reaches a plateau that continues into adulthood (Casey, 2015; Shulman et al., 2016). Another subtle difference between the two models is that the dual systems model hypothesizes independent developmental trajectories, whereas the imbalance model suggests that a dependency between systems such that the maturation of the cognitive control system leads to less reactive motivational system (Shulman et al., 2016). It is also important to note that although these models are useful, adolescents' vulnerability for risk-taking likely involves more complex developmental processes (Casey, 2015; Shulman et al., 2016).

Research shows some support for these models in that adolescents indeed engaged in greater risk-taking behavior in laboratory tasks and show increased levels of self-reported sensation seeking relative to children or adults (Burnett, Bault, Coricelli, & Blakemore, 2010; Lejuez, Aklin, Zvolensky, & Pedulla, 2003; Steinberg, 2008; for review see Schonberg, Fox, & Poldrack, 2011). Longitudinal studies also indicated a linear increase in sensation seeking from childhood to adolescence (Harden & Tucker-Drob, 2011; MacPherson, Magidson, Reynolds, Kahler, & Lejuez, 2010). In particular, one large-scale longitudinal study found that sensation seeking increased from early adolescence (e.g., age 10) to mid-adolescence with declining scores as participants matured into early adulthood (Harden & Tucker-Drob, 2011).

Under neurodevelopmental theories of adolescent risky behavior, it is implied that early maturation of subcortical brain areas representing the socio-emotional system are responsible for increases in risk-taking observed during adolescence (Casey, 2015; Steinberg, 2008). Specifically, it is hypothesized that underlying neurobiological changes in dopaminergic pathways from the ventral tegmental area to the ventral striatum especially nucleus accumbens (NAcc), are at the basis of phenotypic biases toward choosing high-reward options (Ernst,

Romeo, & Andersen, 2009; Galvan, 2010; Shulman et al., 2016). Previous research examining reward sensitivity in the adolescent brain show mixed results, with some studies reporting hyper-reactivity in motivational circuits especially the ventral striatum (Burnett, Bault, Coricelli, & Blakemore, 2010; Galvan et al., 2006; van Leijenhorst et al., 2010), and others indicating hypo-reactivity (Bjork et al., 2004; Bjork, Smith, Chen, & Hommer, 2010). Furthermore, functional and structural imaging studies have provided little to no evidence that inter-individual differences in neural reward sensitivity are related to self-reported risk-taking behaviors in the real world (Braams, van Duijvenvoorde, Peper, & Crone, 2015; for review, see Schonberg, Fox, & Poldrack, 2011; van Duijvenvoorde et al., 2015). For instance, Braams and colleagues (2015) found that adolescents showed increased NAcc activity in response to receiving rewards, but adolescents showing greatest NAcc reward responsivity were not always the same adolescents engaging in high levels of risk-taking.

Taken altogether, support for neurodevelopmental models of adolescent risk-taking is mixed. While some research highlights developmental trends that align with dual systems models, other studies do not. In addition, although adolescents exhibit heightened sensitivity to rewards at the neural level in comparison to adults (Galvan et al., 2006; van Leijenhorst et al., 2010), reward sensitivity does not explain inter-individual differences in real-world adolescent risk-taking (for review see, Schonberg, Fox, & Poldrack, 2011). This prior work suggests that other decision-making processes may be more relevant for guiding adolescents toward risky behavior. One particularly powerful method for identifying the specific decision-making processes guiding risky choice behavior is to utilize model-based approaches in conjunction with functional magnetic resonance imaging (fMRI) to uncover behavioral and underlying neural mechanisms of risky decision-making behavior.

Model-Based Approaches of Risky Decision-Making

Within economics, finance, and decision science, formal mathematical models have been applied to better understand the mechanisms driving risky choice behavior. Under these models, *risk* is typically defined as the variance or standard deviation of potential outcomes (Rothschild & Stiglitz, 1970). There are two types of models that have widely been used to understand risky decision-making: expectation-based and risk-return models.

Expectation-based models have predominately been used to describe how individuals make decisions under uncertainty. These models assert that preferences are a function of the outcome values and probabilities of potential outcomes. The earliest form of these models indicated that the optimal choice is to select the option with the highest expected value in which each option's expected value (*EV*) is the sum of each objective probability, *P*, multiplied by the outcome value, *V*, and is expressed by the formula,

$$EV = \sum (P * V)$$

Expected Utility Theory (EUT), however, assumes that individuals are maximizers of expected utility rather than expected value (Bernoulli, 1954; von Neumann & Morgenstern, 1947). EUT assumes that individuals subjectively represent outcome values in a way that differs from the true or objective outcome value, and allows for the estimation of these subjective preferences for a particular outcome given a myriad of factors. In particular, EUT allows for the assessment of *risk preferences* that indicate inter-individual differences in the level of uncertainty one can tolerate (for review see, Schonberg, Fox, & Poldrack, 2011; Weber & Johnson, 2008). Mathematically, EU is represented by the following functional form,

$$EU = \sum (P * U)$$

where *EU* is equal to the sum of each probability associated with an outcome, *P*, multiplied by the utility of each outcome, *U*. Risk preferences can be described by an individual's utility (*U*) function such that linearity indicates risk neutrality, concavity indicates risk aversion, and convexity indicated risk seeking. Utility of an outcome (*U*) can be described as a function of the monetary value (*V*) and an individual's risk preference, α.

$$U = V^{\alpha}$$

In particular, $\alpha = 1$ corresponds to risk neutral, $\alpha < 1$ corresponds to risk aversion, and $\alpha > 1$ corresponds to risk seeking preferences.

While EUT assumes that individuals may differ in the extent to which they represent values of potential outcomes, it does not make similar assumptions for the probabilities associated with each outcome. On the other hand, Prospect Theory (PT; Kahneman & Tversky, 1979) demonstrated that individuals exhibit systematic biases in the way they represent probability information. In other words, individuals typically tend to overweight small probabilities and underweight large probabilities. Moreover, PT showed that individuals exhibited systematic biases when monetary outcomes were framed as losses relative to gains. In a series of experiments, PT demonstrated that individuals are generally risk averse for high probability gains and low probability losses, and risk seeking for low probability gains and high probability losses (Kahneman & Tversky, 1979; Schonberg et al., 2011). In PT, individuals maximize the value (V) of a prospect using the following function,

$$V = w(p) * v(x)$$

where *w(p)* represents a probability weighting function that captures subjective representations of probability information multiplied by the value function, *v(x)*, of a prospect with regard to a reference point.

Similar to expectation-based models, risk-return models (Markowitz,1959; Weber & Johnson, 2008) are often used in the finance literature to explain risky choice behavior. Risk-return models risky choice behavior as a tradeoff between an option's return or expected value (EV) and its risk (R), corresponding to the option's variance of potential outcomes. The major assumption of these models is that rational decision-makers will maximize the potential return, while concurrently minimizing risk, which can be used to classify approach and avoidance behaviors under uncertainty (Weber & Johnson, 2008; van Duijvenvoorde et al., 2015). Unlike expectation-based models, risk-return models explicitly model individual preferences of risk as a function of an option's objective risk (i.e., variance of potential outcomes). This model can be described using the following mathematical function,

$$WTP = EV - \delta R$$

where willingness to pay for a risky option (WTP) is the difference between each option's EV and an individual's risk preference δ multiplied by an option's objective risk (R).

In sum, model-based approaches (either expectation-based or risk-return) are powerful tools that can be used to provide: (i) clear interpretations regarding the determinants of optimal decision-making behavior, and (ii) a flexible quantitative framework to capture individual differences. Decision neuroscience or neuroeconomics has taken advantage of these model-based approaches by studying which brain networks encode specific choice processes using fMRI. This interdisciplinary approach has been shown to be successful in identifying cognitive and neural mechanisms of risky choice behavior (for review see, Schonberg, Fox, & Poldrack, 2011; van Duijvenvoorde & Crone, 2013), which ultimately advances our understanding of the critical processes guiding risk-taking.

Risky Decision-Making and the Adolescent Brain

Drawing upon previous work in decision neuroscience, risky decision-making arises from computations of reward values as well as the risk or chances of obtaining such valued outcomes (Tobler, O'Doherty, Dolan, & Schultz, 2007). Therefore, optimal choices involve a trade-off between expected rewards and associated risks, in which estimations of risk are equally important as being able to compute expected rewards. Neural computations associated with estimations of risk and value involves overlapping and separable brain areas (Christopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009; d'Acremont & Bossaerts, 2008; Tobler, O'Doherty, Dolan, & Schultz).

Encoding of reward values is associated with responses in the ventral striatum, orbitofrontal cortex, dorsal and ventral prefrontal cortex, and superior and inferior parietal cortices (Bartra, McGuire, & Kable, 2013; Critchley, Mathias, & Dolan, 2001; Kuhnen & Knutson, 2005; Tobler, O'Doherty, Dolan, & Schultz, 2007). A recent meta-analysis of reward processing circuitry in adolescents revealed that adolescents exhibit similar responses to rewarding stimuli in a subcortical network of regions including the ventral and dorsal striatum and posterior cingulate cortex (Silverman, Jedd, & Luciana, 2015). Not surprisingly, adults recruited prefrontal and parietal cortices in response to rewards, while adolescents did not (Silverman, Jedd, & Luciana, 2015). This finding may reflect relatively immature development of cortical brain areas, especially the prefrontal cortex, in adolescents compared to adults.

Encoding of risk or variance of potential outcomes in adults involves a network of regions including the anterior cingulate cortex, dorsal medial prefrontal cortex, and bilateral anterior insular cortex (Kuhnen & Knutson, 2005; Mohr et al., 2010). Greater risk aversion in adults has been related to increased risk-related activation in the inferior frontal gyrus (Christopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009) and the anterior insular cortex

(Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003) in response to increasing risk. Unlike the large body of work that examines reward-related circuitry in adolescence, research investigating risk-related circuitry is very limited. One recent cross-sectional study investigated neural correlates of risk in adolescents (16-19) relative to children and adults, and found that adolescents exhibited greater responses to risk in the insular and dorsal medial prefrontal cortices (van Duijvenvoorde et al., 2015). Moreover, inter-individual differences in adolescent risk sensitivity correlated with activations in the insular and dorsal medial prefrontal cortices such that greater risk aversion was associated with heightened responsivity in these regions (van Duijvenvoorde et al., 2015). In line with these results, adolescents who showed diminished insular cortex responses to increasing risk in addition to decreased cognitive control engaged in higher levels of self-reported health risk behaviors (Kim-Spoon et al., 2016). Taken altogether, these results suggest that inter-individual differences in behavioral and neural sensitivity to risk may explain why some adolescents may be more susceptible to maladaptive risk-taking, and others are not.

Overview

Using a decision neuroscience approach, the present work focused on understanding both inter-individual and intra-individual variability in behavioral risk sensitivity and neural risk processing and their effects on adolescent risky decision-making. Using a longitudinal design, Study 1 examined intra-individual change of behavioral risk sensitivity and neural risk processing within a critical period of adolescence during which a peak in risky behaviors is expected. In addition, Study 1 elucidated inter-individual differences in behavioral risk sensitivity and neural risk processing, as well as the relation between these behavioral and neural indices of risk. Furthermore, Study 1 assessed the extent to which either behavioral risk

sensitivity and neural risk processing were predictive of future self-reported risky behaviors in the real world. In Study 2, we identified inter-individual differences in probability bias that were related to real-world risky behavior using an adapted expectation-based model.

Longitudinal Changes in Neural Correlates of Risk Processing and Prediction of Future Adolescent Risk-Taking

Nina Lauharatanahirun[1,2], Jungmeen Kim-Spoon[1], Brooks King-Casas[1,2]

[1]Department of Psychology, Virginia Tech

[2]Virginia Tech Carilion Research Institute

Longitudinal Changes in Neural Correlates of Risk Processing and Prediction of Future Adolescent Risk-Taking

Abstract

Understanding the cognitive and neurobiological processes underlying risky decision-making during adolescence is key for preventing and reducing behaviors that lead to maladaptive health outcomes. A promising mechanism for guiding adolescents away from risky choices is the extent to which adolescents are sensitive to the likelihood of receiving potential rewards. In order to better understand when adolescents might be most vulnerable for risk-taking, it is necessary to identify the developmental trajectory of potential mechanisms of risky choice behavior. Although the adolescent risky decision making literature is rapidly growing, few studies have shown that processes identified within the laboratory are related to risky behavior in the real world. To this end, the present study investigated the ontogeny of adolescent behavioral risk sensitivity and neural representations of risk, and their prospective relations to self-reported risky behavior. Results showed that adolescents became more sensitive to risk over time, and neural representations of risk changed linearly with increasing activation in bilateral anterior cingulate cortex and insular cortex. Notably, we identified a neural vulnerability in insular risk processing that was predictive of change in self-reported risky behavior over time. This research highlights the normative maturation of risk-related processes during adolescence and identified a neural vulnerability during the beginning of mid-adolescence that may have implications for prevention and amelioration of adverse health risk behaviors.

Introduction

Brain structures and functions undergo significant maturational changes during adolescence that may impact risk-taking behavior (Casey, 2015; Steinberg, 2008). Adolescence is a developmental period characterized by increased exposure to novel experiences and opportunities for engaging in risky behavior where consequences of choices are uncertain. Predominant neurodevelopmental theories suggest that early maturation of motivational circuitry, involving brain areas implicated in decision-making (e.g., ventral striatum, medial prefrontal cortex) result in heightened risk-taking during adolescence (Casey, Getz, & Galvan, 2008; Steinberg, 2008).

One promising motivational mechanism for guiding adolescent risky behavior is *risk* processing (Mohr et al., 2010). Decision-making research has shown that individuals not only consider valued rewards, but also the risk or chance of receiving such rewards when making risky decisions (d'Acremont & Bossaerts, 2008; Tobler, O'Doherty, Dolan & Schultz, 2007; van Duijvenvoorde et al., 2015). Model-based approaches used in decision neuroscience define *risk* as the variability associated with potential outcomes, which is separate from the expected value or potential rewards (for review, see Platt & Huettel, 2008; Schonberg, Fox, & Poldrack, 2011). Although these processes are related, previous neuroimaging research indicates that risk and reward processes recruit separate brain areas during decision-making (d'Acremont & Bossaerts, 2008; Huettel, 2006; Tobler, O'Doherty, Dolan & Schultz, 2007). Risk is generally encoded by the bilateral insular cortex and dorsal medial prefrontal cortex (Mohr, Biele, & Heekeren, 2010; van Duijvenvoorde et al., 2015), while reward is represented in the ventral striatum and ventromedial prefrontal cortex (Richards, Plate, & Ernst, 2013; Silverman , Jedd, & Luciana, 2015).

Previous research has primarily focused on how the adolescent brain processes and responds to valued rewards; however, evidence showing its relevance as a predictor of risky choice outside the laboratory is lacking (Braams, van Duijvenvoorde, Peper, & Crone, 2015; Galvan et al., 2006; Schonberg, Fox, & Poldrack, 2011). Although adolescents exhibit greater reward sensitivity than adults (Galvan et al., 2006; van Leijenhorst et al., 2010), heightened reward sensitivity is rarely related to risk-taking outside the laboratory (Braams, van Duijvenvoorde, Peper, & Crone, 2015; for review, see Schonberg, Fox, & Poldrack, 2011; van Duijvenvoorde et al., 2015). For example, Braams and colleagues (2015) found that adolescents displayed increased nucleus accumbens activity in response to receiving rewards, but those who exhibited the greatest reward responsivity were not always the same adolescents who reported higher levels of risk-taking behavior.

Recent evidence has also shown that adolescents exhibit greater neural sensitivity to increasing risk compared to children and adults, particularly in the insular cortex (van Duijvenvoorde et al., 2015). Notably, insular risk-related processing in adolescents was related to inter-individual differences in risky choice behavior within the laboratory, such that enhanced neural risk sensitivity was associated with greater risk aversion (van Duijvenvoorde et al., 2015). In a small sample of late adolescents, increased insular risk-related processing was related to decreased self-reported risk-taking among adolescents with low cognitive control (Kim-Spoon et al., 2016). Taken together, these findings suggest that neurobehavioral risk sensitivity plays a vital role during adolescent risky decision-making, and may provide insight into the processes that underlie risk-taking in the real world.

Here, we utilize a longitudinal design to examine both inter-individual and intra-individual differences in neurobehavioral risk sensitivity. While cross-sectional designs are

useful and convenient, they do not allow us to characterize the developmental maturation of neurobehavioral risk sensitivity across adolescence. In addition, prior adolescent decision-making studies include a wide range of ages that are often inconsistent, making it difficult to compare results across studies and draw inferences regarding developmental patterns. In the present study, we longitudinally examine how neurobehavioral risk sensitivity changes across a period of adolescence when vulnerability to risk-taking is at its greatest (Burnett et al.,2010; Dahl, 2004). Another advantage of a longitudinal approach is that it allows us to prospectively examine whether neural and behavioral indices of risk at baseline can be used as predictors of future risk-related behavior in the real world. Identifying predictors of risk-taking behavior is crucial for determining which adolescents may be most vulnerable for maladaptive risk-taking.

To this end, adolescents (N=166) engaged in an economic lottery choice task while their blood-oxygen-level-dependent (BOLD) response was monitored using functional magnetic resonance imaging (fMRI) at three time points, approximately one year apart. Using an economic risk-return model (Weber, 2010), we examined (i) how behavioral risk sensitivity changes across adolescence; (ii) how neural correlates of risk processing change across adolescence; and (iii) whether initial behavioral or neural indices of risk predict actual change in risk-taking behavior in the future. See Methods for full details.

Method

Participants. In order to assess developmental changes, adolescents were recruited to participate in a longitudinal study that spanned the critical period of middle adolescence during which increases in risk-taking occur (Dahl, 2004; Steinberg, 2008). Available data from the first three waves of the longitudinal study were included in the current analyses. A total of 164 adolescents (48% female) from the southwest Virginia area participated in an ongoing longitudinal study in

which experiments were completed at three time points approximately one year apart. At Time 1, a total of 144 adolescents (46% female) participated with a mean age of 13.51 years (*SD*=.50). At Time 2, a total of 137 adolescents (45% female) participated with a mean age of 14.51 years (*SD*=.50). At Time 3, a total of 126 adolescents (50% female) participated with a mean age of 15.57 years (*SD*=.52). Inclusion criteria consisted of being either 13 or 14 years old at Time 1, a native English speaker and having vision corrected to be able to see the computer display clearly. Exclusion criteria consisted of the following: claustrophobia, history of head injury resulting in loss of consciousness for more than 10 minutes, orthodontia impairing image acquisition, severe psychopathology (e.g., psychosis), and other magnetic resonance contraindications (e.g., pacemaker, aneurysm clips, neurostimulators, metal in eyes, cochlear implants or other implants). All exclusion criteria were assessed through self-report. Data from participants were excluded from analyses based on meeting the following criteria at any time point: movement greater than 3mm in any direction during the scan (*n*=11), claustrophobia or discomfort with undergoing imaging procedure (*n*=9), braces (*n*=5), severe psychopathology (*n*=2), did not or could not (i.e., moved away) continue participation (*n*=24), image acquisition error (*n*=2), or other magnetic resonance contraindications to (*n*=2).

Measures

Lottery Choice Task. At each time point, adolescents were asked to make choices between pairs of risky gambles in an adapted lottery choice task (Holt & Laury, 2002) while their blood-oxygen-level-dependent (BOLD) response was monitored using functional magnetic resonance imaging (fMRI). Each gamble option included a high and low monetary outcome associated with a probability that the specific outcome would occur. Probabilities were in the form of a pie with ten slices, in which each slice corresponded to ten percent. Each pair of gambles included one

option that was riskier than the other. Risk was calculated using a scale-free measure of variance, coefficient of variation (CV). CV is computed by dividing the standard deviation of potential outcomes by the option's expected value (EV; Weber, Shafir, & Blais, 2004).

$$EV = P_{high} * V_{high} + P_{low} * V_{low}$$

$$CV = \frac{\sqrt{P_{high}(V_{high} - EV)^2 + P_{low}(V_{low} - EV)^2}}{EV}$$

P_{high} and P_{low} is the probability of receiving the high and low outcome, respectively, while V_{high} and V_{low} correspond to the high and low monetary outcome. Prior studies have demonstrated that CV is a better metric of outcome variability relative to other measures (e.g., variance) because variability of a distribution is often represented in relation to the mean rather than in an absolute manner (Bach, Symmonds, Barnes & Dolan, 2017; McCoy & Platt, 2005; Weber, Shafir & Blais, 2004). CV also allows for the comparison of risk sensitivity across different scales or outcome dimensions (Weber, Shafir & Blais, 2004). Since probabilities were the same for both gambles in a given trial, the difference between low and high monetary amounts differentiated the level of risk between options. That is, the option with the smaller difference in monetary outcomes (e.g., \$1.88 - \$1.50 = 0.38, see Figure 1A) indicates relatively low risk compared to the option with the larger difference in outcomes (e.g., \$3.61 - \$0.09 = 3.52, see Figure 1.1. Low-risk options had CV values that ranged from 0.07 to 0.28, while high-risk options ranged from 0.52 to 3.07 (see Appendix A). Monetary outcomes and probabilities randomly varied across trials. Adolescents were instructed that each trial was independent from other trials and was equally likely to be selected for compensation. Compensation was based on the actual results from five randomly selected trials in addition to payment for completion of the study. The task comprised 72 trials and it took approximately 30 minutes to complete.

Trial structure. Adolescents were shown the pair of gamble options and given a fixed four seconds to make a decision. Decisions were made using a magnetic resonance compatible button box. Next, a fixation cross with a jitter of one to three seconds was displayed. Following the fixation period, adolescents were shown the randomly generated outcome based on their selected gamble for a fixed period of two seconds. The inter-trial-interval was jittered between one and three seconds during which another fixation cross was displayed. This design has been optimized for examining decision-related neural responses in previous studies (van Leijenhorst et al., 2006; 2008; 2010).

Health Risk Behavior (HRB). Adolescent health risk behavior was measured using a subset of items from the Things I Do questionnaire (Conger & Elder, 1994; see Appendix B) at each time point through self-report. Based on the Centers for Disease Control's definition of adolescent risk behavior (Eaton et al., 2012; Kann et al., 2016), 14 of the 19 items fell within at least one of the six domains of risk-taking behavior: 1) contributing to unintentional injuries and violence, 2) sexual behaviors contributing to unintended pregnancy and sexually transmitted infections, 3) alcohol and other drug use, 4) tobacco use, 5) unhealthy dietary behaviors, or 6) inadequate physical activity. Due to the lack of variability in participant's responses, three of the 14 items were removed. Examples of the final 11 items include "Smoked a cigarette or used tobacco" and "Drunk a bottle or glass of beer or other alcohol." Adolescents responded to items indicating frequency of behavior as, "0 = not at all", "1= once or twice", or "2 = more than twice". Higher scores on this measure indicated higher risk-taking. For each individual, change in risky behavior was calculated as the difference between Time 1 and Time 3 self-reported health risk behaviors divided by the baseline (i.e., Time 1) assessment: HRB change = HRB at Time 3 – HRB at Time

1) / HRB at Time 1. Positive values indicated an increase in risky behavior over time, whereas negative values indicated a decrease in health risk behaviors over time.

Intelligence. At Time 1, adolescents' verbal intelligence was measured using the Kaufman Brief Intelligence Test (2nd Edition, KBIT; Kaufman & Kaufman, 2004). KBIT is a widely used intelligence assessment used for children and adults. The KBIT-2 verbal intelligence measure is also strongly correlated with other comprehensive measures such as the Wechsler Adult Intelligence Scale (3rd Edition, WAIS-3; Wechsler, 1997, Walters & Weaver, 2003).

Procedure. Adolescent participants completed all study assessments within the same session at each time point. All participants were given instructions for the lottery choice task as well as a practice session of six trials to ensure comprehension of the task. Adolescents were recruited via flyers, recruitment letters, e-mail, and word of mouth. All participants and parent(s) of the participants provided written informed assent/consent in line with Virginia Tech Institutional Review Board guidelines.

Statistical Analyses

Behavioral analysis. To estimate the effects of risk sensitivity across time on the likelihood of choosing a low or high risk gamble, behavioral data from the lottery choice task was analyzed using a generalized logistic linear mixed-effects model using the lme4 package in R (Bates, Maechler, Bolker, & Walker, 2014). Risk sensitivity was defined as the difference between the *CV* of the high and low risk options ($CV_{high} - CV_{low}$). Reward sensitivity was defined as the difference between the *EV* of the high and low risk options ($EV_{high} - EV_{low}$). It is important to note that reward sensitivity in the present study refers to differences in the *objective,* rather than subjective, expected values between options. The wave variable indicated adolescents' choices from Time 1, Time 2 and Time 3, and the likelihood of either choosing the low (coded as 0) or

high (coded as 1) risk gamble was the dependent variable. In order to examine the unique relation between risk and choice behavior apart from reward (a variable related to both risk and choice), reward was included as a covariate in our logistic linear mixed-effects model. The model is formally described as:

Level 1:

$$logit\ (y_{it}) = \pi_{0i} + \pi_{1i}*Risk_{it} + \pi_{2i}*Return_{it} + \pi_{3i}*Wave_{it} + \pi_{4i}*(Risk_{it}*Wave_{it}) + \pi_{5i}*(Return_{it}*Wave_{it}) + \varepsilon_i$$

Level 2:

$$\pi_{0i} = \beta_{00} + \xi_{0i}$$
$$\pi_{1i} = \beta_{10} + \xi_{1i}$$
$$\pi_{2i} = \beta_{20} + \xi_{2i}$$
$$\pi_{3i} = \beta_{30} + \xi_{3i}$$
$$\pi_{4i} = \beta_{40} + \xi_{4i}$$
$$\pi_{5i} = \beta_{50} + \xi_{5i}$$

y_{it} is the response of the *i* participant at the *t* trial, in which $y_{it} = 0$ indicates choosing the low risk gamble and $y_{it} = 1$ indicates choosing the high-risk gamble. Between-subject variance is captured by the random effect ξ, which accounts for the repeated-measures nature of the data. Within-subject variance is captured by the random effect, ε. Fixed effects are represented by the parameter, β. All independent variables in the model were mean centered, in which β_{00} indicates the average likelihood of choosing to take the high-risk gamble for mean risk and reward. Main effects of risk, reward, and wave are represented by β_{10}, β_{20}, and β_{30}, respectively. Interaction effects of risk and reward by wave are represented by β_{40} and β_{50}, respectively. Individual random slopes for risk and reward account for individual differences in sensitivity to risk and reward. Positive values of risk sensitivity indicate a greater likelihood of choosing the high-risk gamble when the difference between CV_{high} and CV_{low} is large (i.e., lower risk sensitivity), and negative values indicate a greater likelihood of choosing the low risk gamble when the difference between CV_{high} and CV_{low} is small (i.e., higher risk sensitivity). Positive values of reward

sensitivity indicate a greater likelihood of choosing the high-risk gamble when the difference between EV_{high} and EV_{low} is large (i.e., increasing expected payoff), and negative values indicate a greater likelihood of choosing the low risk gamble when the difference between EV_{high} and EV_{low} is small (i.e., decreasing expected payoff).

fMRI Acquisition. fMRI data were acquired using a 3T Siemens Tim Trio scanner with a twelve-channel head matrix coil. Anatomical images were collected using a high-resolution magnetization prepared rapid acquisition gradient echo sequence with the following parameters: TR = 1200 ms, TE=2.66 ms, field of view (FoV) = 245x245mm, and 192 slices with the spatial resolution of 1 x 1 x 1mm. Functional images were obtained using the following parameters: slice thickness = 4mm, 34 axial slices, FoV= 220 x 220 mm, repetition time = 2 s, echo time = 30 ms, flip angle= 90 degrees, voxel size = 3.4 x 3.4 x 4 mm, 64x64 grid, and slices were hyper-angulated at 30º from anterior-posterior commissure.

fMRI analysis. Analysis of neuroimaging data was conducted using SPM8 and the Sandwich Estimator toolbox for longitudinal fMRI data (SwE; Guillaume, Hua, Thompson, Waldrop, & Nichols, 2014). Preprocessing of imaging data was performed using the following procedure: data were corrected for excessive head motion using a six-parameter rigid body transformation and realigned, mean functional image was co-registered to the anatomical image, anatomical image was segmented, functional volumes were normalized and registered to the Montreal Neurological Institute (MNI) template, and then smoothed using a 6mm full-width-half-maximum Gaussian filter.

Whole-brain general linear model analysis was conducted to assess neural computations of risk in the adolescent brain. For each subject, decision phase BOLD responses were modeled with a boxcar function representing the length of time it took each participant to make a choice.

Outcome phase BOLD responses were modeled with a duration of two seconds. Two parametric regressors modulating decision phase activation corresponding to the CV of chosen options and EV of chosen options were included in the model. A parametric regressor at the outcome phase indicating whether the subject received the high or low monetary outcome was also included in the model. All regressors included in the model were convolved with a canonical hemodynamic response function. Here, the parametric regressor of interest was the CV of chosen options and the EV of chosen options was included as a covariate of no interest in line with behavioral analysis. Also, six motion parameters were included in the subject-level model as covariates of no interest.

Subject-level contrasts for the regressor of interest – CV of chosen options (i.e., risk processing) – were entered into a group-level model using SwE in order to assess the change in neural risk processing across time as well as the average effect of neural risk processing over time. SwE was used to adequately account for the repeated-measures structure of the data by implementing the sandwich variance estimator (Guillaume, Hua, Thompson, Waldrop, & Nichols, 2014). The marginal regression procedure implemented within SwE also allows for the inclusion of unequal sample sizes across different time points which is a common occurrence in longitudinal studies. This is a strength of using SwE compared to other fMRI toolboxes (McFarquhar et al., 2016). For group-level regression analyses, individual estimates of behavioral risk sensitivity were split into a cross-sectional (time-invariant) and longitudinal (time-varying) component following the procedure outlined in Guillaume et al. (2014). This allowed for the assessment of the following: i) the relation between average neural risk processing and average behavioral risk sensitivity, and ii) the relation between change in neural risk processing across time and change in behavioral risk sensitivity across time.

Prediction of Health Risk Behaviors. A logistic mixed effects analysis was conducted with Time 1 data following the procedure described in the Behavioral Analysis section to retrieve a baseline behavioral phenotype of risk sensitivity. That is, individual estimates of risk sensitivity (i.e., random slopes) from Time 1 were used as the independent variable in subsequent multiple regression analyses. Using a brain-as-predictor approach (see Falk, Cascio, & Coronel, 2015 for overview), subject-level contrasts for parametrically modeled neural data reflecting neural responses to risk level were pooled at the group-level and a one-sample t-test was performed. ROIs were extracted from significant regions in the one-sample t-test meeting a cluster-defining primary threshold of $p < .001$. Eigenvariate values for each region were extracted using a 6mm sphere around the peak voxel coordinates. These eigenvariate values for each subject were then used as neural variables in subsequent multiple regression analyses. Two multiple regression analyses were employed. In the first model, baseline behavioral risk sensitivity and neural risk processing were entered as independent variables in order to test the unique contribution of each in explaining future health risk behaviors at Time 3. In the second model, baseline behavioral risk sensitivity and neural risk processing were used as independent variables to predict behavior change from Time 1 to Time 3 (for calculation, see Measures: Health Risk Behavior).

Results

Behavioral. On average, subjects chose the high-risk gamble 46% at Time 1 (*SD*=.16), 40% at Time 2 (*SD*=.18), and 36% at Time 3 (*SD*=.16). Logistic linear mixed effects analysis revealed that adolescents chose the low risk option for average scores on all other predictors in the model (see Table 1.1). When the difference in riskiness between gamble options was high, adolescents displayed a decreased likelihood of selecting the high-risk gamble on average ($b = -.26$, $p = .009$; see Table 1.1). On the other hand, when the difference in expected reward between gamble

options was high, adolescents showed an increased likelihood of choosing the high-risk option on average (b = 1.02, p < .001; see Table 1.1). These results are consistent are in line with prior work, demonstrating that adolescents are both sensitive to the risks (van Duijvenvoorde et al., 2015) and potential payoffs (Barkley-Levenson & Galvan, 2014) in the lottery choice task. There was also a significant effect of wave, which indicates that adolescents were less likely to choose to the high-risk option over time (see Table 1.1). A significant Risk Sensitivity X Wave interaction was found, indicating that adolescents exhibited greater risk sensitivity (i.e., more likely to choose the low risk option) as they matured. A significant Reward Sensitivity X Wave interaction was also found, which showed that adolescents were more likely to choose options with a higher expected monetary return over time.

We conducted follow-up tests to examine whether the effects of risk and reward on choice behavior were present within each wave. Indeed, adolescents showed main effects of risk (see Table 1.2; all ps <.001) and reward (see Table 1.2; all ps <.001) on risky choice behavior. These results confirm that adolescents are sensitive to risk and reward at each time point. Furthermore, we tested the difference between effects of risk and reward sensitivity on choice behavior in adolescents compared to their parents who serve as a demographically matched sample. Assuming that parents' risk sensitivity might serve as a proxy for what adolescents' risk sensitivity will be in adulthood, results showing no difference between parents and adults suggests that adolescents have reached adult levels of risk sensitivity. On the contrary, if differences existed between parents and adolescents, this would suggest that adolescents' risk sensitivity may not have reached adult levels. We conducted Z-test analyses, which revealed that adolescent risk sensitivity was significantly different, compared to their parents (Z = 2.94, p =.003; see Supplementary Table 1.1). However, there was no significant difference between

adolescent and adult reward sensitivity (Z = -.47, p= .638; see Supplementary Table 1.1). This pair of results suggests that adolescents are still developing the ability to make decisions based on risk assessments, but have already reached adult levels of reward sensitivity (i.e., make choices that maximize their expected monetary payoffs).

Imaging. Using the sandwich variance estimator, which allows for longitudinal fMRI analysis by adjusting the covariance structure of repeated-measures data (see Method), we conducted whole-brain group-level analyses to test for parametric effects of risk during the decision phase of the task controlling for parametric effects of reward. Whole-brain group-level analyses revealed significant hemodynamic responses correlated with parametrically increasing CV for chosen options in the medial prefrontal cortex (especially dorsal anterior cingulate cortex), bilateral insular cortex, and bilateral ventral striatum (see Figure 1.2, Supplementary Table 1.2). Moreover, imaging analyses revealed a significant linear change in the encoding of risk across the three waves such that increased activation was observed in the bilateral anterior cingulate cortex, insular cortex, right pallidum, right thalamus, and right superior orbitofrontal cortex for increasing risk over time (see Figure 1.3, Supplementary Table 1.3). These results are consistent with a large body of literature implicating the aforementioned regions to be involved in the encoding of risk (see meta-analysis, Mohr et al., 2010). To test the extent to which individual risk sensitivity was related to neural risk-related processing, we conducted a multiple regression analysis on the parametric contrast of CV. Our analysis revealed that greater risk sensitivity (i.e., risk aversion) was significantly related to increased activation of bilateral anterior cingulate cortex, bilateral insular cortex, left pallidum, and right caudate (see Figure 1.4, Supplementary Table 1.4). That is, greater risk aversion is related to greater activation in brain areas associated with risk-related processing..

Prediction of Health Risk Behaviors. Two multiple regression models were constructed to test (i) the effects of baseline risk sensitivity and insular risk processing on self-reported health risk behaviors at Time 3, and (ii) the effects of baseline risk sensitivity and insular risk processing on change in health risk behaviors from Time 1 to Time 3 (for detailed variable information, see Prediction of Health Risk Behaviors in Methods). For the first model, our results showed that neither behavioral nor neural indicators of sensitivity to risk at baseline were predictive of future risky behavior at Time 3 (see Table 1.3). Our second regression analysis indicated that insular risk processing was predictive of the change in health risk behaviors from Time 1 to Time 3 (see Table 2). Lower baseline insula activation during the decision phase for increasing levels of risk was related to increases in health risk behavior from Time 1 to Time 3 (see Figure 1.5, Table 1.3), while baseline behavioral risk sensitivity was not predictive of change in risky behavior (see Table 1.3).

Discussion

The purpose of the present study was to investigate how behavioral risk sensitivity and neural risk-related processing develop during a period of adolescence noted for surges in risk-taking behavior (Casey et al., 2008; Dahl, 2004; Steinberg, 2008). Importantly, we also tested whether neurobehavioral correlates of risk are predictive of future engagement in health risk behaviors in the real world. First, our findings demonstrate that behavioral risk sensitivity significantly changes during middle adolescence. Adolescents become increasingly more risk averse as they become older. Second, adolescents' neural representation of risk is consistent with brain areas previously implicated in encoding risk in both adolescent (van Duijvenvoorde et al., 2015) and adult (Mohr, Biele, & Heekeren, 2010) studies. Individual differences in behavioral risk sensitivity were also related to neural representations of risk such that greater risk aversion

corresponded to increased recruitment of risk-related circuitry. Third, the development of risk-related processing in the adolescent brain changed linearly across time, with heightened neural responses for increasing risk in the dorsal anterior cingulate cortex, right anterior insular cortex, and bilateral ventral striatum. Finally, insular risk processing was predictive of change in actual health risk behavior from Time 1 to Time 3 highlighting a potential neural vulnerability that can either increase or decrease the likelihood of future health-related outcomes.

Recent evidence points to the importance of behavioral risk sensitivity and associated neural substrates in guiding individuals toward or away from risky behavior (van Duijvenvoorde et al., 2015; Kim-Spoon et al., 2016). Prior research, however, often utilizes cross-sectional designs and inconsistently defines adolescence using various age ranges making it difficult to draw inferences regarding intra-individual change of neurobehavioral correlates of risk sensitivity. Here, we use a longitudinal design, a neuroeconomic approach, and a large cohort of adolescents to assess the developmental changes associated with how adolescents evaluate and represent risk at a behavioral and neural level. Our design also permitted investigation of the extent to which risky decision-making processes at the beginning of mid-adolescence prospectively influenced real-world risk-taking behavior two years later. Adolescents displayed greater risk averse behavior in the lottery choice task over time, suggesting that they are continuing to develop their behavioral preferences for risk. This is not surprising given the influx of novel experiences and ample opportunities to engage in risky behavior that often occur during the transition from early to middle adolescence. Further support for the idea that adolescents are continuing to develop their behavioral preferences for risk is evidenced by the significant differences in risk sensitivity between adolescents and their parents. If adolescents had already reached adult levels of risk sensitivity, then no difference in risk sensitivity between parents and

adolescents would be expected. Thus, the period between 13 and 16 years old may represent a critical time for shaping adolescents' behavioral preferences for risk that may lead to either risky or safe choices in the future.

Although we found a significant change in reward sensitivity over time, there were no significant differences in reward sensitivity between adolescents and their parents. It can be inferred that adolescents may have already reached adult levels of reward sensitivity, and that development of reward sensitivity potentially occurs earlier than risk sensitivity. Compatible with this rationale, a cross-sectional study using a similar model-based approach and experimental task found that children (relative to adolescents and adults) were not sensitive to alterations of risk, but were quick to detect changes in expected rewards (van Duijvenvoorde et al., 2015). Our results within the context of prior work suggest that calculations of expected rewards may develop earlier, while calculations of risk (i.e., variability of potential rewards) may develop during adolescence and into adulthood. Reward sensitivity within the context of this study refers to the ability to maximize expected monetary payoffs. High reward sensitivity can potentially have two interpretations. First, it could be that reward sensitivity indicates the extent to which adolescents respond to valued rewards (i.e., approach-related tendencies for valued rewards). Second, reward sensitivity could also represent the ability to make accurate calculations regarding the expected value of each option. In other words, reward sensitivity in the context of the lottery choice task may reflect general cognitive ability. To test these two hypotheses, we conducted correlational analyses between estimated reward sensitivity in the lottery choice task, intelligence, and an assessment of reward-specific motivation (Behavioral Activation Reward Subscale (BAS Reward); Carver & White, 1994). Results revealed that reward sensitivity within each wave was significantly related to intelligence, whereas no relation

was found with self-reported reward-specific motivational tendencies (see Supplementary Table 1.5). Taken altogether, these findings imply that reward sensitivity may actually represent the ability to cognitively compute expected value in order to make optimal choices rather than sensitivity to valued rewards.

There is a limited, yet growing literature on how adolescents process risk information in the brain. The present study contributes to this work by examining how the neural representation of risk changes across critical years of adolescence. In line with other studies (Huettel, 2006; Mohr, Biele, & Heekeren, 2010; Paulus, Rogalsky, Simmons, & Stein, 2003; Preuschoff et al., 2008; for review see Platt & Huettel, 2008), we found that adolescents represent risk in a network of regions previously implicated in risk processing including the medial prefrontal cortex, bilateral insular cortex, and bilateral ventral striatum. Importantly, we found that activations in the above-named regions increased for higher levels of risk as adolescents become older. Heightened processing may reflect enhanced sensitivity to risk information occurs as adolescents mature and that this signal strengthens over time to guide adolescents away from potential negative outcomes. Perhaps the developing brain becomes more efficient at calculating potential risks during decision-making, which may explain why a decrease in risky behavior is observed in adulthood compared to other developmental periods (for review, see Defoe, Dubas, Figner, & van Aken, 2015; Levin, Hart, Weller, & Harshman, 2007). Behavioral results are also in line with this interpretation as adolescents become significantly risk averse over time. Risk averse adolescents recruited risk-related brain areas more than those who are behavioral more risk seeking, highlighting that behavioral preferences for risk are related to risk-related neural computations. That is, optimal risk aversion may result from adaptive development of risk-

related neural circuitry, which ultimately functions to signal adolescents away from risky decisions.

Risky decisions made during adolescence, a transformative period of development, may be maladaptive for current and future health outcomes. Thus, identifying predictors of health risk behaviors could aid in prevention and intervention efforts aimed at decreasing risky choices with deleterious outcomes. Here, we showed that the encoding of risk information in the insular cortex around the beginning of mid-adolescence is a potential neural vulnerability for future risky behavior. This finding is important for three reasons: (i) it helps provide an explanation for why some adolescents make risky choices; (ii) it identifies a possible neural biomarker for identifying at-risk adolescents who may be susceptible to increased risky behavior with negative health outcomes; and (iii) it highlights the strength of leveraging a longitudinal design and a model-based approach for understanding neurobehavioral processes of risky decision-making.

References

Bach, D. R., Symmonds, M., Barnes, G., & Dolan, R. J. (2017). Whole-Brain Neural Dynamics of Probabilistic Reward Prediction. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *37*(14), 3789–3798.

Barkley-Levenson, E., & Galván, A. (2014). Neural representation of expected value in the adolescent brain. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(4), 1646–1651.

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2014). Fitting linear mixed-effects models using lme4. *arXiv Preprint arXiv:1406. 5823*. Retrieved from https://arxiv.org/abs/1406.5823

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.

Casey, B. J., Getz, S., & Galvan, A. (2008). The adolescent brain. *Developmental Review: DR*, *28*(1), 62–77.

Conger, D. Elder, R., Glen, H., & Jr. (1994). *Families in Troubled Times: Adapting to Change in Rural America. Social Institutions and Social Change*. Aldine de Gruyter, 200 Saw Mill River Road, Hawthorne, NY 10532.

d'Acremont, M., & Bossaerts, P. (2008). Neurobiological studies of risk assessment: a comparison of expected utility and mean-variance approaches. *Cognitive, Affective & Behavioral Neuroscience*, *8*(4), 363–374.

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), 1–22.

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.

Dennison, M., Whittle, S., Yücel, M., Vijayakumar, N., Kline, A., Simmons, J., & Allen, N. B. (2013). Mapping subcortical brain maturation during adolescence: evidence of hemisphere-and sex-specific longitudinal changes. *Developmental Science*, *16*(5), 772–791.

Eaton, D. K., Kann, L., Kinchen, S., Shanklin, S., Flint, K. H., Hawkins, J., … Others. (2012). Youth risk behavior surveillance—United States, 2011. *Morbidity and Mortality Weekly Report. Surveillance Summaries: MMWR / Centers for Disease Control*, *61*(4), 1–162.

Eckel, C. C., & Grossman, P. J. (2002). Sex differences and statistical stereotyping in attitudes toward financial risk. *Evolution and Human Behavior*, *23*(4), 281–295.

Falk, E. B., Cascio, C. N., & Coronel, J. C. (2015). Neural Prediction of Communication-Relevant Outcomes. *Communication Methods and Measures*, *9*(1-2), 30–54.

Guillaume, B., Hua, X., Thompson, P. M., Waldorp, L., & Nichols, T. E. (2014). Fast and accurate modelling of longitudinal and repeated measures neuroimaging data. *NeuroImage*, *94*, 287–302.

Holt, C. A., & Laury, S. (2002). Risk Aversion and Incentive Effects. https://doi.org/10.2139/ssrn.893797

Huettel, S. A. (2006). Behavioral, but not reward, risk modulates activation of prefrontal, parietal, and insular cortices. *Cognitive, Affective & Behavioral Neuroscience*, *6*(2), 141–151.

Kann, L. (2016). Youth risk behavior surveillance—United States, 2015. *Morbidity and*

Mortality Weekly Report. Surveillance Summaries , *65*. Retrieved from https://www.cdc.gov/mmwr/volumes/65/ss/ss6506a1.htm

Kaufman, A. S., & Kaufman, N. L. (2013). Kaufman Brief Intelligence Test, Second Edition. In *Encyclopedia of Special Education*. John Wiley & Sons, Inc.

Kim-Spoon, J., Deater-Deckard, K., Lauharatanahirun, N., Farley, J. P., Chiu, P. H., Bickel, W. K., & King-Casas, B. (2016). Neural Interaction Between Risk Sensitivity and Cognitive Control Predicting Health Risk Behaviors Among Late Adolescents. *Journal of Research on Adolescence*. https://doi.org/10.1111/jora.12295

Levin, I. P., Hart, S. S., Weller, J. A., & Harshman, L. A. (2007). Stability of choices in a risky decision-making task: a 3-year longitudinal study with children and adults. *Journal of Behavioral Decision Making*, *20*(3), 241–252.

McCoy, A. N., & Platt, M. L. (2005). Risk-sensitive neurons in macaque posterior cingulate cortex. *Nature Neuroscience*, *8*(9), 1220–1227.

McFarquhar, M., McKie, S., Emsley, R., Suckling, J., Elliott, R., & Williams, S. (2016). Multivariate and repeated measures (MRM): A new toolbox for dependent and multimodal group-level neuroimaging data. *NeuroImage*, *132*, 373–389.

Mohr, P. N. C., Biele, G., & Heekeren, H. R. (2010). Neural processing of risk. *The Journal of Neuroscience*, *30*(19), 6613–6619.

Paulus, M. P., Rogalsky, C., Simmons, A., Feinstein, J. S., & Stein, M. B. (2003). Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *NeuroImage*, *19*(4), 1439–1448.

Platt, M. L., & Huettel, S. A. (2008). Risky business: the neuroeconomics of decision making under uncertainty. *Nature Neuroscience*, *11*(4), 398–403.

Preuschoff, K., Quartz, S. R., & Bossaerts, P. (2008). Human insula activation reflects risk prediction errors as well as risk. *The Journal of Neuroscience*, *28*(11), 2745–2752.

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 and Biobehavioral Reviews*, *37*(5), 976–991.

Schonberg, T., Fox, C. R., & Poldrack, R. A. (2011). Mind the gap: bridging economic and naturalistic risk-taking with cognitive neuroscience. *Trends in Cognitive Sciences*, *15*(1), 11–19.

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.

Steinberg, L. (2008). A Social Neuroscience Perspective on Adolescent Risk-Taking. *Developmental Review: DR*, *28*(1), 78–106.

Tobler, P. N., O'Doherty, J. P., Dolan, R. J., & Schultz, W. (2007). Reward value coding distinct from risk attitude-related uncertainty coding in human reward systems. *Journal of Neurophysiology*, *97*(2), 1621–1632.

Tymula, A., Rosenberg Belmaker, L. A., Roy, A. K., Ruderman, L., Manson, K., Glimcher, P. W., & Levy, I. (2012). Adolescents' risk-taking behavior is driven by tolerance to ambiguity. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(42), 17135–17140.

van Duijvenvoorde, A. C. K., Huizenga, H. M., Somerville, L. H., Delgado, M. R., Powers, A., Weeda, W. D., … Figner, B. (2015). Neural correlates of expected risks and returns in

risky choice across development. *The Journal of Neuroscience*, *35*(4), 1549–1560.

van Leijenhorst, L., Crone, E. A., & Bunge, S. A. (2006). Neural correlates of developmental differences in risk estimation and feedback processing. *Neuropsychologia*, *44*(11), 2158–2170.

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.

van Leijenhorst, L., Westenberg, P. M., & Crone, E. A. (2008). A developmental study of risky decisions on the cake gambling task: age and gender analyses of probability estimation and reward evaluation. *Developmental Neuropsychology*, *33*(2), 179–196.

Walters, S. O., & Weaver, K. A. (2003). Relationships between the Kaufman brief intelligence test and the Wechsler adult intelligence scale. *Psychological Reports*, *92*(3), 1111–1115.

Weber, E. U., Shafir, S., & Blais, A.-R. (2004). Predicting risk sensitivity in humans and lower animals: risk as variance or coefficient of variation. *Psychological Review*, *111*(2), 430–445.

Table 1.1

Logistic Linear Mixed Effects Model for Adolescent Behavioral Risky Choice on Risk Sensitivity, Reward Sensitivity, & Wave

Fixed Effects

	b	*SE*	*Z*	*p*
Intercept	-0.15	0.08	-1.68	0.091
Risk Sensitivity	-0.26	0.10	-2.60	0.009
Reward Sensitivity	1.02	0.06	15.61	< .001
Wave	-0.57	0.07	-7.47	< .001
Risk Sensitivity*Wave	-0.60	0.08	-6.77	< .001
Reward Sensitivity* Wave	0.23	0.04	5.32	< .001

Random Effects

	Variance	*AIC*	*deviance*	*p*
Subject (intercept)	1.22	32074	32060	–
Risk Sensitivity	1.15	31108	31090	< .001
Reward Sensitivity	0.59	29949	29925	< .001
Wave	0.78	29116	29084	< .001
Risk Sensitivity*Wave	0.82	28892	28850	< .001
Reward Sensitivity*Wave	0.20	28645	28591	< .001

Table 1.2

Logistic Linear Mixed Effects Model for Adolescent Behavioral Risky Choice on Risk Sensitivity & Reward Sensitivity Within Wave

Fixed Effects

	Wave 1				Wave 2				Wave 3			
	b	*SE*	*Z*	*p*	*b*	*SE*	*Z*	*p*	*b*	*SE*	*Z*	*p*
Intercept	-0.15	0.08	-1.76	0.07	-0.80	0.14	-5.66	< .001	-1.33	0.15	-8.54	< .001
Risk Sensitivity	-0.30	0.10	-3.01	0.002	-0.91	0.15	-5.82	< .001	-1.59	0.18	-8.85	< .001
Reward Sensitivity	1.08	0.07	15.30	< .001	1.45	0.08	16.44	< .001	1.57	0.09	17.09	< .001

Random Effects

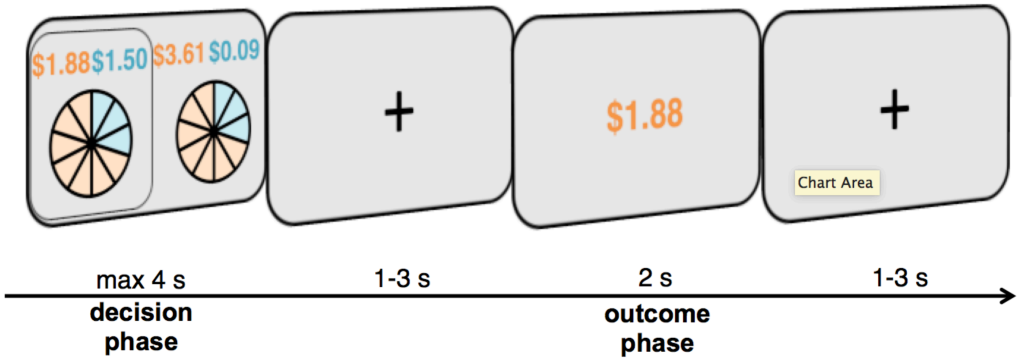
	Variance	*AIC*	*deviance*	*p*	*Variance*	*AIC*	*deviance*	*p*	*Variance*	*AIC*	*deviance*	*p*
Subject (intercept)	1.14	12480	12472	< .001	2.71	9886	9878	< .001	3.11	8677	8669	< .001
Risk Sensitivity	1.03	12138	12126	< .001	2.79	9438	9426	< .001	3.50	8290	8278	< .001
Reward Sensitivity	0.63	11579	11561	< .001	0.90	8891	8873	< .001	0.91	7800	7782	< .001

Table 1.3

Regression Models for Predicting Health Risk Behaviors from Wave 1

	Health Risk Behaviors Wave 3				
	B	*SE (B)*	*ß*	*t*	*p*
Intercept	0.44	0.21	0.35	2.07	0.04
Right Anterior Insula W1	-0.02	0.03	-0.01	-0.64	0.51
Risk Sensitivity W1	0.12	0.06	0.05	1.89	0.06
KBIT Verbal	-0.001	0.004	-0.006	-0.24	0.80
	Change in Health Risk Behaviors from Wave 1 to Wave 3				
	B	*SE (B)*	*ß*	*t*	*p*
Intercept	0.41	0.88	0.46	0.47	0.63
Right Anterior Insula W1	-0.42	0.15	-0.31	-2.77	0.006
Risk Sensitivity W1	0.04	0.26	0.01	0.16	0.86
KBIT Verbal	0.005	0.02	0.03	0.28	0.77

Figure 1.1 Economic Lottery Choice Task



Adolescents made 72 decisions between pairs of risky gambles in an economic lottery choice task (Holt & Laury, 2002). Each gamble consisted of a high and low monetary outcome with an associated probability. Outcomes and probabilities were represented with corresponding colors (orange and blue). The time course of a given trial included a decision phase followed by a jittered fixation interval and an outcome phase, in which participants were shown the results of their choice followed by a jittered inter-trial interval (ITI).

Figure 1.2 Mean Neural Response to Increasing Risk during the Decision Phase Across Waves

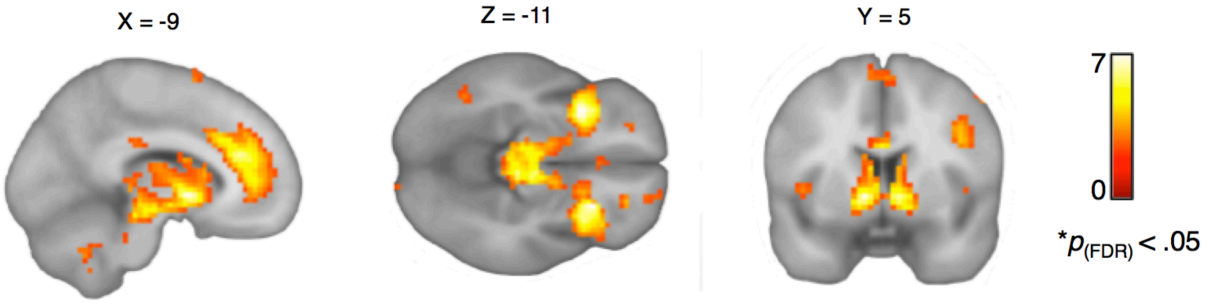


Figure 1.3 Linear Change in Neural Responses to Increasing Risk Across Waves

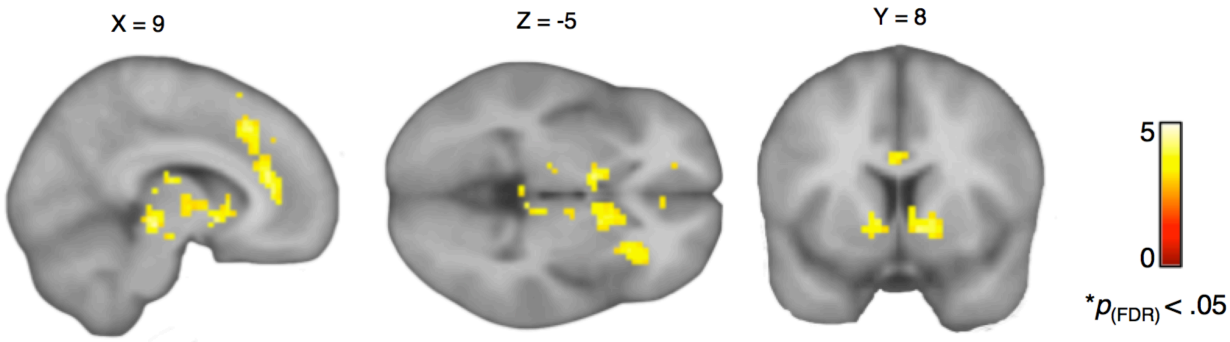
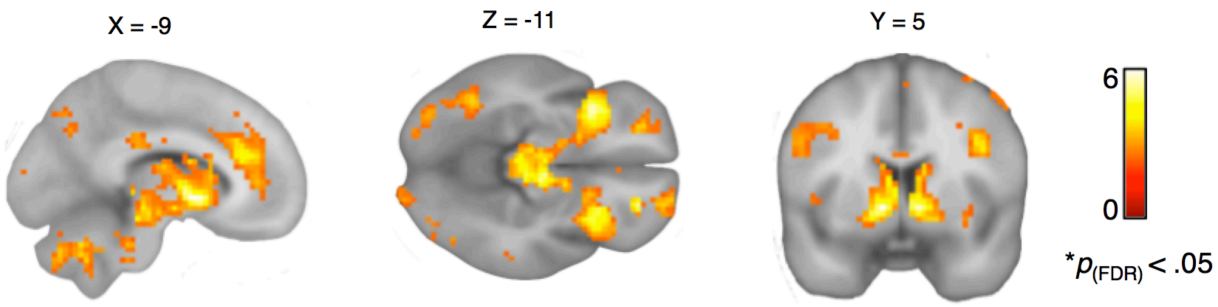
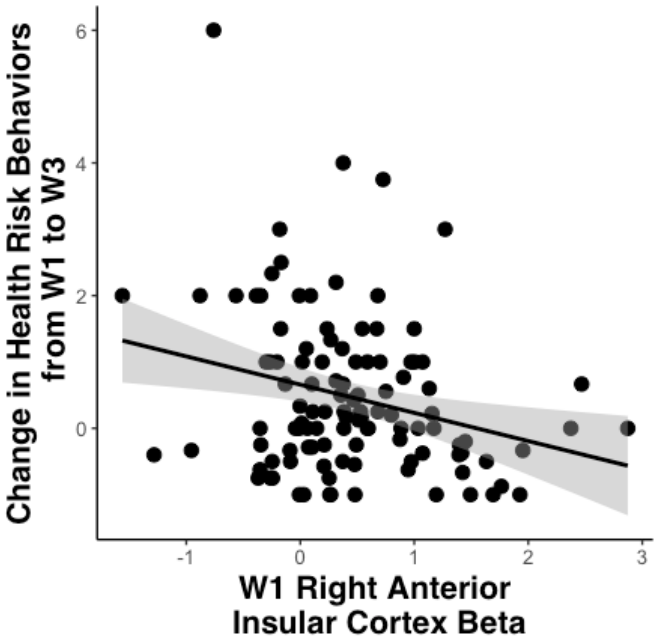


Figure 1.4



Individual risk sensitivity estimates (averaged across three waves for each individual) correlated against mean risk-related BOLD responses, where decreased risk sensitivity (i.e., risk aversion) was related to responses associated with increasing risk (CV).

Figure 1.5 Relation between Wave 1 Insular Risk Processing and the Change in Health Risk Behaviors from Wave 1 to Wave 3



Supplementary Table 1.1

Logistic Linear Mixed Effects Model for Adult Behavioral Risky Choice on Risk Sensitivity & Reward Sensitivity

Fixed Effects				
	b	*SE*	*Z*	*p*
Intercept	-0.30	0.10	-3.02	0.002
Risk Sensitivity	-0.72	0.12	-5.84	< .001
Reward Sensitivity	1.06	0.06	15.53	< .001
Random Effects				
	Variance	*AIC*	*deviance*	*p*
Subject (intercept)	1.49	12411	12403	–
Risk Sensitivity	1.80	11759	11747	< .001
Reward Sensitivity	0.58	11200	11182	< .001

Supplementary Table 1.2

Mean Neural Response to Increasing Risk during the Decision Phase over Time						
			Peak MNI Coordinates			
Cluster #	Region	Size	*x*	*y*	*z*	*Z*
1	R Anterior Cingulate Cortex	4048	6	32	16	7.92
	L Insular Cortex		-33	14	-11	7.85
	R Insular Cortex		27	23	-11	7.74
2	R Precentral Gyrus	50	42	5	31	4.51
3	L Cerebellum	37	-33	-58	-29	4.42
4	R Superior Orbitofrontal Cortex	21	24	44	-11	4.39
	R Middle Orbitofrontal Cortex		18	50	-17	3.62
5	R Precuneus	27	15	-67	40	4.34
6	L Superior Parietal Cortex	53	-18	-64	40	4.15
	L Superior Parietal Cortex		-21	-58	49	3.81
7	L Middle Occipital Cortex	51	-33	-88	-2	4.14
8	R Superior Parietal Cortex	8	30	-64	-50	4.07
9	R Superior Orbitofrontal Cortex	32	21	56	-8	3.64
10	R Cerebellum	14	33	-49	-29	3.54

Note: MNI, Montreal Neurological Institute; L, Left; R, right. Size refers to the number of voxels in the cluster. All clusters $p_{(FDR)} < .05$.

Supplementary Table 1.3

Linear Change in Neural Responses to Increasing Risk Across Time						
			Peak MNI Coordinates			
Cluster #	Region	Size	*x*	*y*	*z*	*Z*
1	R Thalamus	283	3	-19	4	5.15
	R Pallidum		15	5	-8	4.29
2	R Superior Medial Prefrontal Cortex	187	6	23	43	4.74
	R Anterior Cingulate Cortex		9	35	19	4.32
3	L Cerebellum	40	-30	-64	-26	4.02
4	R Insular Cortex	41	30	23	-2	3.97
5	R Middle Frontal Gyrus	17	45	53	19	3.95
6	R Superior Orbitofrontal Cortex	12	18	35	-17	3.77
7	L Anterior Cingulate Cortex	15	-3	8	25	3.68
8	L Insular Cortex	7	-30	14	-11	3.62
9	R Precuneus	8	15	-67	40	3.57
10	R Angular Gyrus	14	33	-64	43	3.44

Note: MNI, Montreal Neurological Institute; L, Left; R, right. Size refers to the number of voxels in the cluster. All clusters $p(\text{FDR}) < .05$.

Supplementary Table 1.4

Neural Correlates of Risk Sensitivity in Response to Increasing Risk during the Decision Phase

			Peak MNI Coordinates			
Cluster #	Region	Size	*x*	*y*	*z*	*Z*
1	L Pallidum	2858	-9	5	-2	6.61
	R Anterior Cingulate Cortex		6	41	4	6.11
	R Anterior Cingulate Cortex		6	32	19	6.11
	L Insular Cortex		-33	17	-11	5.96
	R Anterior Cingulate Cortex		9	35	22	5.94
	R Caudate		9	14	1	5.87
	L Anterior Cingulate Cortex		-6	29	22	5.58
	R Middle Cingulate Cortex		12	35	31	5.54
	R Insular Cortex		33	26	-2	5.45
	L Superior Medial Prefrontal Cortex		-6	32	28	5.34
2	R Precuneus	114	15	-64	37	5.45
3	L Precuneus	133	-18	-64	34	4.95
	L Superior Parietal Cortex		-21	-67	46	4.41
	L Superior Parietal Cortex		-21	-58	49	4.41
4	L Cerebellum	201	-36	-58	-29	4.81
5	R Superior Occipital Cortex	82	33	-73	46	4.80
6	R Inferior Parietal Cortex	107	45	-49	46	4.48
7	L Cerebellum	119	-6	-58	-38	4.43
8	L Inferior Occipital Cortex	57	-30	-85	-5	4.30
9	L Fusiform Gyrus	33	-39	-58	-11	3.96
10	L Middle Orbitofrontal Cortex	13	-24	47	-11	3.94
11	L Inferior Parietal Cortex	21	-42	-49	52	3.67
12	L Precentral Gyrus	29	-57	11	31	3.63
13	L Lingual	9	-18	-91	-14	3.48
14	R Middle Occipital Cortex	11	30	-94	1	3.47

Note: MNI, Montreal Neurological Institute; L, Left; R, right. Size refers to the number of voxels in the cluster. All clusters $p_{(FDR)} < .05$.

Supplementary Table 1.5

Bivariate Correlations Among Reward Sensitivity, Kaufman Brief Intelligence Test (KBIT) Verbal, and Behavioral Activation Reward Subscales (BAS Reward)

		1	2	3	4	5	6	*M*	*SD*
1	Reward Sensitivity W1							1.60	1.10
2	Reward Sensitivity W2	0.47***						2.13	1.29
3	Reward Sensitivity W3	0.33***	0.47***					2.25	1.24
4	KBIT Verbal	0.34***	0.28***	0.41***				43.58	5.82
5	BAS Reward W1	0.05	-0.03	0.04	0.05			3.40	0.41
6	BAS Reward W2	-0.06	-0.004	-0.004	0.02	0.53***		3.39	0.39
7	BAS Reward W3	-0.04	0.03	0.14	0.13	0.51***	0.55***	3.42	0.39

Note. *$p < .05$, **$p \leq .01$, ***$p \leq .001$

Unrealistic Expectations: The Impact of Probability Bias on Adolescent Risky Decision-Making

Nina Lauharatanahirun[a,b], Sheryl Ball[c], Dongil Chung[a], Jason Aimone[a,d], Pearl H. Chiu[a,b], Jungmeen Kim-Spoon[b], Brooks King-Casas[a,b]

[a]Virginia Tech Carilion Research Institute

[b]Department of Psychology, Virginia Tech

[c]Department of Economics, Virginia Tech

[d]Department of Economics, Baylor University

Unrealistic Expectations: The Impact of Probability Bias on

Adolescent Risky Decision-Making

Abstract

Risky behaviors emerging during adolescence have been associated with maturational changes in neural mechanisms of decision-making, with prior research focused on enhanced valuation of rewards as a potential predictor of risky behaviors observed among adolescents. Here, we show biases in the use of probability information, rather than reward valuation, to be systematically related to hemodynamic correlates of risk in bilateral amygdala and associated with real-world risky behaviors among adolescents.

Unrealistic Expectations: The Impact of Probability Bias on Adolescent Risky Decision-Making

Risky decision-making is implicated in the leading causes of death and disease among adolescents in the United States, and recent work using economic models of choice have evaluated potential neurobehavioral mechanisms that can account for poor choices made by adolescents. In this framework[4-5], choices made under risk are a function of the value and probability of receiving potential rewards, with individual differences among adolescents attributed to systematic variation in the way value and probability information are combined to make decisions. For example, risk attitude, captured by the curvature in the relation of value to subjective value (i.e., utility), has been previously thought to underlie risky behavior among adolescents. However, curvature of the utility function has been found to neither predict real-world risky behaviors of adolescents, nor differ from adults[8-10]. Here, we instead examine whether systematic biases in the use of probability information are evident among adolescents, evaluate whether such biases are associated with alternations in neural processing of risk information, and determine whether they are associated with risky behaviors outside of the laboratory.

Prior work has described biases in expectations about the probabilities with which valenced outcomes are likely to occur, with individuals typically expecting desirable outcomes to occur more often and undesirable outcomes to occur less often for oneself, relative to others. These biases are observed across multiple domains, including health, economic, and social outcomes, but vary with individual differences in both prior beliefs and experience. For example, pessimistic biases are observed among depressed individuals who often hold negatively distorted beliefs about the future. Similarly, optimistic biases are reduced among adolescents engaged in

substance use behaviors that typically confer negative consequences in multiple domains of functioning. In the current study, we explore whether similar biases are observed in the use of probability information during risky choice, examine their relation to neural processing of risk, and determine their relation to substance use behaviors of adolescents.

Adolescents (N=159; age=13-14) completed a modified lottery choice task[20] while blood-oxygenated-level-dependent (BOLD) activity was monitored using functional magnetic resonance imaging (fMRI; Fig. 2.1A). Adolescents made a series of choices between pairs of safer and riskier lotteries, defined by the coefficient of variation of each lottery. A computational model including a standard power utility function[4-5] and a linear probability weighting function[13-14,21] was used to estimate individual risk attitudes and probability biases, respectively (See Fig. 2.1B; Supplementary Methods). The linear probability weighting function allowed for the identification of optimistic (or pessimistic) individuals who increase (or decrease) the likelihood of receiving the high value option, while simultaneously decreasing (or increasing) the likelihood of receiving the low value option. Individuals who exhibit no probability bias judge options based on the objective probabilities. Compared to models including risk attitude or probability bias alone, the combined model provided a superior fit of the observed data after accounting for the number of parameters (See Fig. 2.1C, Supplementary Fig. 2.4). In addition, validation of parameter estimates was supported by successful recovery of model parameters (r_{α} =.69, p <.001; r_{Φ} =.75, p < .001). Consistent with prior studies[6,9,12], behavioral results indicate that adolescents on average were risk averse (*M*=.79, *SD*=.73) and exhibited no bias in their use of probability information (*M*= -.02, *SD*=.27), with substantial variability across individuals.

To examine how individual differences in risk attitude and probability bias are related to neural computations of risk processing, estimated individual parameters were used as covariates

against hemodynamic responses to lottery risk; risk was quantified as the coefficient of variation of the chosen lottery, adjusting for the probability bias of each individual. Consistent with prior work in adults[6-7] and adolescents[31], adolescents on average exhibited greater responses in the bilateral medial prefrontal (mPFC) and insular cortices for higher relative to lower risk lotteries (Supp. Fig. 2.1; Supp. Table 2.2). Estimated risk attitudes were correlated with mPFC and insular risk processing, such that risk averse individuals showed greater risk-correlated activity than risk seeking individuals. Individual differences in probability bias were also correlated with mPFC responses (See Fig. 2.2). However, unlike insular responses to risk, individuals' with pessimistic relative to optimistic probability biases exhibited neural responses in the bilateral amygdala, a region implicated in uncertainty and fear processing[22-24](See Fig 2.2).

Taken together, these results indicate that when choosing between risky options, neural processing of risk information among adolescents is differentially related to the way in which they weight probability information and subjectively value rewards in overlapping and distinct neural structures. Among adolescents, the level of risk associated with chosen options was parametrically encoded in the insula and mPFC, and greater activity in these regions was related to greater risk aversion. Such that adolescents with greater risk-correlated responses in the bilateral insula and mPFC were less likely to choose risky options, suggesting encoding of the potential disutility associated with increasing variance (i.e., risk) of outcomes. Enhanced signaling in risk processing regions, such as the insula and mPFC, may lead adolescents away from choosing risky options[6], which is consistent with previous reports in adults[6-7]. Thus, adolescents neither had a greater "taste" for risk nor abnormal neural processing of risk, relative to previous reports of adults[6-7]. Indeed, when compared with their parents, adolescents were no more or less risk averse ($M_{parents}$=.86, $SD_{parents}$= 1.11; $t(316)$=-.64; p=.52).

Of note, these data revealed that pessimistic (relative to optimistic) individuals exhibited a risk-related signal in the bilateral amygdala. This distinct hemodynamic response for probability bias suggests that pessimistic adolescents exhibit an additional risk signal in the amygdala specifically for high-risk options that may be important for motivating behavior. Perhaps, pessimistic (relative to optimistic) adolescents are extra vigilant to low probability outcomes and thus experience increased sensitivity to high-risk situations. Pessimistic probability biases were also correlated with risk processing responses in the mPFC. It may be that increased pessimism or attention to outcomes that have a low likelihood may result in greater amygdala responses that signal other brain regions such as the mPFC to evaluate particularly salient stimuli further[22-23]. Consistent with this notion, the amygdala has been found to play a role in biasing risky choices in previous economic decision-making tasks[25-26].

The individual contributions of subjective valuation and probability bias to risky choice hold implications for how individual differences among adolescents can lead to suboptimal behavior in risky environments. To this end, we assessed whether risk attitudes or probability biases were related to poor decision-making in the real world. Adolescents' self-reported engagement in externalizing behaviors, including smoking and alcohol use, via the Youth Self Report[28] (YSR). Adolescents who scored in the borderline to near clinical range for potential externalizing psychopathology (≥ 65) exhibited significant differences in probability biases, but not in risk attitudes, compared to those with scores in the normal to non-clinical range (< 65; $t(155)=3.19$, $p=.001$). Moreover, high externalizing adolescents displayed pessimistic probability biases ($M=-.27$, $SD=.39$), while low externalizing adolescents exhibited no probability bias ($M=.003$, $SD=.26$). This result is consistent with threshold models of impulsivity[29-30]. In this view, risk-taking individuals are chronically under-aroused in the face of rewards, and therefore

are driven to seek out high rewards to achieve optimal arousal (i.e., meet their threshold). Pessimists who underestimate the likelihood of receiving greater rewards might be driven to sample a rich array of experiences, including substance use, to increase the probability of receiving rewards or meeting their threshold for arousal.

These results highlight probability bias as a novel neurobehavioral mechanism that may explain suboptimal value-based decisions in adolescents. In particular, our findings suggest a linear shift in the use of probability information, consistent with pessimism, that confers risk processing in the bilateral amygdala of adolescents engaged in externalizing behaviors. These data suggest that probability bias is a promising candidate mechanism shaping the development of maladaptive behaviors in adolescents.

References

1. Eaton D.K. et al. *MMWR Surveill Summ* **61**, 1-162 (2012).
2. Vaillant. *Addiction* **98,** 1043-1051 (2003).
3. Chambers R., Taylor J.R., Potenza M.N., *Am J Pychiatry* **160**, 1041-1052 (2003).
4. Bernoulli, D. *Econometrica* **22**, 23-36 (1954).
5. Pratt, JW. *Econometrica* **32**, 122-136 (1964).
6. Mohr P.N.C., Biele, G., & Heekeren, H.R. *J. Neurosci.* **30**, 6613-6619 (2010).
7. Christopoulos, G.I., Tobler, P.N., Bossaerts, P., Dolan, R.J., & Schultz, W. *J. Neurosci.* **29**, 12574-12583 (2009).
8. Sutter, M., Kocher, M.G., Glatzle-Rutzler, D., & Trautmann, S.T. *Am. Econ. Rev.* **103**, 510-531 (2013).
9. Tymula, A., et al. *Proc. Natl. Acad. Sci. U.S.A.* **109,** 17135-17140 (2012).
10. Schonberg, T., Fox., C.R., & Poldrack, R.A. *Trends Cogn. Sci.* **15**, 11-19 (2011).
11. Kahneman, D. & Tversky, A. *Econometrica* **47**, 263-292 (1979).
12. Gonzalez, R. & Wu, G. *Cognitive Psychol.* **38**, 129-166 (2009).
13. Waters et al. *J. Behav. Med.* **34,** 225-235 (2011).
14. Weinsten, N.D. *J. Behav. Med.* **5,** 441-460 (1982).
15. Brewer, N.T. et al. *Health Psychol.* **26,** 136-145 (2007).
16. Gerrard, M., Gibbons, F.X., Benthin, A.C., & Hessling, R.M. *Health Psychol*. **15,** 344-354 (1996).
17. Larsman, P., Eklof, M. & Torner, M. *Safety Sci.* **50**, 1740-1748 (2012).
18. Johnson, R.J., McCaul, K.D., & Klein, W.M.P. *J. Behav. Med.* **25**, 67-82 (2002).
19. Cohn, L.D., Macfarlane S., Yanez, C. & Imai, W.K. *Health Psychol.* **14,** 271-222 (1995).

20. Holt, C.A. & Laury, S.K. *Am. Econ. Rev.* **92**, 1644-1655 (2002).

21. Chapin, J. *Am. J. Psychol.* **3**, 253-262 (2001).

22. Pessoa, L. *Neuropsychologia* **48**, 3416-3429 (2010).

23. Wager, T.D., Phan, K.L., Liberzon, I., & Tayler, S.F. *NeuroImage* **19**, 513-531 (2003).

24. Phelps, E.A. *Curr. Opin. Neurobiol.* **14**, 198-202 (2004).

25. DeMartino, B., Kumaran, D., Seymour, B., & Dolan, R.J. *Science* **313**, 684-687 (2006).

26. Lauharatanahirun, N., Christopoulos, G.I., & King-Casas, B. *Front. Hum. Neurosci.* **6,** 1-7 (2012).

27. Etkin, A., Egner, T., & Kalisch, R. *Trends Cogn. Sci.* **15**, 85-93 (2011).

28. Achenbach, T.M. & Rescorla, L. (Department of Psychiatry, University of Vermont, 2001).

29. Zuckerman, M. (Cambridge University Press, New York, New York, USA, 2004).

30. Beauchaine, T.P., Gatze-Kopp, L., & Mead, H.K. *Biol. Psychol.* **74**, 174-184 (2007).

31. van Duijvenvoorde et al. *J. Neurosci.* **35,** 1549-1560 (2015).

Figure 2.1 Lottery Choice Task and Behavioral Model

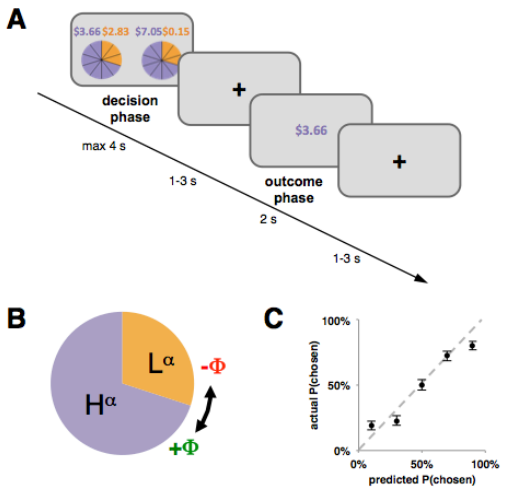
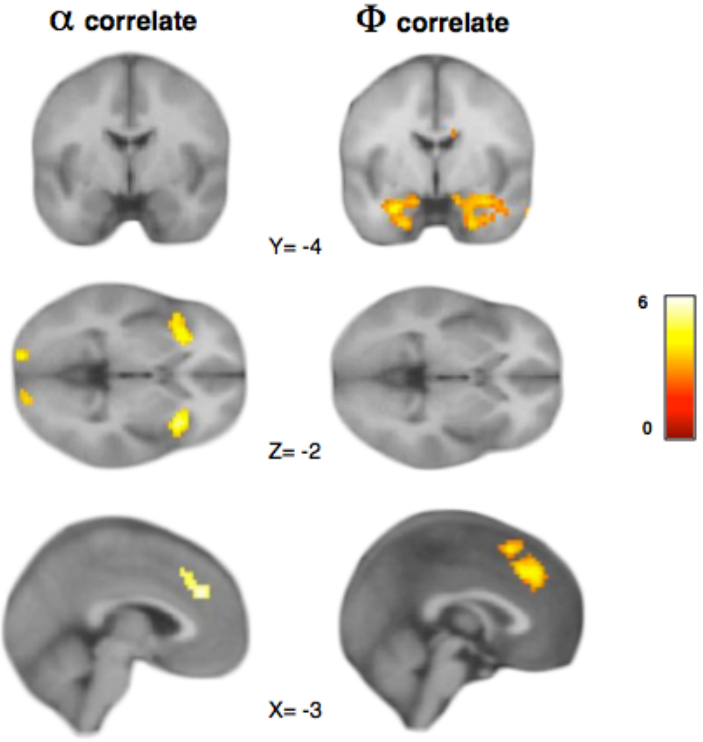


Figure 2.1A: Adolescents made a series of decisions between two gambles in a lottery choice task. For each gamble, a high and low monetary outcome was associated with a specific probability of receiving the outcome. Each probability information was represented as a number of pie slices. For each pair of gambles, one gamble was riskier (higher variance) than the other (lower variance). Probabilities and outcome values varied across trials. 2.1B) To assess economic preferences of risk for each participant, the expected utility of each option was modeled, $EU = (P_{high} + \phi) * V_{high}^{\alpha} + (P_{low} - \phi) * V_{low}^{\alpha}$ where ϕ represents a bias in how people perceive probabilities for the high and low outcomes of a given gamble. Positive values of ϕ indicate an optimism bias in which greater likelihood is assigned to the high value outcome over the low value outcome. Negative values of ϕ indicate an pessimistic bias in which greater likelihood is assigned to the low value outcome over the high value outcome. C) Actual percentage of chosen options in the lottery choice task is plotted as a function of our model's predicted probability of the chosen option. The dotted line indicates perfect prediction.

Figure 2.2 Neural Correlates of Risk Attitude and Probability Bias



Neural correlates of risk attitude and probability bias in response to perceived risk during the decision phase of the lottery choice task. Greater risk aversion relative to risk seeking was associated with neural responses in the bilateral insula (left-middle; left insula: $t(135)=3.42$, $p_{FWE(svc)} < .05$; right insula: $t(135)=4.30$, $p_{FWE(svc)} < .05$) and medial prefrontal cortex (left-bottom; $t(135)=3.56$, $p_{FWE(svc)} < .05$). Greater pessimism relative to optimism was associated with neural responses in the bilateral amygdala (right-top; left amygdala: $t(135)=5.14$, $p_{FWE} < .05$; right amygdala: $t(135)=4.51$, $p_{FWE} < .05$) and medial prefrontal cortex (right-bottom; $t(135)=4.32$, $p_{FWE} < .05$). For all analyses, cluster-defining threshold was $p < .001$.

Supplementary Methods

Participants. A total of 159 healthy developing participants (83 females, 76 males) between the ages of 13 and 14 were recruited from the Southwestern Virginia area. Participants were recruited through word of mouth, posters, internet ads, newspaper ads, and brochures. In addition, participants may have been recruited from a department database that includes previous participants who have participated in various psychological studies and have given consent to be recontacted for other studies. Inclusion criteria consisted of being either 13 or 14 years old and having vision corrected to be able to see the computer display clearly. Exclusion criteria consisted of the following: claustrophobia, history of head injury resulting in loss of consciousness for more than 10 minutes, orthodontia impairing image acquisition, severe psychopathology (e.g., psychosis), and other contraindications to MRI (e.g., pacemaker, aneurysm clips, neurostimulators, cochlear implants, metal in eyes, steel worker, or other implants). All exclusion criteria were assessed through self-report. All participants and parent(s) of the participants provided written informed assent/consent in line with Virginia Tech Institutional Review Board guidelines. Of the 159 participants, 4 participants did not complete the task in the scanner because either they were not comfortable or were not eligible (i.e., braces), 10 participants were excluded for excessive motion during scanning (> 3mm in any direction), and 8 participants were excluded because a GLM model of neural data could not be estimated. After exclusions, a total of 137 participants were included in analysis (75 females, 62 males).

Experimental Design and Procedure. Participants performed a modified lottery choice task while having their blood-oxygen-level-dependent (BOLD) response was monitored via functional magnetic resonance imaging (fMRI). Each participant made a total of 72 decisions,

and on average participants took approximately 30 minutes to complete the task. Each gamble option included a high and low monetary outcome and each associated with a specific probability, represented as a 10-piece pie. Probabilities were the same for each pair of gamble options. We used payoff amounts and probability levels consistent with Holt & Laury, 2002. The original set of Holt/Laury payoffs was rescaled to prevent participants from experiencing practice effects. In a given trial, participants were presented with a pair of gambles for 4 seconds and indicated their decision using an MR-compatible button box. Then, a white fixation cross against a black background was presented for an average of 1.5 seconds (jittered between 1-3 seconds). The winning amount of the selected gamble was then presented for 2 seconds. The inter-trial interval was an average of 1.5 seconds (jittered from 1-3 seconds), during which a white fixation cross was presented against a black background. To incentivize participation in the task, participants were compensated based on their actual winnings from 5 randomly selected trials. Participants were told that each trial is independent from all other trials and is equally likely to be selected for compensation.

Prior to scanning, participants were presented with instructions and given a quiz to ensure comprehension of the task and compensation protocol. Participants then engaged in a practice session of six trials, and were given an opportunity to ask the experimenter any questions. The task was presented on a stimulus presentation PC using Python software. At the end of the fMRI session, participants were debriefed and compensated. In a separate visit, prior to the fMRI session, adolescents completed a series of questionnaires assessing their pubertal development, substance use behaviors, and personality characteristics. Substance use behavior was assessed using a selection of questions from the Youth Behavior Risk Surveillance Survey questionnaire (CDC, 2013).

MRI Acquisition. Functional neuroimaging data were collected on a 3T Siemens Tim Trio MRI scanner with the following parameters: echo-planar imaging, gradient recalled echo; repetition time (TR)=2 seconds; echo time (TE)= 30 milliseconds; flip angle=90˚; 34 axial slices, 4mm slice thickness, 220x220 mm field of view (FoV), 64x64 grid, resulting in voxels that were 3 x 3 x 3 mm, and hyperangulated slices were acquired at 30 degrees from anterior-posterior commissure. The structural scan was acquired using a high-resolution magnetization prepared rapid acquisition gradient echo sequence (TR=1200 milliseconds, TE=2.66 milliseconds, FoV= 245x245 mm, 1 mm slice thickness, 192 slices with special resolution of 1x1x1 mm).

Behavioral Data Analysis. Behavioral data from the lottery choice task was analyzed using a standard economic model of expected utility. In line with a large body of work (Holt & Laury, 2002; Christopoulos et al., 2009; Huettel et al., 2006), individual risk attitudes were modeled using a traditional power utility function (Pratt, 1964; Arrow, 1965) in which the utility of money V, for $V \geq 0$, described by,

$$U(V) = V^{\alpha}$$

where α represents risk attitude with $\alpha < 1$ indicating risk aversion, $\alpha > 1$ indicating risk seeking, and $\alpha = 1$ indicating risk neutrality. To account for unique variance explained by probability bias, individual probability biases were estimated using risk attitude estimates (α) from the standard model above, where expected utility for a particular gamble had the functional form (Gonzalez & Wu, 2009),

$$EU = (P_{high} + \phi) * V_{high}^{\alpha} + (P_{low} - \phi) * V_{low}^{\alpha}$$

where $-1 \leq \phi \leq 1$ and $0 \leq (P_{high/low} \pm \phi) \leq 1$.

Using a maximum likelihood estimation algorithm, behavioral choices for each subject were fit to a logistic function,

$$P(chosen) = \frac{1}{1 + e^{\gamma(EU_{unchosen} - EU_{chosen})}}$$

where $\gamma \geq 0$ reflects the inverse temperature, a measure of relative consistency in choice selection, where greater values indicate more consistency and smaller values indicate less consistency in choices made throughout the lottery choice task.

Model comparison and recovery. We used the Bayesian Information Criterion (BIC) to test the fit of several models to our choice data. Lower values of BIC represent better fit. Compared to an expected monetary value model containing no transformation of value or probability, standard power utility function, and a model containing probability bias alone, our model including both the standard utility function and linear transformation of probability produced a better fit (See Supp Fig. 4). To test the robustness of our model, we simulated choices for each individual in the sample (N=159) using each individual's estimated parameters. Maximum likelihood estimation was used to re-estimate the parameters for each simulated individual using the procedure described in the Behavioral Analysis section. Correlation analyses demonstrated that model recovery was successful for both risk attitude (r_{α}=.69, p <.001) and probability bias (r_{Φ}=.75, p < .001).

Assessment of substance use behavior. To measure suboptimal decision-making behavior in the real world, adolescents self-reported on engagement in externalizing behaviors (e.g., alcohol and drug use) via the externalizing subscale of the Youth Self Report (YSR; Achenbach, 1991). Clinicians often use this measure to assess whether self-reported behaviors indicate potential psychopathology.

fMRI Data Analysis. Neuroimaging data were processed and analyzed using SPM8 (Wellcome Trust Neuroimaging Center). Functional data were corrected for head motion using a six-parameter rigid body transformation. Next, images were realigned, and normalized using parameters from a segmented anatomical image coregistered to the mean EPI. Data were smoothed using a 6mm full-width-half-maximum Gaussian filter.

A general linear model (GLM) was used for all statistical analyses. At the first (subject) level of the GLM, the onset of the decision phase using a boxcar function of 4 seconds, and the onset of the outcome phase using a boxcar function of 2 seconds were included as events. Parametric regressors of the decision phase event representing the perceived risk (i.e., $CV_{\text{perceived}}$) for chosen gambles or the predicted probability for chosen gambles was included. An additional parametric regressor indicating whether subjects received high or low monetary outcomes during the outcome phase was included into the model in order to assess response to rewards. At the second (group) level of the GLM, whole brain analysis was conducted to determine how perceived risk for chosen gambles, predicted probability for chosen gambles, and reward received scales with BOLD response. In addition, to identify how individual differences scale with neural responses to perceived risk of chosen gambles, multiple regression analyses were conducted using individual risk attitude and probability bias values as regressors in separate models.

Construction of Parametric Regressors. To measure risk level, a coefficient of variation (CV_{ϕ}) including subjective instead of objective probabilities was calculated for chosen gambles,

$$EV_{\phi} = \left(P_{high} + \phi\right) * V_{high} + \left(P_{low} - \phi\right) * V_{low}$$

$$CV_{\phi} = \frac{\sqrt{(P_{high} + \phi)(V_{high} - EV_{\phi})^2 + (P_{low} - \phi)(V_{low} - EV_{\phi})^2}}{EV_{\phi}}$$

where P_{high} is equal to the probability associated with the high monetary outcome, P_{low} is equal to the probability associated with the low monetary outcome, ϕ is the estimated probability bias, V_{high} is the high monetary outcome, and V_{low} is the low monetary outcome. Note that $P_{low} + P_{high} = 1$ and that subjective probability was constrained as $0 \leq (P_{high/low} \pm \phi) \leq 1$.

Given the robust results in the risk processing literature (Mohr et al., 2010), we hypothesized that greater hemodynamic response to perceived risk during the decision phase of the lottery choice task would be observed in the bilateral insula and medial prefrontal cortex. Also, based on the large number of studies that report subjective value is encoded in the ventromedial prefrontal cortex (Bartra, McGuire, & Kable, 2013), we expected that subjective value will scale with ventromedial prefrontal cortex responses at both the decision and outcome phases of the lottery choice task. To test these a priori hypotheses, we conducted region of interest (ROI) analyses. ROI analyses were performed using the MarsBar Toolbox. ROIs for each region were generated by creating a 6mm sphere around centroids previously identified in meta-analyses of risk processing (Mohr, Biele, Heekeren, 2010) and subjective value (Bartra, McGuire, & Kable, 2013). Risk processing regions included the right insula (MNI coordinates: 36,24,1), left insula (-31,23,3), and medial prefrontal cortex (-3,37,28). The primary subjective value region was the ventromedial prefrontal (0,40,12). For these ROI analyses, small volume correction with a cluster-level threshold of $p_{FWE} < .05$ was applied to whole brain analyses. For all other analyses, a cluster-level threshold $p_{FWE} < .05$ was applied.

Supplementary Table 2.1. Relations of objective risk activity (CV) vs. risk activity adjusted for probability bias (CVϕ) and individual differences of risk attitude (α) and probability bias (ϕ)

	α				ϕ			
Region	$\beta_{CV\phi}$	β_{CV}	*Z*	*p*	$\beta_{CV\phi}$	β_{CV}	*Z*	*p*
R amygdala	-0.171	-0.068	-0.478	*n.s.*	-3.069	-0.310	-2.715	0.007
L amygdala	-0.083	0.065	-0.629	*n.s.*	-3.460	-0.286	-2.881	0.004
R insula	-0.662	-0.948	1.150	*n.s.*	-2.355	-4.437	1.701	*n.s.*
L insula	-0.571	-1.013	1.703	*n.s.*	-0.919	-3.362	1.843	*n.s.*
dACC	-0.726	-0.941	-0.123	*n.s.*	-3.937	-5.807	1.245	*n.s.*

Supplementary Table 2.2. Neural responses to risk, adjusted for probability bias during the decision phase.

Cluster	Region	Hemisphere	Cluster					Peak					MNI Coordinates		
			p_{FWE}	$p_{FWE(svc)}$	q_{FDR}	p_{unc}	*voxels*	*T*	p_{FWE}	$p_{FWE(svc)}$	p_{FDR}	p_{unc}	*x*	*y*	*z*
1	Anterior Insula / Inferior Frontal Gyrus	Right	0.000	0.005	0.000	0.000	568	8.47	0.000	0.000	0.000	0.000	30	23	-11
								6.58	0.000	*n.a.*	0.000	0.000	39	26	4
2	Anterior Insula / Inferior Frontal Gyrus	Left	0.000	0.005	0.000	0.000	393	7.22	0.000	0.000	0.000	0.000	-36	23	-5
								6.97	0.000	*n.a.*	0.000	0.000	-30	20	-11
								4.24	0.490	*n.a.*	0.101	0.000	-33	14	13
3	Medial Prefrontal Cortex	Bilateral	0.000	0.005	0.000	0.000	1210	8.43	0.000	0.000	0.000	0.000	0	38	16
								6.95	0.000	*n.a.*	0.000	0.000	9	5	-2
								6.25	0.000	*n.a.*	0.000	0.000	6	44	31
4	Supplementary Motor Area	Bilateral	0.003	*n.a.*	0.001	0.000	131	4.80	0.092	*n.a.*	0.024	0.000	9	5	70
								4.74	0.115	*n.a.*	0.028	0.000	-6	8	64
								4.64	0.160	*n.a.*	0.036	0.000	9	14	64

Note: For regions identified a priori, small volume correction (with a cluster-level threshold of $p_{FWE} < .05$) was applied using a 6mm sphere around centroids identified in Mohr et al., 2010.

Supplementary Table 2.3. Neural responses to subjective value at decision and outcome phases.

Cluster	Region	Hemisphere	Cluster					Peak					MNI Coordinates		
			p_{FWE}	$p_{FWE(svc)}$	q_{FDR}	p_{unc}	*Voxels*	*T*	p_{FWE}	$p_{FWE(svc)}$	p_{FDR}	p_{unc}	*x*	*y*	*z*
Decision Phase															
1	Ventromedial Prefrontal Cortex	Right	0.082	0.003	0.061	0.008	71	4.10	0.247	0.000	0.261	0.000	0	47	-14
2	Precuneus	Left	0.001	*n.a.*	0.002	0.000	187	5.51	0.005	*n.a.*	0.027	0.000	-9	-58	19
3	Precuneus	Right	0.031	*n.a.*	0.028	0.000	94	4.51	0.199	*n.a.*	0.245	0.000	12	-55	19
4	Superior Temporal Gyrus	Right	0.001	*n.a.*	0.002	0.000	201	4.65	0.125	*n.a.*	0.245	0.000	69	-19	10
								4.52	0.188	*n.a.*	0.245	0.000	69	-10	10
								4.17	0.497	*n.a.*	0.432	0.000	63	8	-14
5	Occipital Cortex	Left	0.027	*n.a.*	0.028	0.002	97	4.70	0.106	*n.a.*	0.245	0.000	-45	-73	22
								3.97	0.721	*n.a.*	0.432	0.000	-42	-73	31
Outcome Phase															
1	Caudate / Ventromedial Prefrontal Cortex	Bilateral	0.000	0.001	0.000	0.000	1504	5.28	0.014	0.000	0.061	0.000	-12	8	-11
								5.25	0.016	*n.a.*	0.061	0.000	-3	44	-11
								5.04	0.035	*n.a.*	0.069	0.000	18	23	13
2	Occipital Cortex	Left	0.002	*n.a.*	0.001	0.000	155	4.88	0.065	*n.a.*	0.065	0.000	-18	-88	-5
3	Superior Frontal Cortex	Left	0.001	*n.a.*	0.001	0.000	162	4.61	0.163	*n.a.*	0.139	0.000	-18	29	46
4	Lingual Gyrus / Precuneus / Cerebellum	Left	0.001	*n.a.*	0.001	0.000	176	4.44	0.273	*n.a.*	0.141	0.000	-6	-49	1
								3.89	0.843	*n.a.*	0.510	0.000	-6	-55	16
								3.82	0.896	*n.a.*	0.589	0.000	-9	-73	-14

Note: For regions identified a priori, small volume correction (with a cluster-level threshold of $p_{FWE} < .05$) was applied using a 6mm sphere around centroids identified in Bartra et al., 2013.

Supplementary Table 2.5. Neural correlates of risk attitude in response to risk, adjusted for probability bias during the decision phase.

Cluster	Region	Hemisphere	Cluster					Peak					MNI Coordinates		
			p_{FWE}	$p_{FWE(svc)}$	q_{FDR}	p_{unc}	*voxels*	*T*	p_{FWE}	$p_{FWE(svc)}$	p_{FDR}	p_{unc}	*x*	*y*	*z*
1	Anterior Insula	Left	0.127	0.009	0.106	0.010	52	3.42	0.999	0.006	0.734	0.000	-33	20	1
2	Anterior Insula	Right	0.086	0.009	0.106	0.006	59	4.30	0.429	0.001	0.518	0.000	36	20	-2
3	Medial Prefrontal Cortex	Left	0.984	0.012	0.717	0.296	7	3.56	0.994	0.006	0.681	0.000	-3	35	31
4	Angular Gyrus	Left	0.041	*n.a.*	0.098	0.003	73	4.88	0.429	*n.a.*	0.518	0.000	-63	-55	37

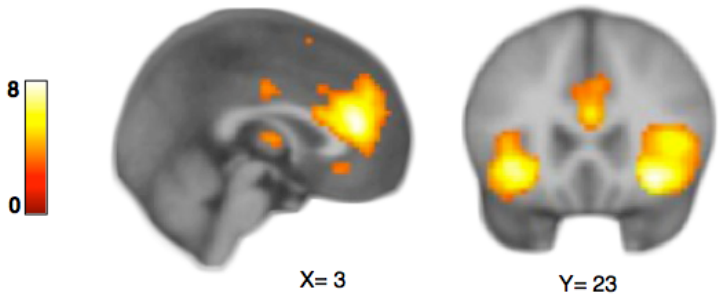
Note: For regions identified a priori, small volume correction (with a cluster-level threshold of $p_{FWE} < .05$) was applied using a 6mm sphere around centroids identified in Mohr et al., 2010.

Supplementary Table 2.6. Neural correlates of probability bias in response to risk, adjusted for probability bias during the decision phase.

Cluster	Region	Hemisphere	Cluster					Peak					MNI Coordinates		
			p_{FWE}	$p_{FWE(svc)}$	q_{FDR}	p_{unc}	*Voxels*	*T*	p_{FWE}	$p_{FWE(svc)}$	p_{FDR}	p_{unc}	*x*	*y*	*z*
1	Amygdala / Parahippocampal Gyrus	Right	0.018	*n.a.*	0.062	0.003	113	5.14	0.012	*n.a.*	0.048	0.000	24	-10	-32
								3.86	0.620	*n.a.*	0.381	0.000	33	-4	-20
2	Amygdala / Parahippocampal Gyrus	Left	0.023	*n.a.*	0.062	0.004	107	4.51	0.111	*n.a.*	0.103	0.000	-27	-4	-26
								4.14	0.337	*n.a.*	0.249	0.000	-24	-13	-20
								4.13	0.347	*n.a.*	0.249	0.000	-21	-7	-35
3	Medial Prefrontal Cortex	Bilateral	0.044	0.004	0.092	0.007	88	4.32	0.205	0.001	0.175	0.000	3	26	43
								3.93	0.542	*n.a.*	0.341	0.000	0	35	37
4	Inferior Temporal Gyrus / Parahippocampal Gyrus	Right	0.007	*n.a.*	0.054	0.001	144	5.28	0.007	*n.a.*	0.041	0.000	60	-19	-26
								4.74	0.051	*n.a.*	0.103	0.000	51	-16	-26
								4.57	0.091	*n.a.*	0.103	0.000	33	-22	-23

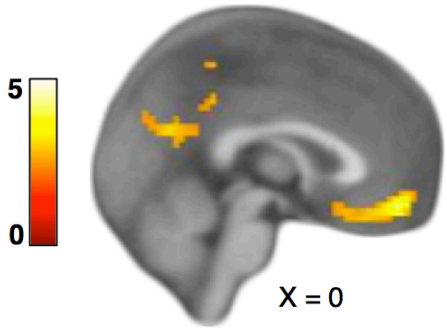
Note: For regions identified a priori, small volume correction (with a cluster-level threshold of $p_{FWE} < .05$) was applied using a 6mm sphere around centroids identified in Mohr et al., 2010.

Supplementary Figure 2.1. Neural responses to risk, adjusted for probability bias during the decision phase.



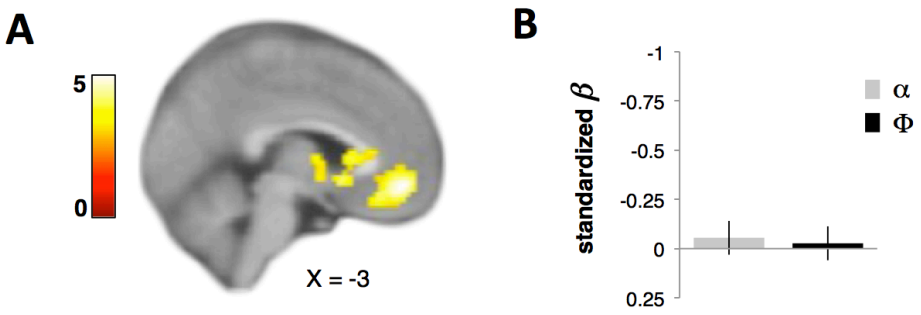
S2.1. Adolescents displayed greater hemodynamic responses in the medial prefrontal cortex (left; $t(136)=8.47$, $p_{FWE} < .05$) and bilateral insula (right; left insula: $t(136)=7.22$, $p_{FWE} < .05$; right insula: $t(136)=8.43$, $p_{FWE} < .05$) in response to higher levels of risk (i.e., coefficient of variation) relative to lower levels for chosen options during the decision phase of the lottery choice task. A cluster defining threshold of $p < .001$ was used for all analyses.

Supplementary Figure 2.2. Neural responses to subjective value during the decision phase.



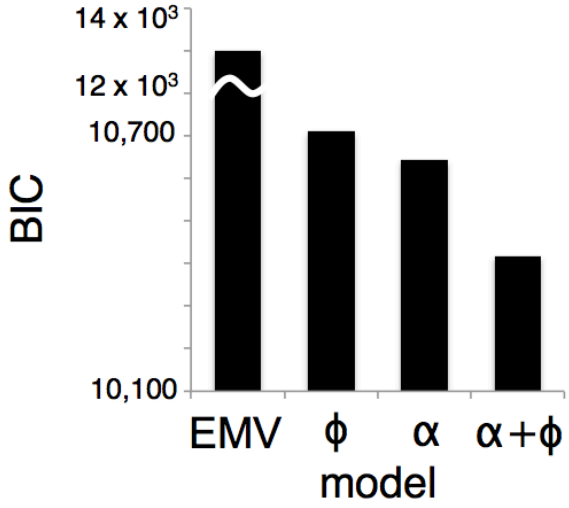
S2.2. Adolescent participants exhibited a subjective valuation signal consistent with prior studies (Clithero & Rangel, 2013; Hare, Camerer & Rangel, 2009, Chung et al., 2015) in the ventromedial prefrontal cortex in response to chosen options with higher (relative to lower) predicted probabilities during the decision phase of the lottery choice task, $t(136)=4.10$, $p_{FWE(SVC)} < .05$, with a cluster defining threshold $p < .001$.

Supplementary Figure 2.3. Neural responses to reward during the outcome phase



S2.3 A.) Adolescents displayed heightened hemodynamic responses in the ventromedial prefrontal cortex (vmPFC) to high versus low outcomes during the outcome phase of the lottery choice task, $t(136)=5.25$, $p_{FWE} < .05$, with a cluster defining threshold $p < .001$. **B.)** Individual risk attitude and probability bias estimates showed no relation to the vmPFC responses during the outcome phase. The lack of a relation during the outcome phase demonstrates that individual differences in the transformation of values and probabilities are specific to neural computations of risk rather than processing of rewards.

Supplementary Figure 2.4. Model comparison



S2.4. Bayesian Information Criterion (BIC) values for i) expected monetary value model (EMV; no transformation of value or probability); ii) probability bias model; iii) risk attitude model; and iv) the model containing both risk attitude and probability bias. Lower values of BIC indicate better fit to data.

General Discussion

The goal of the current work was to gain a broad understanding of the cognitive and neurobiological mechanisms that drive risk-taking, with the aim of informing prevention and intervention efforts targeting reduced risk-taking. To this end, the current work leveraged methods from multiple disciplines (i.e., behavioral economic models, developmental theory, fMRI) to examine how adolescents evaluate risk information during decision-making. Findings from both studies indicated that adolescents exhibited inter-individual differences in risk preferences; these individual differences were related to the recruitment of risk-related circuitry, suggesting a neural signature representative of behavioral risk sensitivity. Our results emphasized that some adolescents demonstrated notable proclivity toward risk, while others did not, and that adolescents were capable of processing risk in a similar way relative to adults (for meta-analysis, see Mohr, Biele, & Heekeren, 2010). Suggesting that the adolescent brain has the functional capacity to carry out neural computations of risk at the beginning of middle adolescence.

Study 1 also showed that sensitivity to risk information increases as adolescents become older, implying that the adolescent brain becomes more efficient at encoding risk over time. This result speaks to the importance of considering adolescence as a heterogeneous developmental period where fluctuations in risk processing have strong influence on decision-making. An inherent strength of Study 1 was the utilization of a longitudinal design and large cohort of adolescents, which allowed for the prospective examination of risk processing effects on future risky behavior. The longitudinal design also allowed us to account for the maturation of neurobehavioral mechanisms of risky choice, which cross-sectional studies are unable to accomplish. More generally, these findings shed light on an existing debate in economics and

psychology concerning the stability of risk preferences. No consensus has been reached as to whether risk preferences are stable traits or states that change over time. Our findings support the latter by showing that adolescent risk preferences are not only unstable but that they linearly increase over time.

Much of the adolescent risky decision-making literature utilizing model-based approaches have yet to link inter-individual differences in decision-making processes (either risk or reward) to risk-taking in the real world. This is an important connection to be made if the goal is to use research to inform existing prevention and intervention efforts aimed at decreasing risk-taking. Our results from both studies are promising for two reasons. First, Study 1 revealed that adolescents who exhibited decreased sensitivity to risk in the insular cortex were more likely to engage in risky behavior compromising their health two years later. This finding represents a potential neural vulnerability that exists at the beginning of middle adolescence that prospectively influences future risk-taking. Second, Study 2 used an adapted expected utility model to show that adolescents have unrealistic expectations regarding the probability of receiving favorable outcomes and these expectations are related to self-reported substance use behavior. Although laboratory tasks have previously been thought to be limited in capturing real-world decision-making behavior (Richards, Plate, & Ernst, 2013), both of the studies presented here demonstrated that decision-making processes expressed in the laboratory can translate to environments outside the laboratory.

Taken altogether, our results suggest that the motivational system described within neurodevelopmental "dual-systems" theories may actually be more complex than previously thought (Casey, 2015; Steinberg, 2008). The overactive motivational system has been attributed primarily to reward-related processes reflecting the bulk of previous research focused on

understanding reward sensitivity during adolescence (Barkley-Levenson & Galvan, 2014; Braams, van Duijvenvoorde, Peper, & Crone, 2015; Galvan et al., 2006; Silverman, Jedd, & Luciana, 2015; van Leijenhorst et al., 2010). Although adolescents have been found to be more sensitive to rewarding stimuli compared to adults (Barkley-Levenson & Galvan, 2014; Galvan et al., 2006; van Leijenhorst et al., 2010), no relation between adolescent reward sensitivity and real world risk-taking has been found (for review, see Pfeifer & Allen, 2012; Schonberg, Fox, & Poldrack, 2011). The present work illuminates the complexity of the proposed motivational system and highlights risk sensitivity as a promising neurobehavioral mechanism worthy of future research given its prospective and concurrent relation to real-world risk-taking.

Limitations & Future Directions

While the current work makes important contributions to the study of adolescent risky decision-making, future studies should expand on the research presented here in order to comprehensively understand how risk processes influence adolescent risk-taking. Future work examining time points both before and after middle adolescence may better uncover when risk-related circuitry begins to develop as well as more fully capture the developmental trajectory of these processes. In order to substantiate probability bias as a potential neurobehavioral mechanism of risk-taking, future studies should replicate the current findings and examine behavioral biases and neural processes within a sample of adolescents who exhibit high levels of risky behavior. Given that our study focused on a normative sample, it is possible that our current findings only apply to a relatively risk-averse population. Longitudinal investigation of probability bias and associated neural substrates in both low- and high-risk adolescents could reveal the processes that distinguish maladaptive developmental pathways, as well identify target time periods for intervention in high-risk populations.

In order to holistically characterize risky decision-making in adolescence, future research should also examine whether motivational processes synergistically influence risky decision-making. Since it is well known that both reward and risk sensitivity are related and separately influence risky decision-making (d'Acremont & Bossaerts, 2008; Christopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009; Tobler, O'Doherty, Dolan, & Schultz, 2007), it might be the case that reward sensitivity depends on risk sensitivity resulting in risky choice behavior. For instance, adolescents may exhibit incongruent sensitivities toward reward and risk such that risky choice is actually the product of high reward sensitivity and low risk sensitivity. Whereas, risk averse behavior might be the result of an individual who exhibits low reward sensitivity in addition to high risk sensitivity guiding him or her toward less risky options. Additionally, prior work has suggested that neural risk processing and cognitive control processes in the adolescent brain interact to predict adolescent health risk behaviors such as substance use and risky sexual behavior (Kim-Spoon et al., 2016), suggesting that individual differences in cognitive control may help account for relations between neural risk sensitivity and adolescent risk-taking. That being said, it is important for future work to concurrently study the developmental trajectory of risk processing and cognitive control processes in the adolescent brain, as well as the relation between these processes and adolescent risky behavior. Research in this area could inform current neurodevelopmental theories and provide testable hypotheses. For instance, if neurodevelopmental theories are accurate, we might predict a buffering effect between cognitive control and the relation between risk processing and risk-taking.

Although our results indicated that adolescents become more risk averse over time, we are unable to explain the specific mechanisms driving this pattern. Prominent theories in developmental psychology have emphasized the importance of contextual factors such as home

environment and peer influence as well as biological factors such as pubertal development in shaping the development of risk-taking behavior during adolescence into adulthood. For instance, adolescents have been shown to increase in risk-taking when amongst peers (Chein, O'Brien, Uckert, & Steinberg, 2011) and decrease in risk-taking when being observed by their mothers (Telzer, Ichien, & Qu, 2015). Future work is needed to directly examine how these factors (and their interactions) contribute to neural and behavior risk processes and subsequent health outcomes. Another context that may be an important consideration for future research is the type of uncertainty experienced during risky decision-making. The risky decision-making task used in both studies focused on neurobehavioral responses to *risk,* a type of uncertainty that describes situations in which the probabilities of outcomes are completely known. However, most risky decision-making situations in the real world are often *ambiguous*. That is, ambiguous decisions involve choosing between alternatives in which the probabilities are partially to completely unknown. Previous research has shown that adolescents are more ambiguity tolerant compared to adults which may explain why adolescents engage in relatively more risk-taking (Blankenstein, Crone, van den Bos, & van Duijvenvoorde, 2016; Blankenstein, Peper, Crone, & van Duijvenvoorde, 2017; Tymula et al., 2012). Based on our results in Study 2, adolescents exhibited unrealistic expectations regarding the probabilities of potential outcomes. These findings lead us to speculate that probability bias may also influence ambiguity preferences, such that congruency or incongruency between these preferences may lead to deviations from choice predictions. Further research is needed to investigate how ambiguity preferences and underlying neural correlates mature throughout adolescence.

Risk-taking during adolescence is often described as maladaptive; however, adolescent risk-taking can be adaptive for healthy development by promoting learning through exploration

and approach toward novel experiences. In order to better understand the mechanisms of maladaptive risky behavior, it is critical to study how risky decision-making processes develop within adaptive and maladaptive risk-taking domains, in addition to identifying the developmental pathways leading to adaptive versus maladaptive risky behavior. Regarding adaptive risky behavior, it may be that behavioral and neural sensitivity to risk may potentially guide adolescents toward health promotion behaviors, while concurrently leading them away from harmful health risk behaviors.

Conclusions

In summary, the current work advances our knowledge of the roles behavioral and neural risk sensitivity play in adolescent risky decision-making. In particular, our results characterize the developmental trajectory of behavioral and neural risk sensitivity during a crucial period of adolescence in which susceptibility to risk-taking is at its greatest. Most importantly, this work identifies potential neurobehavioral determinants of adolescent risk-taking that may be effective for the development of individualized prevention and intervention programs.

References

Barkley-Levenson, E., & Galván, A. (2014). Neural representation of expected value in the adolescent brain. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(4), 1646–1651.

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.

Benes, F. M. (1989). Myelination of cortical-hippocampal relays during late adolescence. *Schizophrenia Bulletin*, *15*(4), 585.

Bernoulli, D. (1954). Exposition of a New Theory on the Measurement of Risk. *Econometrica: Journal of the Econometric Society*, *22*(1), 23–36.

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*, *24*(8), 1793–1802.

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.

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.

Blakemore, S.J., & Robbins, T. W. (2012). Decision-making in the adolescent brain. *Nature Neuroscience*, *15*(9), 1184–1191.

Blankenstein, N. E., Crone, E. A., van den Bos, W., & van Duijvenvoorde, A. C. K. (2016). Dealing With Uncertainty: Testing Risk- and Ambiguity-Attitude Across Adolescence.

Developmental Neuropsychology, *41*(1-2), 77–92.

Blankenstein, N. E., Peper, J. S., Crone, E. A., & van Duijvenvoorde, A. C. K. (2017). Neural Mechanisms Underlying Risk and Ambiguity Attitudes. *Journal of Cognitive Neuroscience*, 1–15.

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*, *35*(18), 7226–7238.

Brenhouse, H. C., Sonntag, K. C., & Andersen, S. L. (2008). Transient D1 dopamine receptor expression on prefrontal cortex projection neurons: relationship to enhanced motivational salience of drug cues in adolescence. *The Journal of Neuroscience*, *28*(10), 2375–2382.

Burnett, S., Bault, N., Coricelli, G., & Blakemore, S.-J. (2010). Adolescents' heightened risk-seeking in a probabilistic gambling task. *Cognitive Development*, *25*(2), 183–196.

Casey, B. J. (2015). Beyond simple models of self-control to circuit-based accounts of adolescent behavior. *Annual Review of Psychology*, *66*, 295–319.

Casey, B. J., Giedd, J. N., & Thomas, K. M. (2000). Structural and functional brain development and its relation to cognitive development. *Biological Psychology*, *54*(1-3), 241–257.

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). Retrieved from http://onlinelibrary.wiley.com/doi/10.1111/j.1467-7687.2010.01035.x/full

Christopoulos, G. I., Tobler, P. N., Bossaerts, P., Dolan, R. J., & Schultz, W. (2009). Neural correlates of value, risk, and risk aversion contributing to decision making under risk. *The*

Journal of Neuroscience, *29*(40), 12574–12583.

Critchley, H. D., Mathias, C. J., & Dolan, R. J. (2001). Neural activity in the human brain relating to uncertainty and arousal during anticipation. *Neuron*, *29*(2), 537–545.

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.

d'Acremont, M., & Bossaerts, P. (2008). Neurobiological studies of risk assessment: a comparison of expected utility and mean-variance approaches. *Cognitive, Affective & Behavioral Neuroscience*, *8*(4), 363–374.

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), 1–22.

Ernst, M., Romeo, R. D., & Andersen, S. L. (2009). Neurobiology of the development of motivated behaviors in adolescence: a window into a neural systems model. *Pharmacology, Biochemistry, and Behavior*, *93*(3), 199–211.

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*, *26*(25), 6885–6892.

Galvan, A. (2010). Adolescent development of the reward system. *Frontiers in Human Neuroscience*, *4*, 6.

Giedd, J. N. (2004). Structural magnetic resonance imaging of the adolescent brain. *Annals of the New York Academy of Sciences*, *1021*, 77–85.

Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., … Thompson, P. M. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proceedings of the National Academy of Sciences of*

the United States of America, *101*(21), 8174–8179.

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.

Huettel, S. A. (2006). Behavioral, but not reward, risk modulates activation of prefrontal, parietal, and insular cortices. *Cognitive, Affective & Behavioral Neuroscience*, *6*(2), 141–151.

Huttenlocher, P. R. (1990). Morphometric study of human cerebral cortex development. *Neuropsychologia*, *28*(6), 517–527.

Kahneman, D., & Tversky, A. (1979). Prospect Theory: An Analysis of Decision under Risk. *Econometrica: Journal of the Econometric Society*, *47*(2), 263–291.

Kuhnen, C. M., & Knutson, B. (2005). The neural basis of financial risk-taking. *Neuron*, *47*(5), 763–770.

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.

MacPherson, L., Magidson, J. F., Reynolds, E. K., Kahler, C. W., & Lejuez, C. W. (2010). Changes in sensation seeking and risk-taking propensity predict increases in alcohol use among early adolescents. *Alcoholism, Clinical and Experimental Research*, *34*(8), 1400–1408.

Markowitz, H. (1959). *Portfolio Selection, Efficient Diversification of Investments*. J. Wiley.

Masten, A. S., & Cicchetti, D. (2010). Developmental cascades. *Development and Psychopathology*, *22*(3), 491–495.

Metcalfe, J., & Mischel, W. (1999). A hot/cool-system analysis of delay of gratification: dynamics of willpower. *Psychological Review*, *106*(1), 3–19.

Mohr, P. N. C., Biele, G., & Heekeren, H. R. (2010). Neural processing of risk. *The Journal of Neuroscience*, *30*(19), 6613–6619.

Paulus, M. P., Rogalsky, C., Simmons, A., Feinstein, J. S., & Stein, M. B. (2003). Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *NeuroImage*, *19*(4), 1439–1448.

Paus, T. (2005). Mapping brain maturation and cognitive development during adolescence. *Trends in Cognitive Sciences*, *9*(2), 60–68.

Peper, J. S., & Dahl, R. E. (2013). The Teenage Brain: Surging Hormones—Brain-Behavior Interactions During Puberty. *Current Directions in Psychological Science*, *22*(2), 134–139.

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.

Raznahan, A., Lee, Y., Stidd, R., Long, R., Greenstein, D., Clasen, L., … Giedd, J. N. (2010). Longitudinally mapping the influence of sex and androgen signaling on the dynamics of human cortical maturation in adolescence. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(39), 16988–16993.

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 and Biobehavioral Reviews*, *37*(5), 976–991.

Rothschild, M., & Stiglitz, J. E. (1970). Increasing risk: I. A definition. *Journal of Economic Theory*, *2*(3), 225–243.

Schonberg, T., Fox, C. R., & Poldrack, R. A. (2011). Mind the gap: bridging economic and naturalistic risk-taking with cognitive neuroscience. *Trends in Cognitive Sciences*, *15*(1), 11–19.

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.

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.

Steinberg, L. (2008). A Social Neuroscience Perspective on Adolescent Risk-Taking. *Developmental Review: DR*, *28*(1), 78–106.

Telzer, E. H., Ichien, N. T., & Qu, Y. (2015). Mothers know best: redirecting adolescent reward sensitivity toward safe behavior during risk-taking. *Social Cognitive and Affective Neuroscience*, *10*(10), 1383–1391.

Tobler, P. N., O'Doherty, J. P., Dolan, R. J., & Schultz, W. (2007). Reward value coding distinct from risk attitude-related uncertainty coding in human reward systems. *Journal of Neurophysiology*, *97*(2), 1621–1632.

Tymula, A., Rosenberg Belmaker, L. A., Roy, A. K., Ruderman, L., Manson, K., Glimcher, P. W., & Levy, I. (2012). Adolescents' risk-taking behavior is driven by tolerance to ambiguity. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(42), 17135–17140.

van Duijvenvoorde, A. C. K., & Crone, E. A. (2013). The teenage brain: a neuroeconomic approach to adolescent decision-making. *Current Directions in Psychological Science*, *22*(2), 108–113.

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.

van Leijenhorst, L., Westenberg, P. M., & Crone, E. A. (2008). A developmental study of risky decisions on the cake gambling task: age and gender analyses of probability estimation and reward evaluation. *Developmental Neuropsychology*, *33*(2), 179–196.

Weber, E. U., & Johnson, E. J. (2008). Decisions under uncertainty: Psychological, economic, and neuroeconomic explanations of risk preference. *Neuroeconomics: Decision Making and the Brain*, 127–144.

Willoughby, T., Good, M., Adachi, P. J. C., Hamza, C., & Tavernier, R. (2013). Examining the l ink between adolescent brain development and risk-taking from a social–developmental perspective. *Brain and Cognition*, *83*(3), 315–323.

Appendix A

Holt & Laury Gamble Information

Gamble Information (High Probability, Low Probability, High Outcome, Low Outcome, Expected Value, Coefficient of Variation)

Low-Risk Option						High-Risk Option					
High Probability	Low Probability	High Outcome	Low Outcome	EV	CV	High Probability	Low Probability	High Outcome	Low Outcome	EV	CV
20%	80%	$2.00	$1.60	1.68	0.12	20%	80%	$3.85	$0.10	0.85	1.63
30%	70%	$2.00	$1.60	1.72	0.14	30%	70%	$3.85	$0.10	1.23	1.55
40%	60%	$2.00	$1.60	1.76	0.15	40%	60%	$3.85	$0.10	1.60	1.45
50%	50%	$2.00	$1.60	1.80	0.15	50%	50%	$3.85	$0.10	1.98	1.33
60%	40%	$2.00	$1.60	1.84	0.14	60%	40%	$3.85	$0.10	2.35	1.20
70%	30%	$2.00	$1.60	1.88	0.13	70%	30%	$3.85	$0.10	2.73	1.04
80%	20%	$2.00	$1.60	1.92	0.12	80%	20%	$3.85	$0.10	3.10	0.85
90%	10%	$2.00	$1.60	1.96	0.09	90%	10%	$3.85	$0.10	3.48	0.60

Appendix B

THINGS I DO

These next questionnaires are about things you might do. Please answer truthfully. Your answers to the questions are confidential. Here is a list of things some kids might do.
After you read each statement, indicate how often you have done each thing: Never, Once or Twice, or More than Two Times IN THE PAST YEAR.

How many times in the past year have you...

	Not at all	Once or Twice	More than Twice
1. Ridden in a car without a seatbelt	0	1	2
2. Ridden on a bike without a helmet	0	1	2
3. Done something dangerous on a dare	0	1	2
4. Carried a weapon somewhere	0	1	2
5. Threatened to beat up someone to make them do something	0	1	2
6. Taken part in a gang fight	0	1	2
7. Skipped school without permission	0	1	2
8. Had a fist fight with another person	0	1	2
9. Purposely set a fire in a building or in any other place	0	1	2
10. Hurt an animal on purpose	0	1	2
11. Smoked a cigarette or used tobacco	0	1	2
12. Drunk a bottle or glass of beer or other alcohol	0	1	2
13. Used or smoked marijuana, grass, pot, weed	0	1	2
14. Taken or stolen something not yours worth a lot, like a video game	0	1	2
15. Taken or stolen something not yours and worth little, like candy	0	1	2
16. Gotten into someplace like a movie or game without paying	0	1	2
17. Run away from home	0	1	2
18. Broken into a building to take or steal something	0	1	2

19. Purposely damaged or destroyed property that wasn't yours	0	1	2