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Voor mijn ouders

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Chapter 1

General introduction

Scope

As human beings, we face many uncertainties in our decision-making. For example, when deciding to run a red light on our way to work, we do not know if this will result in a fine, cause a traffic accident, or save time. Or, when deciding to go out on the ice after the first frost of the season, it is difficult to anticipate whether we will fall through the ice or enjoy winter fun. Even a simple decision such as flipping a coin involves uncertainty: we do not know if the outcome is heads or tails. In these examples, a decision-maker is presented with a choice that involves risk, that is, outcomes may occur with a certain probability. Although a decision-maker may have some idea of the possible range of outcomes of their decisions (e.g., causing a traffic accident or not; falling through the ice or not; flipping heads or tails), he/she may lack information about the exact *probabilities* of these different outcomes. That is, in some of these examples, the exact probabilities of the different outcomes are known (for example, the chance of heads in a coin flip is 50%). In behavioral economics, this is referred to as explicit risk, or *risk* for short (Tversky & Kahneman, 1992). In other instances, these probabilities may not be known (for example, the chance of falling through the ice is unknown). This is referred to as ambiguous risk, or *ambiguity* (Tversky & Kahneman, 1992). Whether decisions involve risk (uncertain outcomes with a *known probability*) or ambiguity (uncertain outcomes with an *unknown probability*), influences our actual tendency to engage in taking risks to a great extent (Tversky & Kahneman, 1992; Tymula, Rosenberg Belmaker, Ruderman, Glimcher, & Levy, 2013). For instance, adults are generally averse to risk, and even more averse to ambiguity (Camerer & Weber, 1992). Although how we approach risks can be considered to be a stable trait, there may be developmental life periods in which our risk preferences change.

A developmental period possibly associated with greater risk-seeking preferences is adolescence, which is the transition phase between childhood and adulthood (Somerville, Jones, & Casey, 2010; Steinberg, 2008). In particular, adolescents display higher levels of risk taking in daily life, such as excessive substance use and reckless behavior in traffic, compared to children and adults (Eaton et al., 2008; Steinberg, 2008). Many experimental psychological studies on developmental changes in risk taking have used paradigms that involve explicit risks. However, real life predominantly presents ambiguous risks. In addition, defining how adolescents generally deal with (i.e., avoid or seek out) risk and ambiguity remains rarely done. Moreover, even though adolescence is described as a period of heightened risk taking on average, there are pronounced individual differences in observed risk-taking behavior (not all adolescents are risk takers), which remain largely overlooked (Bjork & Pardini, 2015). In addition, risk taking may not necessarily be negative, but may be useful such as when taking risks to explore the environment or to help others (Hartley & Somerville, 2015; Do, Guassi-Moreira, & Telzer, 2017). Finally, few studies have aimed to link experimental risky choice behavior to indices of risk taking in real life. Therefore, in this thesis I examine risk taking in adolescents as a multi-measure tendency that may be driven by behavioral preferences towards risk and ambiguity; and by assessing individual variation in these preferences and their relation to real-life risk taking. In addition to behavioral measures, I use a neuroscientific approach to study the underlying mechanisms of these different aspects of risk taking. Including measures of the function and structure of the brain enables to study whether distinguishable aspects of risk taking are driven by different neural systems and how these relate to developmental and individual differences in risk taking.

In sum, the main goals of this thesis are twofold. First, I study fundamental processes underlying risky decision-making. To this end, I make use of behavior modelling and functional neuroimaging to decompose the behavioral and neural mechanisms underlying risky choice behavior in adolescence, under conditions of risk (known probabilities) and ambiguity (unknown probabilities). Second, given the positive and negative aspects of risk taking, I study to what extent individual differences in risk-taking tendencies inform our understanding of adolescence as a period of risks and opportunities (Crone & Dahl, 2012). Here, I combine self-report measures with functional and structural neuroimaging. The current introduction starts out with an overview of risky decision-making and associated neural networks, followed by an overview of current models on adolescent development, and ends with an outline of the empirical chapters.

Risky business?

Decision-making under uncertainty: risk and ambiguity

Risky decisions always involve a level of uncertainty about what outcome will result from what choice (Platt & Huettel, 2008). To what extent this variability in outcome is known or unknown is referred to as explicit risk or ambiguous risk, respectively (Tversky & Kahneman, 1992). One of the first behavioral studies on how individuals deal with these two aspects of risky decision-making was Ellsberg (1961), who asked participants in a series of experiments to bet money on one of two vases filled with marbles. The first vase contained a known distribution of black and red marbles (50:50), whereas the second vase contained 100 black and red marbles in an unknown distribution. Participants preferred the first vase (with the known distribution) for drawing a black marble. Yet strikingly, when participants were asked to bet between vases for grabbing a red marble, participants again preferred the first vase. Because participants kept betting on the first vase with the known distribution of marbles, their prior beliefs about the distribution of the second vase (namely, that there are more red marbles in this vase) were contradicted. That is, one cannot simultaneously believe that there are both more and less black marbles in the second vase. These findings became known as the Ellsberg Paradox (Ellsberg, 1961) and illustrate individuals' aversion to unknown distributions. This research was extended by other classic behavioral economic work, showing that even though individuals are averse to both risk and ambiguity, most individuals show an even stronger aversion to ambiguity than risk alone (Camerer & Weber, 1992; Ellsberg, 1961; Von Gaudecker, Van Soest, & Wengström, 2011). However, even though in general, people are risk and ambiguity averse, risk and ambiguity preferences are correlated weakly at best, indicating they may differentially drive risk-taking behavior (Tversky & Kahneman, 1992). Furthermore, there are pronounced individual differences in risk and ambiguity preferences (Levy, Snell, Nelson, Rustichini, & Glimcher, 2010).

An elegant way to capture individuals' preference for risk and ambiguity is to present participants with an economic choice paradigm, in which specific task parameters (such as the gain probabilities, gain amounts, and ambiguity levels) are systematically varied, and individuals' choice behavior is analyzed (e.g., see Tymula et al., 2013). Specifically, by using a model-based approach, an individual's preferences towards risk and ambiguity can be estimated, otherwise known as *risk attitude* and *ambiguity attitude*. These measures are a reflection of an individual's behavioral tendency to shy away from, or seek out, risk and ambiguity, and therefore range from risk and ambiguity averse, to risk and ambiguity seeking tendencies (Levy et al., 2010). The advantage of this formal decomposition of risky choice behavior is

that it results in isolated measures of behavioral preferences under risk and under ambiguity. However, to understand whether risk and ambiguity are differentially processed within, and between, individuals, a fundamental understanding of the underlying mechanisms driving these processes is key.

A neuroeconomic perspective

With the rise of cognitive neuroscience studies (Poldrack, 2008), researchers have been more and more able to study the underlying mechanisms of risky decision-making. First, with structural magnetic resonance imaging (MRI), one can examine the relation between brain volume and individuals' choice preferences (e.g., see Levy, 2016). Second, functional MRI allows researchers to examine the function of the brain, for instance during a risky choice task, in relation to individuals' choice preferences. This 'neuroeconomic' approach, which combines insights from economics, psychology, and neuroscience, is a valuable addition to understanding the mechanisms underlying various aspects of the risky decision-making process (Glimcher & Rustichini, 2004). That is, whereas an economic and psychological approach is typically focused on modelling and understanding choice behavior, neuroscience provides a mechanistic account of the underlying, fundamental, processes. As such, the combination of behavioral and neural substrates of risky choice behavior (e.g., relating risk sensitivity to brain activation), ultimately provides much more explanatory power of what drives risk taking than either approach

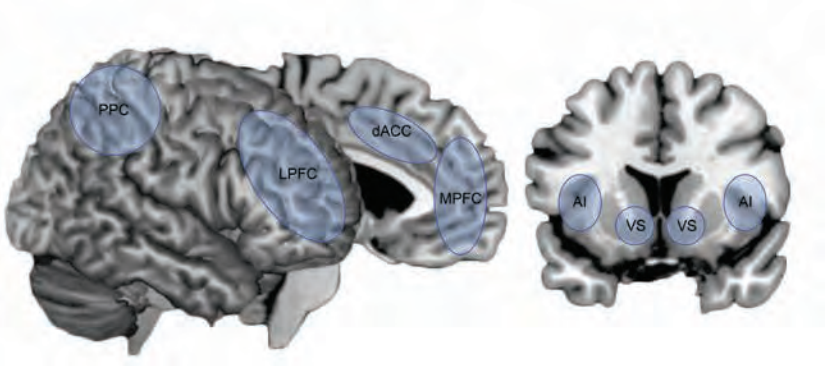

Figure 1. *Regions implicated in various aspects of risky choice behavior. PPC = posterior parietal cortex; LPFC = lateral prefrontal cortex; dACC = dorsal anterior cingulate cortex; MPFC = medial prefrontal cortex; AI = anterior insula; VS = ventral striatum. Figure based on the reviews by Knutson & Huettel, 2015; Mohr et al, 2010; Platt & Huettel, 2008.*

alone (Glimcher & Rustichini, 2004; Van Duijvenvoorde & Crone, 2013). Unraveling whether activation in the same, or in different, brain regions codes risk and ambiguity contributes to our understanding on whether these two aspects of risky decision-making differentially impact overt choice behavior.

Prior studies with adults have charted which brain regions are involved in risky decision-making *in general* (see Figure 1 below; for comprehensive reviews and meta-analyses, see Knutson & Huettel, 2015; Mohr, Biele, & Heekeren, 2010; Platt & Huettel, 2008). For instance, the ventral striatum (VS) and the (ventro)medial prefrontal cortex (PFC) have been associated with processing reward outcomes (Bartra, McGuire, & Kable, 2013; Delgado, 2007; Sescousse, Caldú, Segura, & Dreher, 2013) and reward learning (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). In addition, the anterior insula, dorsal anterior cingulate cortex (dACC/dorsomedial PFC), and ventrolateral PFC, typically respond to increasing uncertainty (Levy, 2016; Mohr et al., 2010), while dorsolateral PFC and posterior parietal cortex (PPC) have been associated with making executive judgments about probability and value (Huettel, Song, & McCarthy, 2005). However, note that these brain systems are a *general* reflection of risky decision-making, and may not be specific to conditions of risk (known probabilities) or ambiguity (unknown probabilities). That is, the few studies on the neural coding of risk and/or ambiguity (preference) have yielded mixed findings within these brain systems (e.g., see Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005; Huettel, Stowe, Gordon, Warner, & Platt, 2006; Levy et al., 2010). Moreover, these studies have been conducted in relatively small samples of adults. Thus, there is a need to further investigate the neural mechanisms underlying risk and ambiguity attitude, in larger samples, and importantly, across adolescent development. That is, although some studies have started to focus on *behavioral* risk and ambiguity attitudes in adolescence (e.g., Tymula et al., 2012; van den Bos & Hertwig, 2017), it remains unstudied how their neural mechanisms are manifested in adolescence. This is not only a developmental phase characterized by ongoing neural changes, but also by heightened risk-taking behavior.

Prevailing models of risk-taking development in adolescence

Adolescence, or the developmental phase from childhood to adulthood, is associated with pronounced changes in brain development (Giedd, 2004; Giedd et al., 1999). Specifically, while some subcortical volumes (such as the amygdala) follow an inverted U-shaped trajectory, others (such as the nucleus accumbens of the striatum), follow a linear decrease across adolescence (Mills, Goddings, Clasen, Giedd, & Blakemore, 2014). Cortical gray matter follows a gradual inverted U-shaped trajectory, peaking between childhood and adolescence, and stabilizes across adolescence and early

adulthood (Mills et al., 2014; Mills et al., 2016). Importantly, the development of these brain regions do not all occur at the same rate. For instance, the development of parietal and prefrontal regions, involved in cognitive control, is relatively protracted (continuing well into the early twenties) compared to the development of subcortical regions (Lenroot & Giedd, 2006; Mills et al., 2014). These profound structural changes have inspired influential theoretical models on adolescent (brain) development. For instance, it has been proposed that the 'imbalance' between relatively fast-maturing subcortical, socio-affective brain regions and relatively slow-maturing cortical, cognitive control regions (and their interconnections), underlies heightened risk taking typically observed in adolescence, such that these affective regions are hyperactive compared to these cognitive control regions (Casey, Jones, & Hare, 2008; Casey, 2015; Somerville & Casey, 2010; Steinberg, 2008). Furthermore, this imbalance may be especially salient in 'hot', or affectively-laden, contexts, resulting in elevated levels of risk taking, such as when behaviorally reinforcing decision outcomes are provided (Figner, Mackinlay, Wilkening, & Weber, 2009), in a peer context (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011) and, suggestively, in other contexts that may be a more naturalistic reflection of risk taking in real life, such as ambiguity (Defoe, Dubas, Figner, & van Aken, 2015).

These 'imbalance' models thus describe changes in risky decision-making across adolescence and in various decision contexts, and are useful when making general assumptions about adolescents on a group level. However, one potential drawback of these models is that they may overlook prominent individual differences that are observed between adolescents. Extending these insights, recent literature highlights the importance of examining individual differences in behavioral and brain development, stressing that adolescence is not the same for each individual (e.g., see Foulkes & Blakemore, 2018). Prior developmental neuroimaging studies show that individual differences in various risk-taking tendencies relate to neural activation in the VS, (ventro)medial PFC, DMPFC, insula, and lateral PFC (for a comprehensive review, see Sherman, Steinberg, & Chein, 2017). These regions are in line with neural findings reported in adults (see Figure 1). However, like adult studies, these adolescent studies too have included relatively small samples, nor have they explicitly focused on conditions of risk versus ambiguity. Moreover, the relation with real-life risk taking is relatively understudied. In this thesis, I therefore decompose risky choice behavior into underlying risk and ambiguity attitude, assess individual variation in these attitudes, and examine how these measures relate to neural activation and to risk taking in real life.

Finally, recent related neurodevelopmental models have proposed that adolescence may not only be a developmental phase characterized by maladaptive

behaviors such as health-detrimental risk taking, but may be a flexible phase characterized by risks *and* opportunities (e.g., Crone & Dahl, 2012). For instance, risk-taking behavior may be adaptive, such as when taking risks to explore new environments (Hartley & Somerville, 2015; Romer, Reyna, & Satterthwaite, 2017) or to help others (i.e., prosocial risk taking; Do, Guassi Moreira, & Telzer, 2017). Moreover, adolescence is also a developmental phase during which positive, other-oriented behaviors emerge, such as prosociality and social perspective taking (Blakemore & Mills, 2014; Dumontheil, Apperly, & Blakemore, 2010; Güroğlu, van den Bos, & Crone, 2014). However, a formal investigation of this view of adolescence (i.e., of positive and negative developmental trajectories and their underlying neural pathways) is currently lacking. Therefore, in addition to a fundamental approach on adolescent risky choice behavior, I address this broader theme of adolescence as a developmental phase of risks and opportunities, by relating individual differences in real-life measures of (risky) decision-making to functional and structural neuroimaging measures.

Outline of the thesis

In sum, the goals of this thesis are twofold. First, I decompose risky choice behavior into their underlying components (risk and ambiguity attitudes), and investigate their neural mechanisms in adolescence. Second, I focus on how individual differences in real-life (risky) decision-making contribute to our understanding of adolescence as period of risks and opportunities. These two goals are further outlined in the following five empirical chapters.

In **chapter 2**, I administered a behavioral 'wheel of fortune' task in a large sample of adolescents, spanning a wide age range (N = 157, 10-25 years). In this task, participants were asked to choose between two wheels of fortune. One wheel represented a sure, but relatively small, gain, whereas the other wheel reflected a gamble with varied amount, probability, and ambiguity level. Using a model-based method, individuals' risk and ambiguity attitude were estimated. In this study I tested the age-related trajectories of risk and ambiguity aversion, and how individual differences in risk and ambiguity attitude are related to indices of real-life risk taking and reward sensitivity. Furthermore, given the saliency of the peer-context in adolescent risk taking (e.g., Steinberg, 2008), I also included a social condition in which participants were presented with choices from a high risk-taking peer before making their own choice, and tested whether adolescents' risk and ambiguity attitude became more aligned with the peers' choices. This study thus aimed to get

a thorough understanding of behavioral risk and ambiguity attitude in adolescence, by focusing on their age-related changes, relations to real life, and robustness in a social context.

In **chapter 3** I describe a functional neuroimaging study with 50 adult participants (18-28 years). Here I aimed to disentangle behavioral and neural measures of risk and ambiguity processing within individuals. That is, I aimed to get a fundamental understanding of risk and ambiguity attitudes and their neural correlates (during choice and choice outcome) in an adult sample. This allowed me to test whether these factors separately drive observed risky choice behavior, and whether these relied on distinct or overlapping neural substrates. To this end I used two versions of the wheel of fortune task. First, I administered the behavioral wheel of fortune task to estimate risk and ambiguity attitude. Second, I related these estimations to neural activation during a straightforward monetary gambling task: a simplified fMRI version of the wheel of fortune task which included a choice phase (choosing to gamble or not) and a reward outcome phase (gain and no gain), under conditions of risk and ambiguity. The resulting insights set the stage for further testing in an adolescent population.

Chapter 4 builds on the findings reported in chapters 2 and 3, and describes a study in which it was further tested how risk and ambiguity attitudes are coded in the brain, in a second adolescent sample spanning a broad age range (N = 188, 12-22 years). However, here, I integrated participants' separately estimated risk and ambiguity attitudes, with the fMRI task during choice, on a trial-by-trial basis. That is, I inferred participants' individual *subjective value* of the choices presented in the fMRI task. While prior studies have investigated effects of objective expected value (i.e., the probability * amount of a risky option) in adolescence (e.g., Van Duijvenvoorde et al., 2015) , few studies have focused on *subjective* value coding, nor on whether this differs for risky and ambiguous decision contexts. Moreover, subjective, rather than objective, expected value tracking may be a more sensitive reflection of individual valuation processes. In this study I examined which brain regions positively and negatively scaled with subjective value under risk and under ambiguity in a large sample of adolescents.

Next, in **chapter 5** (N = 198, 12-25 years, including the sample of chapter 4), I focused on the relation between neural risk and ambiguity processing and individual differences in task-based (i.e., proportion gambling) and real-life (i.e., self-report measures) risk-taking tendencies. Although many prior studies have investigated brain-behavior associations of risk taking, few have included actual risk-taking behaviors inside and outside the laboratory in one comprehensive study (e.g., see Sherman et al., 2017). In addition, these brain-behavior associations have not been studied under conditions of risk versus ambiguity, both during choice (choosing to

gamble or not) and during outcome (processing rewards versus no rewards). Thus, to understand what drives risk taking in adolescence, multiple predictors of behavior on the individual level were included during gambling, as well as during reward-outcome processing.

Moving from this multidimensional perspective on adolescent risk taking, in **chapter 6** I further studied self-reported real-life risk-taking behavior and their underlying behavioral and neural predictors. Moreover, I also focused on prosocial behavior, that is, behaviors intended to benefit someone else. As such, the aim of this study was to understand which behavioral and neural underpinnings were predictive of these two seemingly paradoxical behaviors that emerge across adolescence in tandem; and whether adolescence can be conceived as a developmental phase of both risks and opportunities (Crone & Dahl, 2012). In this three-wave biannual longitudinal study (N = 210, 12-29 years at the final wave, including those participants of chapters 4 and 5), I predicted risk-taking and prosocial behavior from longitudinal behavioral data on approach tendencies and social functioning. In addition, I included longitudinal structural neuroimaging data (which follow the most consistent within-individual patterns of change), and focused on regions previously implicated in risk-taking as well as prosocial tendencies: the nucleus accumbens and the medial prefrontal cortex.

Finally, in **chapter 7** I summarize the empirical chapters, and provide a general discussion of the findings.

Chapter 2

Dealing with uncertainty: Testing risk- and ambiguity-attitude across adolescence

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Abstract

Attitudes to risk (known probabilities) and attitudes to ambiguity (unknown probabilities) are separate constructs that influence decision making, but their development across adolescence remains elusive. We administered a choice task to a wide adolescent age-range (N=157, 10-25 years) to disentangle risk- and ambiguity-attitudes using a model-based approach. Additionally, this task was played in a social context, presenting choices from a high risk-taking peer. We observed age-related changes in ambiguity attitude, but not risk attitude. Also, ambiguity aversion was negatively related to real-life risk taking. Finally, the social context influenced only risk attitudes. These results highlight the importance of disentangling risk- and ambiguity-attitudes in adolescent risk taking.

Keywords: adolescence, risk-taking, risk, ambiguity, social context, peer advice

Introduction

Adolescence, which encompasses the developmental phase between childhood and adulthood, has often been described as a period of increased risk taking (Crone & Dahl, 2012; Somerville, Jones, & Casey, 2010; Steinberg, 2008). Typically, risk taking is defined as choosing the option with the highest outcome variability (Defoe, Dubas, Figner, & van Aken, 2015), that is, an action that may lead to greater benefits, but may also lead to negative outcomes, at the expense of certainty. During adolescence engagement in substance abuse, deviant behavior, unprotected sex, and reckless driving increase and peak (Eaton et al., 2008), often accompanied, if not strengthened, by the presence of peers (Chassin, Hussong, & Beltran, 2004; Simons-Morton, Lerner, & Singer, 2005). This potential rise in risk-taking behavior is associated with pronounced neural changes in brain networks including subcortical structures (such as the ventral striatum) and cortical regions (such as the prefrontal cortex). It has been suggested that the different maturational rate of these brain regions, and their connectivity patterns, lead to a "neural imbalance", which may result in increased reward sensitivity, risk taking, peer susceptibility, and attenuated impulse control (Crone & Dahl, 2012; Somerville & Casey, 2010; Steinberg, 2008). However, there are large individual differences (not *all* adolescents are risk takers) and contextual influences (adolescents are not *always* risk takers) that are not yet well understood (Casey, Jones, & Hare, 2008; Harden & Tucker-Drob, 2011). The current research examined determinants of risky decision-making in adolescence, by testing the role of risk versus ambiguity, and by examining the role of social influence on risk taking. These two contexts have previously been found to play an important role in explaining variance in risk taking (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011; Tymula et al., 2012), but no study to date has examined these factors across adolescence in one comprehensive study.

Risk and ambiguity

Although the *outcomes* of risky prospects are often certain (e.g., you know exactly how much you may win or lose in a gambling game), the probabilities may be presented under different conditions varying in uncertainty (Tversky & Kahneman, 1992). First, risk taking can occur under conditions in which the probabilities are known, reflecting explicit risk (e.g., the probability of heads in a coin toss is 50%). Second, risk taking can occur under conditions in which the probabilities are not known, reflecting ambiguous risk (e.g., the probability of causing an accident when running a red light is unknown). Thus, in conditions of risk versus ambiguity the *probabilities* of different outcomes vary in uncertainty. Indeed, real life often presents ambiguous

risks (running a red light), rather than explicit risks (a coin toss). Prior developmental studies, however, have often used paradigms that only involve gambles with known probabilities (Braams, Peters, Peper, Guroglu, & Crone, 2014; Burnett, Bault, Coricelli, & Blakemore, 2010; Defoe et al., 2015; Van Leijenhorst, Westenberg, & Crone, 2008), or used paradigms that start out ambiguous but in which the ambiguity is reduced over time via learning or experience (Chein et al., 2011; Crone & van der Molen, 2004; Lejuez, Aklin, Zvolensky, & Pedulla, 2003; Van Duijvenvoorde, Jansen, Bredman, & Huizenga, 2012) and therefore cannot distinguish between these two elements of risk taking. Individuals' risk-taking behavior may be driven by both one's attitude towards risk (i.e., a taste for risk, known probabilities) and one's attitude towards ambiguity (i.e., a tolerance for uncertainty, unknown probabilities (Tversky & Kahneman, 1992), indicating the importance of disentangling these attitudes in studies on adolescent risk taking.

Previous research showed that adults tend to dislike both risk (Von Gaudecker, Van Soest, & Wengström, 2011) and ambiguity (Ellsberg, 1961) indicating that generally, adults are risk- and ambiguity-averse. However, risk- and ambiguity-attitudes are correlated weakly at best (Levy, Snell, Nelson, Rustichini, & Glimcher, 2010; Tymula, Rosenberg Belmaker, Ruderman, Glimcher, & Levy, 2013), suggesting that these attitudes indeed reflect different elements of risk taking. Most importantly, a recent study found pronounced differences in these elements of risk taking in adolescents (12-17 years) and adults (30-50 years). Tymula et al. (2012) showed that although both age groups were risk- and ambiguity-averse, adolescents were less ambiguity averse, and unexpectedly more risk averse, than adults (Tymula et al., 2012). Also, ambiguity attitude, but not risk attitude, was related to indices of adolescent real-life risk taking, particularly the frequency of reckless behavior. These results highlight a relatively higher tolerance to ambiguity in adolescence that may relate to the increased risk taking observed in adolescence compared to adulthood (see Defoe et al., 2015). Additionally, a recent study comparing children (8-9 years) with adults (19-27 years; Li, Brannon, & Huettel, 2014), observed that despite an intact bias towards the familiar (e.g., preferring known books over unknown books), ambiguity-aversion was not yet present in childhood. This indicates that adolescence may be the start of developing ambiguity-aversion as observed in adulthood, or may show unique risk- and ambiguity-tolerance relative to children and adults. Thus, the exact developmental trajectory of risk- and ambiguity-aversion remains unknown.

Here, we aim to further address this question by testing whether risk- and ambiguity-attitude follow a linear trajectory (e.g., ambiguity aversion increases with age) or a quadratic trajectory (e.g., a tolerance to ambiguity peaking in adolescence) into young adulthood. Furthermore, we explicitly aim to link individual differences

in risk-and ambiguity-attitude with differences in self-reported real-life risk-taking behavior and reward sensitivity. Self-report measures are an important addition to the current study, as they serve as validation of our paradigm and explain how risk taking in the laboratory reflects risk-taking behavior in real life. Specifically, we were interested in the behavior subscales of the Adolescent Risk-taking Questionnaire (ARQ, frequency of risk-taking behaviors in daily life; Gullone, Moore, Moss, & Boyd, 2000), and the Behavioral Inhibition System/Behavioral Approach System questionnaire (BIS/BAS, reward sensitivity; Carver & White, 1994). These questionnaires have previously been associated with ambiguity attitude (Tymula et al., 2012) and risk-taking tendencies in adolescence (Braams, van Duijvenvoorde, Peper, & Crone, 2015; Van Duijvenvoorde et al., 2014), respectively.

Social influence

Besides a rise in risk-taking behavior, adolescents also show a shift in orientation towards peers, and some have suggested that these processes are strongly related (Chein et al., 2011; Gardner & Steinberg, 2005). For instance, risk-taking behavior typically takes place in groups and studies have shown that merely the presence of peers may lead to increased risk taking (Gardner & Steinberg, 2005) and greater activation in reward-sensitive areas in the brain during risk taking (Chein et al., 2011; Steinberg, 2004). Although most studies until now have focused on peer presence, peers may also be a source of information for choice behavior. Consistently, a recent study with adults focused on the influence of observing peers' choices (Chung, Christopoulos, King-Casas, Ball, & Chiu, 2015). Specifically, it was shown that merely observing other people's choice of gambles changes the subjective value of those gambles. Also, in a study with adolescents (12-17 years) and adults (18+ years), advice from an 'expert economist' had stronger effects on adolescents than on adults, with the adolescents approaching adult-like (i.e., risk-averse) risk attitudes in the presence of advice (Engelmann, Moore, Monica Capra, & Berns, 2012). These studies suggest that information retrieved by observing others is integrated in one's own choice process. As a first step to test whether adolescents' risk- and ambiguity-attitude is influenced by a social context, we presented an additional condition in which adolescents were presented with the same gambles, but in which choices from a high risk-taking peer were presented. Here, we focus particularly on the shift in risk- and ambiguity-attitudes between the solo and the social condition.

The current study

Taken together, we aim to study the developmental trajectory of risk-and ambiguity-attitudes across adolescence, and to what extent these attitudes relate to real-life

risk-taking behavior. Second, we test the influence of a social context on risk- and ambiguity-attitude across adolescence. Based on the few previous studies we expect that developmental changes in risk attitude are less pronounced compared to changes in ambiguity attitude, which may increase or peak particularly in early- to mid-adolescence. Also, we expect that although both risk- and ambiguity attitude may relate to individuals' real-life risk-taking behavior, this relation may be stronger for ambiguity attitude given that this more likely reflects real-life risks (i.e., unknown probabilities rather than known probabilities). Finally, we expect that a social context influences participants' risk- and ambiguity-attitudes, particularly in early- to mid-adolescence.

To these ends, we developed a wheel-of-fortune gambling task modeled after Tymula et al. (2012) that included risky choices (known risks) and ambiguous choices (unknown risks) that was administered to a wide adolescent age-group (ages 10-25, *N*=162). A novel aspect of this study was that we applied a model-based approach derived from economics to estimate individual's risk-and ambiguity-attitudes from this specific set of items (Gilboa & Schmeidler, 1989). This is a relatively new approach in developmental research (Tymula et al., 2012) and allows to distinguish individuals' subjective, rather than objective, preferences for risky and ambiguous choices, a central question in economic theory (Camerer & Weber, 1992; Knight, 2012). In addition, participants completed questionnaires on their individual level of risk taking in daily-life situations (ARQ) and reward-sensitivity (BIS/BAS). This provides valuable information with respect to validation of our paradigm and how risk taking in the laboratory reflects real-life risky behavior. Moreover, participants played these gambles by themselves (solo) or when choices from an age-matched peer were present (social). Specifically, peer choices were manipulated to include a more risk-seeking and ambiguity-seeking attitude to investigate to what extent participants' attitudes were swayed.

Method

Participants

One hundred sixty-two participants (85 female) ages 10-25 completed the wheel-of-fortune task. Participants were recruited from a primary school (10-12 year olds, *n* = 37), a secondary school (14-16 year olds, *n* = 40), higher vocational institutes (17-20 year olds, *n* = 31), and universities (21-25 year olds, *n* = 52), in the Netherlands. Written informed consents were provided by the participants themselves or by a parent in the case of minors. Recruitment, written informed consent, and procedures were approved by the local ethics committee. Participants were given a flat rate of

10 Euro (21-25 year olds) or a small present (10-20 year olds) for their participation. Additionally, to increase motivation and include a real-life consequence, participants were explained that one trial would be randomly picked out from their choices and that they could win this amount via a lottery in their class. Eventually, one participant from each class won his amount.

Five participants were excluded from all analyses: three because they did not show any variation in choice behavior, making it impossible to estimate risk- and ambiguity-attitudes, and two for violations of stochastic dominance in more than 50% of the trials. Stochastic dominance violations occur when one option is better than another option in all respects, but the suboptimal option is chosen (Birnbaum & Navarrete, 1998). In the current task, dominated choices occurred when presented with a 5 Euro safe choice and a 5 Euro gamble (see task description). Choosing the gamble would be a violation of stochastic dominance, as it is impossible to benefit from the gamble compared to the safe option. Consistently violating stochastic dominance may indicate a limited understanding of the task. These exclusion criteria have been applied before in Tymula et al. (2012; 2013). The final sample therefore included 157 individuals (84 female, M_{age} = 17.04 years, SD_{age} = 4.58, range = 10.00-25.63 years), evenly distributed over four continuous age groups (10-12 years: n = 37, 19 female; 14-16 years: n = 39, 21 female; 17-20 years: n = 31, 12 female; 21-25 years: n = 50, 32 female). A χ^2-test indicated no significant gender differences between age groups (χ^2 (3, N(157) = 5.01, p = .17). IQ was estimated for the three youngest age groups using a short version of the Raven Standard Progressive Matrices (SPM; Raven, Raven, & Court, 1998). The average estimated IQ scores were within the normal range (M = 102.11 , SD = 12.81), but correlated with age (r = -.22, p = .023). However, adding IQ as a covariate in the subsequent analyses did not result in any significant effects of IQ nor changed the results, indicating that intelligence did not influence behavior on the task.

Wheel-of-fortune task

In a wheel-of-fortune task (see Figure 1), mimicked after (Ernst et al., 2004; Tymula et al., 2012), participants were asked to make a series of choices between pairs of wheels. One consistent option was a sure wheel that would always yield a gain of 5 Euro. The other option was a gambling wheel that could yield higher gain-amounts, but also entailed a chance to win nothing (0 Euro), depicted with blue (winning) and red (not winning) parts. The gain-amount, gain-probability and ambiguity-level associated with the gambling wheel varied from trial to trial, allowing to estimate participants risk attitude (to known probabilities) and ambiguity attitude (to unknown probabilities). The amount of gain varied between 5, 8, 20 and 50 Euro. In risky trials, the gain-probability of risky gambling wheels (i.e., wheels with known

probabilities) varied between 0.125, 0.25, 0.375, 0.50, 0.625, and 0.75. In ambiguous trials, the gambling wheel was obscured by a grey lid that covered more or less of the gambling wheel. The ambiguity-level of ambiguous gambling wheels (i.e., wheels with unknown risks) varied between 25%, 50%, 75%, and 100% (see Figure 1C). In these ambiguous wheels, the visible parts always included the same relative size of red and blue parts. Combining all gain-amounts and gain-probabilities resulted in 24 unique risk trials, and combining all gain-amounts and ambiguity-levels resulted in 16 unique ambiguous trials.

Risky wheels were explained to the participants as wheels with winning (and not winning) parts that could vary in size, indicating that the chance of winning (and not winning) could also vary. Ambiguity levels were explained to the participants as a lid that could vary in size and hence cover more or less of the gambling wheel. To ensure that participants understood that the blue and red parts under the ambiguous lids could vary randomly, participants were explicitly shown all possible wheels that could lie beneath each type of lid during instruction of the task.

The wheel of fortune task was played in a solo (Figure 1A) and a social condition (Figure 1B). Participants played three repetitions of all unique risky and ambiguous trials in each condition, resulting in a total of 240 trials (120 per condition).

In the solo condition, participants indicated their responses with a left or right button press, without a maximum response time. After their decision a yellow selection frame appeared around the chosen wheel. The social condition (Figure 1B) was similar to the solo condition, except that a picture of a peer was included on screen (matching the participant's age group and gender) during each choice. Before the participant's own choice, the choice of the peer was presented by a grey selection frame around one of the wheels. Subsequently, the participants were able to indicate their choice irrespective of the peer's choice. For each age group and gender a set of ten standardized pictures were used (Gunther Moor, Crone, & van der Molen, 2010). For each participant one of these pictures was randomly drawn, matched for age group, and presented throughout the social condition. Participants were explicitly instructed that the observed peer-choices were from another participant of the same age. In reality, our peer-manipulation was programmed as a risk-taking peer, given that the cutoff of gambling for the peer was set to an objective expected value (EV) > 3 Euro of the gambling wheel (i.e., the EV of the safe option was always 5 Euro), with the exception that the peer did not violate stochastic dominance in the 5 Euro gambling items. These settings resulted in a risk attitude of the peer of α = 1.44 (indicating an extreme risk-seeking attitude), and an ambiguity attitude of β = -.85 (indicating an extreme ambiguity-seeking attitude). As a control measure, we included four additional trials in which the peer did violate stochastic dominance.

These trials were added to check if participants would not blindly mimic the peer's choices. However, this rarely happened (i.e., 3.3% of the time).

All participants first played a solo block of trials followed by a social block. To account for order effects, participants subsequently played another solo block followed by a social block, or vice versa (counterbalanced across subjects). Preliminary one-way ANOVAs did not reveal an effect of block order on overall gambling in risk trials (p = .95), nor on overall gambling in ambiguity trials (p = .36). Last, to control for key preference and effects of attention, we counterbalanced the position of the blue and red parts of the wheels (left, right, bottom, and top of the wheel), and the position of the ambiguous lids (top or bottom of the wheel), across trials. That is, each stimulus had four possible color configurations (except for the 50:50 explicit risky wheels and the 100% ambiguous wheels, which had two possible color configurations), one of which was randomly chosen on each trial. Finally, the different wheels (gamble, safe) were randomly displayed left and right on the screen.

Questionnaires and exit questions

To test for relations between estimated risk- and ambiguity-attitudes and indices of real-life risk taking, participants completed the *behavior* scale of the Adolescent Risk taking Questionnaire (ARQ; Gullone et al., 2000), a measure of one's real-life risk-taking behavior (as opposed to the *perception* scale of the ARQ, which is a measure of one's perception towards real-life risk taking; Gullone et al., 2000). That is, participants indicated on a 5-point Likert scale the frequency with which they engaged in risky activities (with 1 indicating *never* and 5 indicating *very often*). Examples include 'Snow skiing', 'Drinking and driving' and 'Having unprotected sex'. The ARQ *behavior* scales consists of four subscales: Thrill-seeking, Rebellious, Reckless, and Antisocial behavior. The ARQ has been validated in 925 participants between the ages of 11 and 19 years old (Gullone et al., 2000). To test for relations with reward-sensitivity, participants completed the Behavioral Inhibition System/Behavioral Approach System questionnaire (BIS/BAS; Carver & White, 1994), which measures avoidant and appetitive motives for reaching a desirable goal (e.g., reward sensitivity). This questionnaire contains 24 items on a 4-point Likert scale ranging from 1 (*very true for* me) to 4 (*very false for me*). Examples include 'When I get something I want, I feel excited and energized' and 'I crave excitement and new sensations'. The BIS/BAS questionnaire consists of four subscales: BIS, BAS Fun Seeking, BAS Reward Responsiveness, and BAS Drive. Due to class absence, eight participants did not complete the ARQ questionnaire (two 17-20 year-olds and six 21-25 year-olds), and nine participants did not complete the BIS/BAS questionnaire (three 17-20 year-olds and the same six 21-25 year-olds).

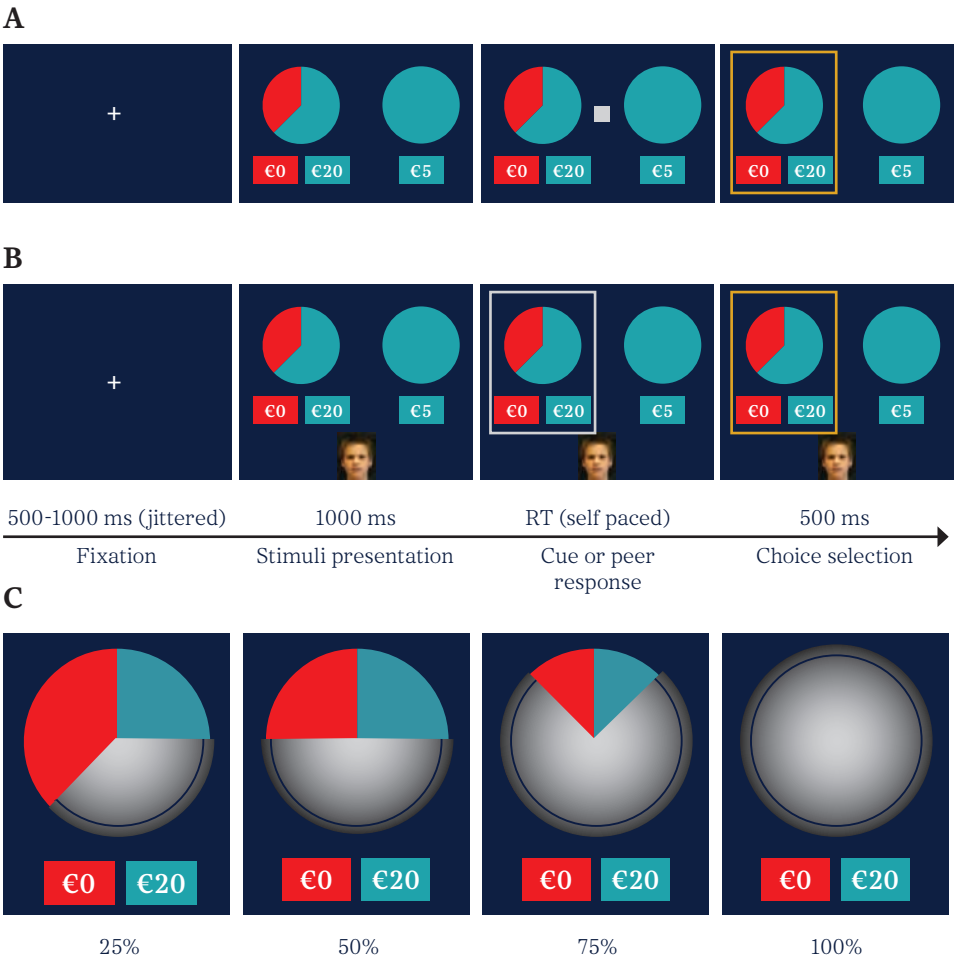


Figure 1. A. *Example of a risk trial in the solo condition. Participants were presented with a jittered fixation cross between 500-1000 ms (with increments of 100 ms), after which the wheels appeared (a gambling wheel varying in gain-probability, gain-amount and ambiguity-level) and a sure wheel (a consistent gain of 5 Euro). After 1000 ms a centered cue appeared, allowing the participants to respond. A yellow selection frame (500 ms) confirmed the participant's choice.* ***B.*** *Example of a risk trial in the social condition. The timing of social trials was similar to the solo condition. In addition to the gambling wheel and the sure wheel, an anonymous peer (matching the participant's gender and age) appeared. After 1000 ms this peer's response appeared, allowing the participants to respond. A yellow selection frame (500 ms) confirmed the participant's choice.* ***C.*** *Examples of the ambiguous gambling wheels. The lid could cover a varying proportion of the wheel.*

Additionally, all participants completed a number of exit questions about the anonymous peer in the wheel of fortune task. These questions considered the participants' opinion on how much they believed the decisions of the peer, how wise they found the decisions of the peer, how smart they found the peer, and how influenced they were by the decisions of the peer, on a scale from 0 to 9 with anchors *not at all true for me* and *completely true for me*.

Procedure

Participants played the wheel-of-fortune task individually in a quiet space at their school or university. Instructions were delivered individually and before starting the task it was ensured all participants understood the task. Participants were given a number of examples and completed seven practice trials before starting. The wheel-of fortune task took approximately twenty minutes to complete. Participants completed the Raven SPM, and the questionnaires on paper-and-pencil or online using Qualtrics (www.qualtrics.com) in a separate session from the wheel-of-fortune task. After the experimental procedure, participants were debriefed by explaining that the choices of the peer were computer-generated. Participants reported to modestly believe the decisions of the peer (M = 3.44, SD = 2.18, range 0-9), but this did not correlate with age (p = .96), indicating all participants reported to believe the decisions of the peer to a similar degree.

Data analyses

To check whether all participants had a basic understanding of the task (e.g., are sensitive to increasing probability, ambiguity level, and amount), conventional ANOVAs were used on the task data. These analyses set the stage for testing our hypotheses. For further analyses with model-based estimations of risk- and ambiguity-attitudes (hierarchical) multiple regressions were used.

Model-based analysis: Risk and ambiguity.

Our main focus was to estimate risk- and ambiguity-attitudes of each participant using a model-based approach and use these attitudes for subsequent analyses. The advantage of such a model-based approach is twofold. First, it is an elegant way of estimating an integrative choice model that simultaneously estimates risk- and ambiguity-attitude. Second, it allows for an explicit comparison with previous studies using a similar model-based approach (Tymula et al., 2012; 2013), which has been successfully applied to a developmental sample (Tymula et al., 2012).

To estimate the risk- and ambiguity-attitudes of each participant, we modeled the subjective value (EU) of the choice option using a widely used power utility function

with an additional term to account for ambiguity attitudes (Gilboa & Schmeidler, 1989; Levy et al., 2010; Tymula et al., 2012):

$$EU(x,p,A) = (p - \beta * \frac{A}{2}) * x^{\alpha}$$

where x represents the amount of money that could be won, p is the probability, A the ambiguity level, α the risk attitude, and β the ambiguity attitude. In the current gain trials, an $\alpha = 1$ indicates a linear utility function and thus risk neutrality. An $\alpha < 1$ indicates a concave utility function and thus risk aversion, whereas $\alpha > 1$ indicates convexity and thus risk seeking.

To obtain subjective value, the utility of an option was multiplied with the probability of outcome. In this specific case, the level of ambiguity was taken into account. That is, p was the objective probability of winning, and β was the individual ambiguity attitude to be estimated. A is the objective ambiguity-level. An ambiguity-neutral participant would have an estimated $\beta = 0$. An ambiguity-averse participant would behave as if the winning probability was less than the objective 0.5 probability ($\beta > 0$). An ambiguity-seeking participant would behave as if the winning probability was more than the objective 0.5 probability ($\beta < 0$).

We used the simplex algorithm of the general-purpose optimization toolbox (*optim*) in R for model fitting (R Core Team, 2015). To model trial by trial choices we used a logistic choice rule to compute the probability (P_{Gamble}) of choosing the risky/ambiguous option as a function of the difference in subjective value EU_{Gamble} and EU_{Sure}. To account for the observed stochasticity in choice, we also modeled the decisions of participants as susceptible to an error (μ):

$$\Pr(\textit{ChoseGamble}) = \frac{1}{1+\exp(-(EU_{risky} - EU_{sure}) / \mu)}$$

To account for local minima in estimated parameters this function was refitted using a grid search procedure. The resulting risk- and ambiguity-parameters were used in subsequent analyses using conventional regressions.

Results

Task understanding

In the following analyses we report the data from the solo condition only (but see 'Risk- and ambiguity-attitudes in the social condition').

Stochastic dominance violation

To investigate understanding of the choice task, we determined first-order stochastic dominance violations. That is, in some trials, subjects chose between a sure gain of 5 Euro and a gambling wheel that offered a risky or an ambiguous chance of winning 5 Euro. In such trials it is impossible to benefit by choosing the gambling wheel. Thus, an economically rational subject should always choose the certain amount over the gamble (but see (Kahneman & Tversky, 1979). The participants (after exclusions, see 'Participants') rarely chose this gambling wheel (M = .02, SD = .07). A linear regression revealed no significant age effect on choosing this lottery over the sure gain (p = .28). This indicates that although subjects occasionally violate dominance, this rarely happened in the current task and age-range.

Sensitivity to gain-probability, ambiguity-level, and gain-amount

Next, to investigate understanding of the task, we tested participants' choice behavior in response to changes in level of gain-probability, ambiguity-level, and gain-amount in conventional repeated measures ANOVAs with age group as a between-subjects variable. These revealed significant main effects on choice behavior of gain-probability, ambiguity-level, and gain-amount, with higher gain-probability, lower ambiguity-level, and higher gain-amount leading to an increased likelihood to gamble (all p's < .001). No significant interactions with age group were found (all p's > .09), and visualization of these effects indicated highly similar patterns across the four equally-spaced age groups (see Figure 2). Thus, all participants indicated a basic understanding of the task.

Finally, we compared gambling in the ambiguous items to gambling in the 50:50 explicit risky items. Considering that this is how one should treat an ambiguous gamble (i.e., with a 50% chance of winning, Tymula et al., 2012), less gambling in ambiguous items versus this option would indicate ambiguity aversion. Indeed, participants generally gambled less in the ambiguous items (M = .28, SD = .16), compared to the 50:50 explicit risky items (M = .46, SD = .17), as shown by a paired samples t-test ($t(156)$ = -14.35, p < .001). This replicates prior studies (Ellsberg, 1961; Levy et al., 2010) and sets the stage for testing our hypotheses on risk- and ambiguity-attitudes.

Risk- and ambiguity-attitude: Model-based analyses

To more formally estimate individuals' risk- and ambiguity-attitude we used a model-based approach (Tymula et al., 2012; Tymula et al., 2013), see Methods for further specification. When plotting the individually estimated risk- and ambiguity-attitudes we observed that people were generally risk- and ambiguity-averse (see Figure 3A for a visualization of the data).

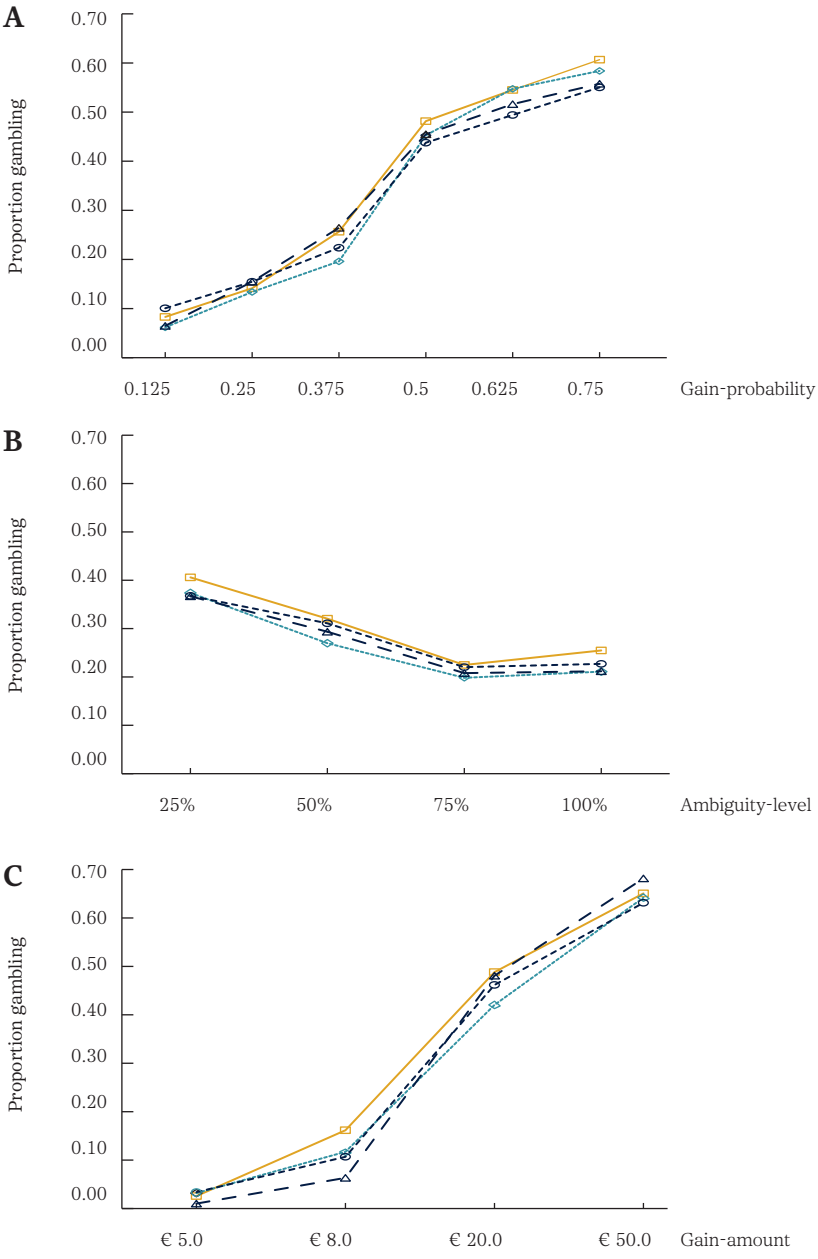


Figure 2. *Visualization per age group of the effects of* ***A)*** *gain-probability,* ***B)*** *ambiguity-level and* ***C)*** *gain-amount, on proportion of gambling.*

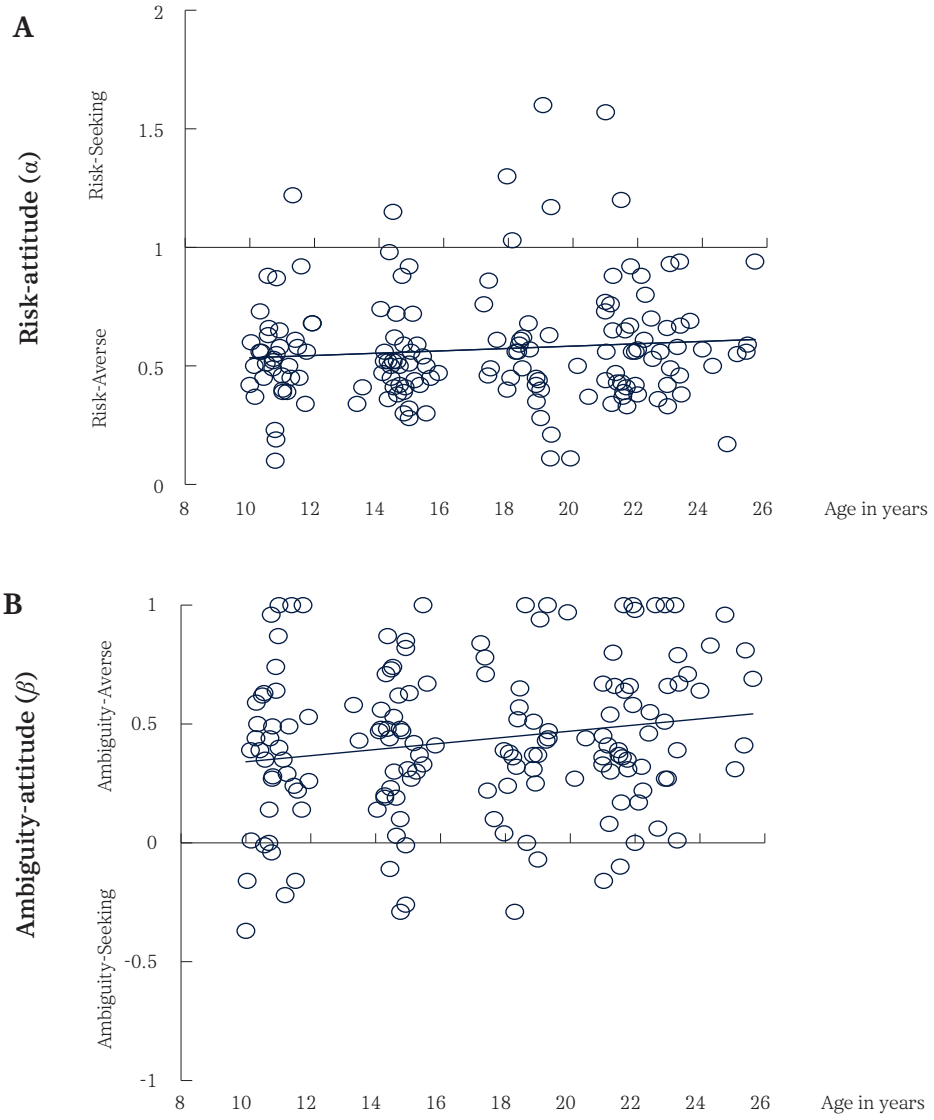
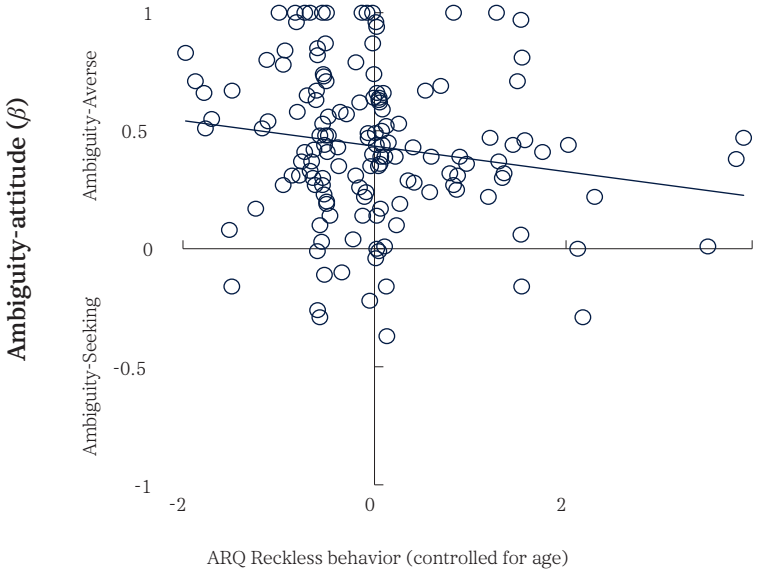


Figure 3. *A. Risk attitude (y-axis) across age (x-axis). a's smaller than 1 indicate risk aversion, whereas a's larger than 1 indicate risk seeking. Most subjects across all ages were risk averse and this did not change with age.* ***B****. Ambiguity attitude (y-axis) across age (x-axis). β's larger than 0 indicate ambiguity-aversion, whereas β's smaller than zero indicate ambiguity-seeking. Most subjects were ambiguity averse, and this aversion increased linearly with age.* ***C.*** *Relation between the ARQ Reckless behavior scale (controlled for age) and ambiguity attitude. More reckless behavior was related to less ambiguity-aversion.*

C



That is, most risk attitudes (α's) were < 1 (*M* = .57*, SD* = .24) and most ambiguity attitudes (β's) were > 0 (*M* = .43*, SD* = .32).

Our main goal was to test for linear and quadratic age effects on risk- and ambiguity-attitudes. Hierarchical multiple regressions, with the linear effect of age as the first predictor and the quadratic effect of age as the second predictor, revealed no significant linear age effect on estimated risk attitude (p = .25), nor a quadratic effect of age (*p-change* = .79). To test whether gender would have an effect on risk attitude, we added gender as a third predictor above age linear and age quadratic. The model with gender explained additional variance (ΔR^2 = .04, *F-change*(1,153) = 4.75, *p-change* = .031, *b* = .08, *SE* = .04), and showed that males (*M* = .61, *SD* = .24) were slightly more risk seeking than females (*M* = .53, *SD* = .24). No significant interactions between age (linear or quadratic) and gender were observed.

A similar analysis with estimated ambiguity attitude showed that ambiguity-aversion increased linearly with age (R^2 = .034, F(1,155) = 5.40, p = .021, *b* = .01, *SE* = .006), but did not show a quadratic effect of age (*p-change* = .41). No significant main effect of gender, nor interactions between gender and age were observed. Thus, ambiguity attitude, but not risk attitude, changed significantly with age. A correlation between these attitudes showed that risk- and ambiguity-attitude were not significantly correlated (r = .05, p = .51).

Individual differences

Next, we aimed to test whether the estimated risk- and ambiguity-attitudes were related to indices of self-reported real-life risk taking behaviors (ARQ; Gullone et al., 2000) and reward sensitivity (BIS/BAS; Carver & White, 1994).

First, we observed that self-reported risk taking (ARQ) increased linearly across age for reckless behavior (b = .07, SE = .009, p < .001), rebellious behavior (b = .18, SE = .015, p < .001), and antisocial behavior (b = .06, SE = .01, p < .001). To test which ARQ subscale(s) best explained risk- and ambiguity-attitudes, we performed multiple regressions (using backward selection), with risk- and ambiguity-attitudes as dependent variables and the ARQ subscales as independent variables. To control for age (linear), this variable was always included in the model. We observed that ambiguity attitude was best explained by the model with age and ARQ Reckless behavior (R^2 = .07, F(2,146) = 5.19, p = .007). As reported above, ambiguity-aversion increased linearly with age (b = .02, SE = .007, p = .002). Interestingly, reckless behavior was negatively related to ambiguity attitude, with more reckless behavior related to less ambiguity-aversion (b = -.11, SE = .05, p = .041, see Figure 3C). No significant models were observed for risk attitude.

Because some of the items of the Reckless behavior scale might not have been applicable to the youngest participants (e.g., 'Having unprotected sex'), we inspected the relation between ambiguity-aversion and reckless behavior for participants of 14 years and older (leaving n = 110 participants), using a partial correlation (controlling for age). A similar effect was observed in which risk-taking behavior was related to ambiguity attitude (r = -.18, p = .059), but not to risk attitude (p = .87).

Second, for self-reported reward-sensitivity (BIS/BAS) we observed that BAS Drive increased linearly with age (b = .14, SE = .035, p < .001). BAS Reward responsiveness showed a quadratic pattern (b = .02, SE = .01, p = .035), which was best described as an emerging pattern of increased reward responsivity in young adulthood. However, the BIS/BAS subscales were not related to either risk- or ambiguity-attitude.

Risk- and ambiguity-attitudes in the social condition

We added a first step in the current study to test for context effects of risk- and ambiguity-attitudes. Particularly we aimed to test to what extent the social condition influenced risk- and ambiguity-attitudes. To this end we calculated risk- and ambiguity-attitudes in the social condition with the same model-based approach as in the solo condition (see Methods for model specification). One participant (a late adolescent) did not complete the social blocks of the task due to time constraints, leading to n =156 in further analyses on the social condition.

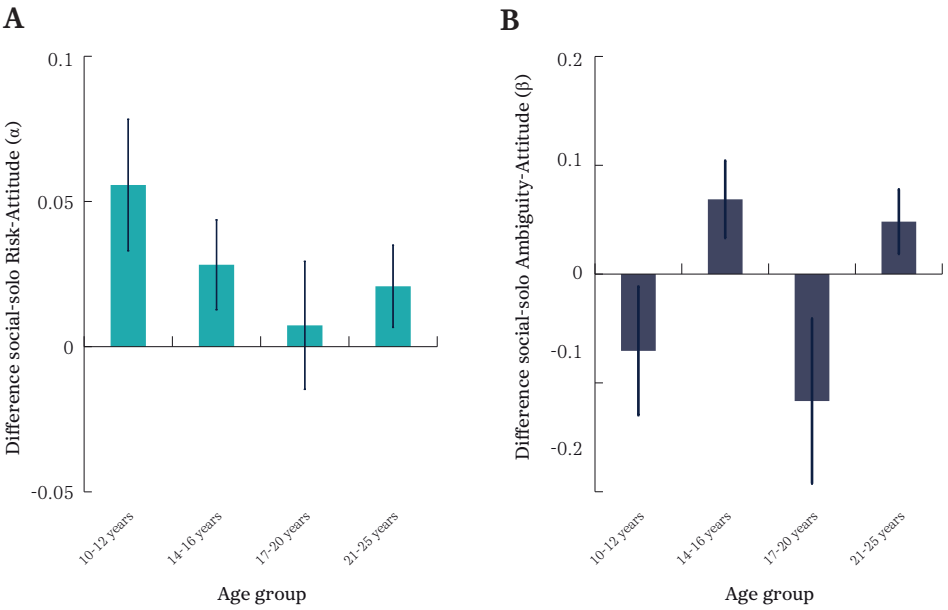


Figure 4. A. *Visualization of the difference between the social minus the solo condition for risk attitude, plotted per age group. Note that a positive score means individuals became more risk seeking in the social condition compared to the solo condition. Particularly the youngest ages became more risk seeking in the social compared to the solo condition.* ***B.*** *Visualization of the difference between the social minus the solo condition for ambiguity attitude, plotted per age group. A positive score means individuals became more ambiguity averse, whereas a negative score means individuals became more ambiguity-seeking in the social condition compared to the solo condition. There was no significant effect of the social condition. Error bars represent +1/-1 SE around the mean.*

To assess the influence of the social condition on participants' attitudes, we first ran a repeated measures ANOVA on risk attitudes, with condition (solo, social) as a within factor, and the linear and quadratic effects of age as covariates. With respect to risk attitude, we observed a significant main effect of condition ($F(1,153) = 5.37$, $p = .022$, $\eta_p^2 = .034$), with participants becoming more risk seeking in the social condition ($M = .59$, $SE = .02$) compared to the solo condition ($M = .56$, $SE = .02$). In addition, we observed a significant age (linear)*condition interaction ($F(1,153) = 4.06$, $p = .046$, $\eta_p^2 = .026$), and an age (quadratic)*condition interaction at trend level ($F(1,153) = 3.56$, $p = .061$, $\eta_p^2 = .023$). We have visualized these age effects in Figure 4A, where we have plotted the difference score between risk attitude in the social condition minus the solo condition. A similar analysis on ambiguity attitude

showed no significant effects of condition, or age (see Figure 4B). When gender was included, this factor did not interact with condition or condition*age effects in both the risk- and ambiguity-attitudes analyses. To control for the self-report rating of peer believability, we added this rating as a covariate in addition to the linear and quadratic effect of age on the ANOVA for risk attitude. This analysis revealed no significant interaction between the believability rating and condition (p = .424), nor did it change the results, indicating that this rating did not influence the effect of condition that we observed.

Discussion

This study focused on distinguishing determinants of risky choice across adolescence by testing attitudes towards risk (contexts with explicit probabilities) and ambiguity (contexts with unknown probabilities) across adolescence (ages 10-25 years). We observed that ambiguity attitude, but not risk attitude, changed with age, with younger adolescents being more ambiguity-tolerant (i.e., less averse) than older adolescents and young adults. Moreover, ambiguity attitude, but not risk attitude, was related to self-reported real-life reckless behavior, with less ambiguity-averse attitudes related to more reckless behavior. Finally, we observed an effect with respect to the social condition: risk-, but not ambiguity-attitude, tended to change between the solo and social context, with participants becoming more risk-seeking in the social context. The discussion is organized alongside the line of these main findings.

Risk- and ambiguity-attitudes across adolescence

Age effects

First, we tested for age-related changes in individuals' risk- and ambiguity-attitudes. Model fits showed that most participants were risk averse and ambiguity averse, as has been observed in adult studies (Ellsberg, 1961; Levy et al., 2010; Von Gaudecker et al., 2011), but note that considerable individual differences were present (see Figure 3A an 3B). Over the course of adolescence, ambiguity aversion increased monotonically into early adulthood. In contrast, we observed no age-related differences in risk aversion. These findings highlight a distinct developmental trajectory of risk- versus ambiguity-attitude, which concurs with findings that these attitudes separately drive risk-taking behavior (Tymula et al., 2012) and are uncorrelated (Levy et al., 2010), a pattern we also observe in this study.

The finding that ambiguity-aversion increases with age replicates prior research (Tymula et al., 2012) that showed that adolescents were more ambiguity-tolerant than adults. However, our results extend this finding by showing that ambiguity-tolerance

was highest in the youngest ages (10-12 years) and decreases into young adulthood. Prior research found that children (8-9 years) did not yet show ambiguity-aversion (Li et al., 2014). That is, when children and adults were asked which gamble they preferred (a risky or an ambiguous gamble), children were equally likely to choose the ambiguous or the risky option, whereas adults chose the risky option more often. In addition, children were willing to pay as much for betting on an ambiguous gamble versus a risky gamble, whereas adults were willing to pay more for the risky gamble. Both findings highlight that children, in contrast to adults, did not yet distinguish between risk and ambiguity (Li et al., 2014). Possibly, early adolescence is the start of ambiguity aversion in decision-making, a question that should be addressed in future research including even younger children.

In contrast, risk attitudes did not change significantly across adolescence. Previous studies using paradigms with *known* probabilities have generally shown little age differences in overall risk-taking levels (Eshel, Nelson, Blair, Pine, & Ernst, 2007; Van Leijenhorst et al., 2008; Wolf, Wright, Kilford, Dolan, & Blakemore, 2013). This absence of age differences has been explained by relatively mature cognitive abilities, and understanding of probabilities, in adolescence (Van Leijenhorst et al., 2008). On the other hand, heightened adolescent risk taking has been shown in explicit risky-choice paradigms when immediate rewards and losses are present, resulting in a "hot" decision context (Figner et al., 2009, Burnett et al., 2010). Thus, under conditions of known probabilities, age differences may appear only under higher emotional load, although future research should formally address this hypothesis.

Age-related change may be more pronounced in ambiguous decision-tasks such as the Iowa Gambling Task (IGT; Bechara, Damasio, & Damasio, 2000), the Balloon Analogue Risk taking Task (BART; Lejuez et al., 2003) and the Stoplight task (Chein et al., 2011). A comparison of a non-informed ("ambiguous") and informed (risky) IGT, also observed that particularly in the ambiguous task, choice behavior became more advantageous across adolescence (Van Duijvenvoorde et al., 2012). However, most of these ambiguous decision-tasks include immediate feedback, which may result in a heightened emotional load, but also inherently drive learning. Learning may explain some of these age-related changes in decision-making (Eppinger, Hämmerer, & Li, 2011; Van Duijvenvoorde et al., 2012; Van Duijvenvoorde, Jansen, Griffioen, Van der Molen, & Huizenga, 2013). The current study is, to our knowledge, one of the first to compare adolescents' risk taking under risky (known) and ambiguous (unknown) decision contexts in a task that does not require learning. Our finding that ambiguity attitude was driven by age-related change and risk attitude was not, suggests that ambiguity may differently influence risk taking across adolescence, and is perhaps a better reflection of real-life risk taking, in which age differences are prominent.

Individual differences

This relation between attitudes and real-life risk taking was further tested by relations with self-reported risk taking. With increasing age, reckless behavior (such as drinking and driving) increased. Interestingly, we observed that this scale was related to ambiguity-, but not risk attitude. Specifically, more ambiguity-aversion was related to less real-life reckless behavior. This finding highlights that ambiguity attitude may be a characteristic that is particularly driving individuals' real-life risk-taking tendencies, and is consistent with findings in a previous study relating ambiguity attitudes and self-reported risk taking, particularly reckless behavior (Tymula et al., 2012). Given the relatively modest effect observed in the current study, this relation needs to be replicated in further studies, and extended to adolescent populations with a wider range of risk-taking behaviors (i.e., with less and more extreme risk-taking tendencies).

Prior research has defined reckless behavior as actions that carry strong connotations of serious negative consequences, such as injury and death (Arnett, 1992). Indeed, the ARQ reckless behavior subscale of Gullone et al. (2000) consists of items such as 'Drinking and driving', 'Speeding', 'Having unprotected sex', and 'Stealing cars and going for joy rides', all of which can have a strong negative long-term impact, and may be typically framed in the domain of health-safety decisions (Blais & Weber, 2006; Figner & Weber, 2011). This is a decision domain in which risky behavior may particularly rise during adolescence (Van Duijvenvoorde, Blankenstein, Weber, & Figner, *in prep*). Tentatively it may be suggested that explicit decision-making tasks reflect real-life risk taking to a lesser degree than ambiguous tasks, because risks in real-life rarely present known probabilities.

Although we did not observe a relation between real-life risk taking and risk attitude, nor in reward-sensitivity and risk attitude, there were considerable individual differences in aversion to risk. Whether individual differences in risk attitudes reflect other aspects of real-life risk taking, or perhaps more cognitive aspects of risk taking (understanding of probability, intelligence, etc.) will need to be determined in future studies.

Social context

Finally, we explored whether risk- and ambiguity-attitude changed between a solo and a social context, in which choices from a high risk-taking peer were presented. The social context tended to only influence risk attitude, with individuals becoming more risk seeking in the social context. This shift in risk attitudes significantly differed with age. When we plotted the difference between the social minus the solo condition, as a measure of the effect of the social condition, we observed the effect was strongest in the youngest age group (10-12 years). Thus these findings indicate

an overall sensitivity to peers' choices, but strongest in this age range. Finally, this finding seems to indicate that people are somewhat more swayed by peer behavior in explicit risk compared to ambiguous conditions. This suggest that risk taking may vary under different conditions of social advice. Prior studies have demonstrated peer effects on adolescent risk taking in both ambiguous (Chein et al., 2011; Gardner & Steinberg, 2005) and more explicit risk taking tasks (Smith, Chein, & Steinberg, 2014) although few explicitly compared these risk-taking situations. Future studies will need to confirm whether peers have more, or similar, effects in risky and ambiguous contexts compared to the current study.

When presenting peer's choices it has been suggested that the combination of individuals' behavior and peer behavior may also play an important role in the level of peer influence. That is, a recent study showed that although peer behavior may influence individuals' risk taking, this influence was greater when peer choices were aligned with individual preferences (Chung et al., 2015). That is, for risk-averse individuals the influence of safe peer choices will be greater (i.e., a bias in conforming to safe options) than risky peer choices, and vice versa. Here, we only used risky peer choices (in a relative risk- and ambiguity-averse sample). An interesting next step may be to include both risk-averse and risk-seeking peers. In combination with a model-based approach (see Chung et al., 2015), such a design may disentangle individual differences in adolescents' conformity to peers across risky and ambiguous contexts.

Limitations and future directions

To our knowledge, the current study is the first to compare risk- and ambiguity-attitudes across a wide adolescent age-range, using a validated model-based approach. However, this study also suffered from some limitations that should be addressed in future research. First, we did not have estimates of IQ for the oldest age group. However, we believe it is unlikely IQ would have had an effect on task behavior for the oldest age group, because (1) all age groups showed similar sensitivity to gain-probability, ambiguity-level and gain-amounts and (2) IQ did not appear to influence task behavior in the three younger age groups. Nevertheless, future studies should include an IQ assessment for all participants from all ages.

Second, although a Chi-square test indicated that there were no significant gender differences across the different age groups, gender was not well matched across the two older age groups, with particularly more males than females in the 17-20 year-old group, and more females than males in the 21-25 year-old group. However, when including gender in our analyses, results of age-related changes in risk- and ambiguity-attitude, or the effect of social context, did not change. We observed that in general, males were more risk seeking, but not more ambiguity seeking, than

females. This finding is in line with previous studies showing that generally, males are more risk taking (Byrnes, Miller, & Schafer, 1992; Van Leijenhorst et al., 2008). In future studies it is important to have an equal distribution of both genders in each age group to test the role of gender in more detail.

Third, in the current study the self-reported believability of the social manipulation ranged from very low to very high, but was relatively low overall. Including peer-believability as a covariate did not influence our results of the social condition, in which we particularly observed that people became more risk seeking when presented with a risk-seeking peer. It may be the case that this explicit self-report is not a reliable measure, because it may have resulted in the participants actively questioning the peer, whereas they may not have done this throughout the experiment. Nonetheless, future studies should for instance increase the personal association felt with a social-influence group (e.g., Knoll, Magis-Weinberg, Speekenbrink, & Blakemore, 2010), or perform control experiments to compare social versus non-social influence (e.g., Klucharev, Hyto, Rijpkema, Smidts, & Fernández, 2009).

Fourth, the current study focused particularly on the gain domain, which may have caused our participants to be particularly risk averse. That is, individuals tend to be relatively risk averse when gains are at stake, but risk seeking when losses are at stake (Tversky & Kahneman, 1992). Future studies could benefit from also including a loss domain, which may provide better insight of risky choice across adolescence under conditions varying in uncertainty.

Finally, we investigated age as an important factor of interest, but we did not include puberty measurements. Puberty typically starts between ages 10-13 and influences structural and functional development of limbic and prefrontal systems (Peper & Dahl, 2013). Pubertal development appears to contribute to increased adolescent sensation-seeking (Forbes & Dahl, 2010) and reward-sensitivity, as shown by heightened neural activation in the nucleus accumbens (Braams et al., 2015). These findings suggest that pubertal development may relate to individual differences in risk- and ambiguity-attitude. Future research may further establish the relation between risk- and ambiguity-attitudes, puberty, and the associated neural development.

Conclusion

The current study highlights the potential of a model-based approach to decompose overt risk-taking levels into underlying determinants of adolescent risk taking: risk- and ambiguity-attitudes. These distinct influences on risk taking were found to have different developmental trajectories, and provide complementary insights into

adolescent risky decision-making. This study confirmed an emerging ambiguity-aversion across adolescent development, and its relation with risk taking in daily life, and provides suggestions for including a social context in future adolescent risk-taking research. Future studies using neuroimaging methods may allow us to further understand the underlying mechanisms of these separate aspects of risk taking, which may impact adolescent risky decision-making in different ways.

Chapter 3

Neural mechanisms underlying risk and ambiguity attitudes

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Abstract

Individual differences in attitudes to risk (a taste for risk, known probabilities) and ambiguity (a tolerance for uncertainty, unknown probabilities) differentially influence risky decision-making. However, it is not well understood whether risk and ambiguity are coded differently within individuals. Here, we tested whether individual differences in risk and ambiguity attitude were reflected in distinct neural correlates during choice and outcome processing of risky and ambiguous gambles. To these ends, we developed a neuroimaging task in which participants (N = 50) chose between a sure gain and a gamble which was either risky or ambiguous, and presented decision outcomes (gains, no gains). From a separate task in which the amount, probability, and ambiguity level were varied we estimated individuals' risk and ambiguity attitudes. Although there was pronounced neural overlap between risky and ambiguous gambling in a network typically related to decision-making under uncertainty, relatively more risk-seeking attitudes were associated with increased activation in valuation regions of the brain (medial and lateral orbitofrontal cortex), whereas relatively more ambiguity-seeking attitudes were related to temporal cortex activation. Additionally, although striatum activation was observed during reward processing irrespective of a prior risky or ambiguous gamble, reward processing following an ambiguous gamble resulted in enhanced dorsomedial prefrontal cortex activation, possibly functioning as a general signal of uncertainty coding. These findings suggest that different neural mechanisms reflect individual differences in risk and ambiguity attitude, and that risk and ambiguity may impact overt risk-taking behavior in different ways.

Key words: risk, ambiguity, attitude, functional MRI, individual differences

Introduction

Many of our decisions are characterized by an element of risk, that is, an uncertainty in the outcomes we might encounter. For instance, we may place a bet in a game of roulette hoping to win large amounts of money (with the risk of losing money), or we may smoke with the risk of developing cancer. However, a fundamental difference in these types of risk is that in the former case the probabilities of the possible outcomes are known (e.g., the chance of winning in roulettes when betting on the color black is slightly less than 50%), while in the latter case the probabilities are unknown (e.g., one does not know the exact chance of developing cancer). This distinction between known and unknown risks has long been acknowledged in the decision-making literature as 'explicit' risk and 'ambiguous' risk, respectively (Knight, 1921; Tversky & Kahneman, 1992; henceforth referred to as risk and ambiguity). Classic behavioral experiments have shown that risk and ambiguity are distinct types of uncertainty that both influence our choice behavior (Ellsberg, 1961). That is, although generally people are both averse to risk and ambiguity, and show a stronger aversion to ambiguity than risk alone, individuals' preferences for risk and ambiguity are often uncorrelated (Ellsberg, 1961; Von Gaudecker, Van Soest, & Wengström, 2011). Even though prior studies have examined the neural mechanisms underlying these distinct types of uncertainty, it is not yet well understood if risk and ambiguity at the neural level can be disentangled within individuals.

In general, two main brain systems have been implicated during decision-making (for a review, see Platt & Huettel, 2008). First, a system that responds to reward-contingencies has been related to the ventral striatum (VS) and ventral medial prefrontal cortex (PFC)/orbitofrontal cortex (OFC) (Bartra, McGuire, & Kable, 2013; Knutson, Taylor, Kaufman, Peterson, & Glover, 2005; Kuhnen & Knutson, 2005; Levy & Glimcher, 2012; O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). This valuation system may reflect the subjective (Levy, Snell, Nelson, Rustichini, & Glimcher, 2010) or objective (van Duijvenvoorde et al., 2015) expected value of the choice at hand, but is also related to processing rewarding outcomes (Delgado, Nystrom, Fissell, Noll, & Fiez, 2000) and producing learning signals (O'Doherty, 2004). A second system, including the insular cortex, lateral PFC, dorsolateral PFC, and posterior parietal cortex (PPC) is more central to the evaluation of the uncertainty of choice options (Levy, 2016; Mohr, Biele, & Heekeren, 2010; Platt & Huettel, 2008) with the PPC being particularly important for assessing probabilities (Huettel, Song, & McCarthy, 2005). Thus, while a system of subcortical (VS) and cortical (medial PFC) regions appears to be responsible for choice valuation and

reward learning, a cortical system (insula, lateral PFC, PPC) may be more related to executive, computational processes in risky decisions, such as assessing uncertainty.

Several prior neuroimaging studies have tested for associations between decisions under risk and/or ambiguity and brain activation. That is, one study that compared risky and ambiguous gambling observed increased activation for ambiguity compared with risk in the amygdala and medial OFC, while risk compared with ambiguity elicited more activation in the striatum (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005). However, another study observed increased activation for ambiguity compared with risk in the insula, lateral PFC, and PPC (Huettel, Stowe, Gordon, Warner, & Platt, 2006). Both studies concluded that these brain regions are responsible for resolving uncertainty. Yet similar patterns of activation for both risk and ambiguity have also been observed, with overlapping activation in the medial PFC, PPC, amygdala, and striatum (Levy et al., 2010). Thus, although these studies found areas of activation typical for decision-making (i.e. valuation and uncertainty coding), it is not yet well understood whether risky and ambiguous decision-making rely on distinct neural mechanisms.

A valuable addition to studying the neural specificity of risk and ambiguity processing may be to include individuals' preferences, i.e., attitudes, towards uncertainty. While someone's risk attitude reflects to what extent one makes a trade-off between outcome magnitudes (e.g., the size of a monetary reward) against the probability of that outcome, ambiguity attitude reflects how one deals with the uncertainty around outcome probabilities (i.e., pessimistic or optimistic about the unknown probabilities; e.g., see Levy, 2016). An elegant way to estimate these preferences is by formally modelling risk and ambiguity attitude from tasks in which the gain probability, gain amount, and level of ambiguity are varied. Behaviorally, this model-based method has been applied successfully in developmental samples (Blankenstein et al., 2016; Tymula et al., 2012) as well as in adults (Tymula, Rosenberg Belmaker, Ruderman, Glimcher, & Levy, 2013) and provides a sensitive measure of someone's risk and ambiguity preferences.

Several studies have started to relate individuals' risk or ambiguity attitudes to neural activity in decision-making. For instance, a number of studies observed that greater risk aversion was related to greater activation in inferior frontal gyrus, lateral PFC, and lateral OFC, both with model-based estimations of risk aversion (Christopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009; Tobler, O'Doherty, Dolan, & Schultz, 2007), as well as with model-free risk-averse behavior (Fecteau et al., 2007; Knoch et al., 2006). Contrary, a greater risk-*seeking* attitude has also been positively related to activation in the lateral OFC, ventromedial PFC, and PPC (Engelmann & Tamir, 2009; Huettel et al., 2006; Tobler et al., 2007). Individual

differences in ambiguity attitude have been studied to a lesser extent. Some studies revealed that more ambiguity *aversion* was related to increased activation in lateral OFC (Hsu et al., 2005) and medial PFC (Pushkarskaya, Smithson, Joseph, Corbly, & Levy, 2015), whereas another study found greater activation in a neighboring region (ventrolateral PFC) with more ambiguity-*seeking* attitudes (Huettel et al., 2006). These previous studies, carried out in relatively small samples (e.g., n = 16, Tobler et al., 2007; n = 10, Engelmann & Tamir, 2009; n = 16, Hsu et al., 2005; n = 13, Huettel et al., 2006), thus show conflicting findings and did not yet disentangle risk and ambiguity attitudes within individuals.

In the current study we aimed to examine the neural correlates of decision-making under risk and ambiguity, and study the association with individual differences in risk and ambiguity attitudes in a sample of 50 healthy adults (a recommended minimal sample size for analyses of individual differences (Yarkoni, 2009; Yarkoni, Poldrack, Van Essen, & Wager, 2010)). To get a robust measure of neural activation during risky and ambiguous gambling and subsequent outcome processing, we administered a straightforward monetary gambling task. Here participants chose between a consistent sure gain and a gambling option, which was either risky or completely ambiguous, and presented subsequent reward outcomes (gain or no gain). We were particularly interested in the neural response during an active gamble, because previous studies have shown that decision-making and subsequent reward processing is more robust when an active choice is made rather than passively viewing the stimuli (Rao, Korczykowski, Pluta, Hoang, & Detre, 2008; Studer, Apergis-Schoute, Robbins, & Clark, 2012; Tricomi & Delgado, 2004).

To derive risk and ambiguity attitudes, we modelled each individual's risk and ambiguity attitude from a separate behavioral task administered after the MRI session (see also Blankenstein et al., 2016; modeled after; Tymula et al., 2012; Tymula et al., 2013). This enabled us to investigate the relation between risk and ambiguity attitudes and brain activation during risky and ambiguous gambling. Although prior findings are mixed, one region that has relatively consistently been associated with risk attitude is the OFC/medial PFC (e.g. Engelmann & Tamir, 2009; Tobler et al., 2007). In the current study we therefore expected that individual differences in risk attitude would be associated with neural activation in the OFC/medial PFC during risky gambling. Alternatively, risk attitudes may correlate more specifically with neural activation related to assessing uncertainty and probabilities such as the lateral PFC and PPC (Christopoulos et al., 2009; Fecteau et al., 2007; Huettel et al., 2006; Knoch et al., 2006). Fewer studies have investigated relations between ambiguity attitude and brain activation (Huettel et al., 2006; Hsu et al., 2005; Pushkarskaya et al., 2015). A central hypothesis based on this prior work would be that individuals'

tendency to seek out ambiguity is related to control regions in the brain such as the lateral PFC (Huettel et al., 2006).

Furthermore, the association between risk versus ambiguity within a choice at hand and processing subsequent reward outcomes (gain or no gain) has yet to be examined. That is, although it is well known that processing rewards is related to increased activation in the VS and medial PFC (e.g., see Delgado et al., 2000), to our knowledge no study to date has explicitly disentangled reward processing after a risky gamble from reward processing after an ambiguous gamble. Given that behavior in response to risk and ambiguity differs (Ellsberg, 1961; Von Gaudecker et al., 2011), it is possible that processing rewards after risk and ambiguity yields different responses in the reward circuitry of the brain as well. Thus, in addition we explored whether processing rewards after risk or ambiguity would yield differential activation in regions typically associated with reward (i.e., VS and ventral medial PFC), and whether this differential reward-related activation was associated with individual differences in risk and ambiguity attitudes.

Method

Participants

Fifty-seven participants (30 women) between 18 and 28 years took part in this study. All participants were recruited via local advertisements in the Netherlands and provided written informed consent. This study was approved by the institutional review board of the Leiden University Medical Centre. All anatomical scans were cleared by a radiologist and no abnormalities were reported. Participants were screened for MRI contra indications and neurological or psychiatric disorders, had normal or corrected-to-normal vision, and were right handed. Five participants reported to have been diagnosed with a disorder, including depression, anxiety, ADHD, and cyclothymic disorder (a mild form of bipolar disorder). These participants were scanned but were excluded from all analyses. Note that when we reran our analyses including these participants, this did not qualitatively affect our results. In addition, one participant was excluded because of too few trials in which the gambling option was chosen (i.e., <10 gambles) and one participant due to excessive head motion in the scanner (i.e., > 3 mm). The final sample therefore included 50 healthy participants (25 women) (M_{age} = 23.71 years, SD_{age} = 2.56, range: 18.85 – 28.46).

Wheel of fortune task

fMRI task

*P*articipants played a wheel of fortune task (Figure 1) in which they were asked to make a number of choices between pairs of wheels, presenting a safe (a consistent sure gain of €3) versus a gambling option which could yield more money (€31, €32, €33, or €34; varied to keep participants engaged in the task) but could also yield nothing (€0). The gambling wheel presented either a risky or an ambiguous gamble. In the risky gambles the probabilities were known, with blue indicating the portion of the wheel corresponding to gain, and red indicating the portion of the wheel corresponding to no gain. In the ambiguous gambles the probabilities were completely hidden by a gray 'lid' with a question mark on it. Participants played 92 trials: 46 ambiguous and 46 risky trials, which were presented inter-mixed. Of the risky trials, 30 trials reflected a gamble with a 50% gain probability, 8 trials reflected a gamble with a 75% gain probability, and 8 trials reflected a gamble with a 25% gain probability (Figure1B).

After the choice, participants were presented with reward feedback (gain or no gain; Figure 1C). This was done to investigate effects of risk and ambiguity within the choice at hand on subsequent reward processing, and to study potential effects of risk and ambiguity attitude on reward processing following a risky or ambiguous gamble. We programmed the experiment such that the probabilities presented in the wheels (25%, 50%, 75%) matched the actual possibilities of winning when choosing to gamble. For example, for the 50% risk trials, there was a 50% chance of winning when choosing the gamble. That is, the computer, on a trial-by-trial basis, randomly selected (without replacement) either gain or no gain in half of the trials. The order of gains and no gains was randomized for each participant. We observed that on average participants' experienced probabilities in risky and ambiguous gambles matched the presented probabilities. Finally, on each trial, the computer randomly selected (without replacement) one of the four possible amounts (€31, €32, €33, €34) to display on a trial-by-trial basis. Thus, although each individual was exposed to the same distribution of probabilities, the amount varied per trial. Reward feedback for gains was presented as the amount in blue. Reward feedback for no gains was presented as €0 in red. To motivate participants to frequently choose the gamble option, the expected value (EV, the amount of a choice option multiplied by its probability) of the gamble option was considerably higher than the EV of the safe option (which was always €3). This enabled the comparison of brain activation during gambling under risk to brain activation during gambling under ambiguity and during their corresponding outcomes.

The task was presented in the MRI scanner via E-prime (Psychology Software Tools) and started with a 500 ms fixation cross, after which the wheels appeared. After

1000 ms, a gray square appeared in the center of the screen cuing the participants to respond. Responses had to be given within a 3000 ms interval. Participants responded to the task with their right index finger (to select the wheel on the left) and right middle finger (to select the wheel on the right). After the response was made, a gray selection frame appeared around the chosen wheel, confirming the participant's choice. This remained visible for the duration of the 3000 ms interval. In case of no response, the words 'TOO LATE' appeared in the center of the screen for

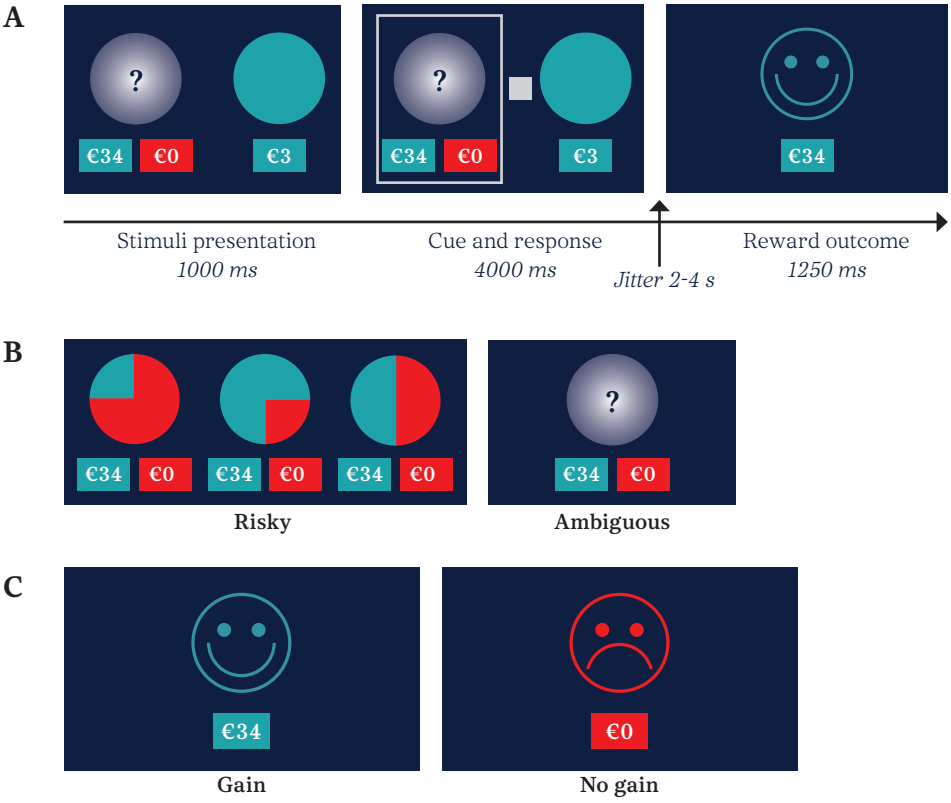


Figure 1. A*. Example of the trial sequence of the fMRI task showing an ambiguous trial with gain as reward outcome. Each trial started with a 500 ms fixation cross, after which the wheels appeared. After 1000 ms, a grey square appeared in the center of the screen prompting the participants to respond. A response had to be given within 3000 ms. A gray selection frame confirmed the participant's choice. After a jittered fixation cross (2000-4000 ms with increments of 500 ms) participants were presented with the reward outcome of their choice (gain or no gain), which was visible for 1250 ms. The next trial began after an inter-trial-interval with intervals varying between 0 and 9350 ms (jittered).* ***B.*** *The different gambling wheels.* ***C.*** *Gain and no gain outcomes.*

1250 ms, after which the next trial began. This happened only in 0.67% of the trials and these trials were excluded from all analyses. A jittered fixation cross (2000-4000 ms with increments of 500 ms) separated the choice phase from the outcome phase. The reward outcomes (gain, no gain, or safe gain) were presented for 1250 ms. The optimal trial sequence (i.e., the ordering of risky and ambiguous trials) and the inter-trial-intervals were chosen using OptSeq (Dale, 1999), with jittered intervals varying between 0 and 9350 ms (M = 1961 ms). The 500 ms fixation cross that preceded each trial was not part of the inter-trial-interval.

Finally, we randomly displayed the different wheels (gamble, safe) left and right on the screen. In addition, the risky wheels had varying color configurations that were presented randomly on a trial-by-trial basis, with the blue proportion of the wheel displayed in the left or right portion of the wheel (in the case of 50% probability trials), or the upper left, upper right, lower left, or lower right portion of the wheel (in the case of 25% and 75% probability trials).

Behavioral task

To scrutinize individuals' risk and ambiguity attitudes, a behavioral version of the wheel of fortune task was administered after the fMRI session as validated previously (Blankenstein et al., 2016) and modeled after Tymula et al. (2012). To derive sensitive measures of risk and ambiguity attitudes from individuals that could not be influenced by changes in the decision environment, no outcomes were provided in this task.

In this behavioral task, the gambling wheel varied in amount (€5, €8, €20, or €50), probability (0.125, 0.25, 0.375, 0.50, 0.625, or 0.75), and ambiguity level (0%, 25%, 50%, 75%, or 100%). The level of ambiguity was manipulated by varying the size of the 'lid' covering the wheel. Combining all amounts with all probabilities resulted in 24 unique risk trials. Combining all amounts with all ambiguity levels resulted in 16 unique ambiguous trials. All trials were presented twice, resulting in a total of 80 trials, which were used to estimate individuals' risk and ambiguity attitudes (see 'Model-based estimations of risk and ambiguity attitudes' section).

The task was presented after the fMRI session via E-prime (Psychology Software Tools). Each trial started with a jittered fixation cross (between 500 and 1000 ms, with increments of 100 ms) after which the wheels appeared. After 1000 ms a gray square appeared in the center of the screen, prompting the participants to respond using their right index finger (left wheel) and middle finger (right wheel). Response time was self-paced. A yellow selection frame confirmed the participant's choice (500 ms). Similar to the fMRI task, we controlled for effects of attention and key preference, by counterbalancing the position of the blue and red parts of the wheel

(left, right, bottom, and top of the wheel) and the position of the ambiguous lids (top or bottom) across trials. Finally, the different wheels (gamble, safe) were randomly displayed left and right on the screen.

Procedure

Participants received instructions on the MRI session in a quiet laboratory room. Next the wheel of fortune fMRI task was explained. Participants were instructed that the ambiguous wheel could reflect a gamble of any of the risky probabilities (25%, 50%, 75%), and they practiced 10 trials on a laptop. Participants were told that after the task, the computer would randomly select the outcomes of three trials, of which the average amount was paid out in addition to a standard pay-out fee. Eventually the computer randomly selected a rounded average of a gain trial, a no gain trial and a safe gain trial, which amounted to an additional payout of €11 or €12. The wheel of fortune task was presented in two runs of nine minutes each, with a short break in between. Stimuli were presented on a screen, which was visible via a mirror that was placed on the head coil. Participants responded to the task with their right index finger (to select the wheel on the left) and right middle finger (to select the wheel on the right) using a button box that was attached to the participant's leg. Head movements were restricted by inserting foam padding between the participant's head and the head coil. After the MRI session, participants completed the behavioral version of the wheel of fortune task, which lasted approximately twenty minutes. Here participants were given a hypothetical choice task and instructed to choose their preferred option. We explained the different levels of ambiguity by showing the different 'lids' that could vary in size and cover more or less of the wheel, and show the wheels that could lie underneath these lids. Participants played three practice trials before the task began.

Model-based estimations of risk and ambiguity attitudes

To estimate each participant's risk and ambiguity attitude from the behavioral task we modeled the subjective value (or expected utility; EU) of each choice option by using a power utility function with an additional term to take into account ambiguity attitude (Blankenstein et al., 2016; Gilboa & Schmeidler, 1989; Levy et al., 2010; Tymula et al., 2012):

$$EU(x,p,A) = (p - \beta * \frac{A}{2}) * x^{\alpha}$$

In this equation, x denotes the amount, p the probability, A the ambiguity level, α the risk attitude, and β the ambiguity attitude. An α of 1 indicates a purely linear utility

function, indicating a risk-neutral attitude. An $\alpha < 1$ indicates a concave utility function and thus a risk-averse attitude. Conversely, an $\alpha > 1$ indicates convexity and thus a risk-seeking attitude. To assess subjective value, we multiplied the utility of a choice option with the probability of the (hypothetical) outcome. Here, the ambiguity level was taken into account, with p as the objective probability, β the individual ambiguity attitude to be estimated, and A the objective ambiguity level. A β of 0 indicates an ambiguity-neutral attitude, meaning the individual is unaffected by the level of ambiguity. A $\beta > 0$ indicates an ambiguity-averse attitude, meaning the individual would behave as if the probability is less than the objective probability (50%). Finally, a $\beta < 1$ would indicate an ambiguity-seeking attitude, in which case the individual would behave as if the probability is more than the objective probability.

For model fitting, the simplex algorithm of the general purpose optimization toolbox (optim) in R was used (R Core Team, 2015). To model trial by trial choices, a logistic choice rule was used to compute the probability of choosing the gamble option (Pr(*ChoseGamble*) as a function of the difference in subjective value of the gamble (EU_{Gamble}) and the safe option (EU_{Safe}). In addition, to account for possible stochasticity in choice, we modeled the decisions of participants as susceptible to an error (μ):

$$\Pr(ChoseGamble) = \frac{1}{1 + \exp\left(-\left(EU_{Gamble} - EU_{Safe}\right) / \mu\right)}$$

We refitted this function using a grid search procedure to account for local minima in the estimated parameters. The resulting risk and ambiguity attitudes were used as predictors of brain activation in whole-brain regressions. To facilitate interpretation, ambiguity attitude was recoded, such that higher values indicate a more seeking attitude.

MRI data acquisition

We used a 3T Philips scanner (Philips Achieva TX) with a standard whole-head coil. Functional scans were acquired during two runs of 246 dynamics each, using T2* echo-planar imaging (EPI). Volumes covered the whole brain (repetition time (TR) = 2.2 s; echo time (TE) = 30 ms; sequential acquisition, 38 slices; voxel size 2.75 x 2.75 x 2.75 mm; field of view (FOV) = 220 x 220 x 114.68 mm). We discarded the first two volumes to allow equilibration of T1 saturation effects.

MRI data analyses

Preprocessing

The data were analyzed using SPM8 (Wellcome Department of Cognitive Neurology, London). Images were corrected for slice timing acquisition and rigid body motion.

Functional volumes were spatially normalized to EPI templates. Translational movement parameters never exceeded 3 mm (<1 voxel) in any direction for any participant or scan (movement range: 0.00 – 1.19 mm, M = .058, SD = .020). The normalization algorithm used a 12-parameter affine transform with a nonlinear transformation involving cosine basis function, and resampled the volumes to 3 mm^3 voxels. Templates were based on MNI305 stereotaxic space. The functional volumes were spatially smoothed using a 6 mm full width at half maximum (FWHM) isotropic Gaussian kernel.

General-Linear model

To perform statistical analyses on individual subjects' data we used the general linear model in SPM8. The fMRI time series were modeled as a series of two events convolved with the hemodynamic response function (HRF). The onset of the choice phase was modeled with a duration of choice (1000 ms + response time; see Figure 1). Events were modeled separately for gambling under risk and gambling under ambiguity, and for choosing the safe option under risk and choosing the safe option under ambiguity. This resulted in four conditions in the choice phase: Gamble Risk, Gamble Ambiguity, Safe Risk, and Safe Ambiguity. The onset of the feedback phase (second event) was modeled with zero duration. We modeled gain and no gain after a risky or ambiguous gamble, and safe gain after a risky or ambiguous safe choice. This resulted in six conditions in the feedback phase: Gain Risk, No Gain Risk, Gain Ambiguity, No Gain Ambiguity, Safe Gain Risk, Safe Gain Ambiguity. Given that outcomes are based on choices, a participant who gambled more frequently viewed more gain and no gain feedback than a participant who chose the safe option (€3) more frequently. However, the participants gambled a considerable number of times on average (*M* = .77, *SD* = .18). This translated into the participants experiencing 36 gains on average (*SD* = 8.21, range = 18-46) and 35 no gains (*SD* = 8.33, range = 17-46) after gambling. Hence all participants experienced at least 18 gains and 17 no gains, thus leaving a sufficient number of trials for our fMRI analyses on reward outcomes. Furthermore, to check that the prior outcome (gain, no gain), did not influence the neuroimaging results during gambling, we also tested a separate general linear model that included whether the gamble was preceded by a gain or a no gain. Because results remained similar between the two models, we only report the more parsimonious model without reward outcome modelled in the gambling conditions.

Trials on which the subjects failed to respond were modeled separately as a covariate of no interest. Additionally, six motion parameters were included as nuisance regressors. The least-squares parameter estimates of the height of the best-fitting canonical HRF for each condition separately were used in pairwise contrasts.

These pairwise comparisons resulted in subject-specific contrast images, which were used for second-level group analyses. All second-level group analyses were conducted with Family Wise Error (FWE) cluster correction ($p < .05$, with a primary voxel-wise threshold of $p < .001$ (uncorrected) (Woo, Krishnan, & Wager, 2014) or FWE voxel correction ($p < .05$), indicated where needed. To visualize patterns of activation in clusters identified in the whole-brain regressions we used the MarsBaR toolbox (Brett, Anton, Valabregue, & Poline, 2002; http://marsbar.sourceforge.net). Coordinates of local maxima are reported in MNI space.

Two types of models. - In addition to our main model with all various probability trials (i.e. 25%, 50% and 75% gain probability), we also include in the tables which clusters are present in a model with the ambiguous trials and risky trials with a 50% probability only. The latter was done because objectively, the ambiguous trials reflect a 50% probability (e.g. Tymula et al., 2012; Levy 2016). For the model with 50% probability risk trials only, we modeled the other probability risk trials (25%, 75%) as covariates of no interest.

Results

Behavioral results

Behavioral task

Results from the model-based estimations showed that participants were predominantly risk and ambiguity averse. That is, most risk attitudes were below 1 (M =.63, SD = .21, range = .30 − 1.03) and most ambiguity attitudes (after recoding) were below 0 (M = -.30, SD = .37, range = -1.0 to .66). This general pattern of aversion to risk and ambiguity coincides with prior research (Huettel et al., 2006; Levy et al., 2010), although the range of the attitudes, and inspection of scatter plots, indicated considerable individual differences in aversion to risk and ambiguity (see Figure 2A).

Finally, we observed a moderate negative relation between risk and ambiguity attitude, indicating that more risk seeking was relation to less ambiguity seeking (r = -.22, p = .124, Figure 2A). However, this relation was not significant, echoing prior studies that have predominantly found non-significant relations between these phenomena (Blankenstein et al., 2016; Bossaerts, Ghirardato, Guarnaschelli, & Zame, 2010; Levy et al., 2010; Tymula et al., 2013; van den Bos & Hertwig, 2017).

fMRI task

In the fMRI task, when choosing between the safe option and the gamble option (risky or ambiguous), participants gambled significantly less in the ambiguous than in the risky trials, as indicated by a paired samples *t*-test ($t(49) = -2.35$, $p = .023$, $M_{Ambig} = .75$, $SD_{Ambig} = .25$, $M_{Risk} = .82$, $SD_{Risk} = .14$). This effect was more pronounced when comparing the ambiguous trials to the 50% probability risk trials only ($t(49) = -4.61$, $p < .001$, $M_{Ambig} = .75$, $SD_{Ambig} = .25$, $M_{Risk50} = .90$, $SD_{Risk50} = .18$). Furthermore, when gambling, participants responded slower in the ambiguous trials than in the risky trials in both the model with all trials ($t(49) = 4.09$, $p < .001$, $M_{Ambig} = 653.73$,

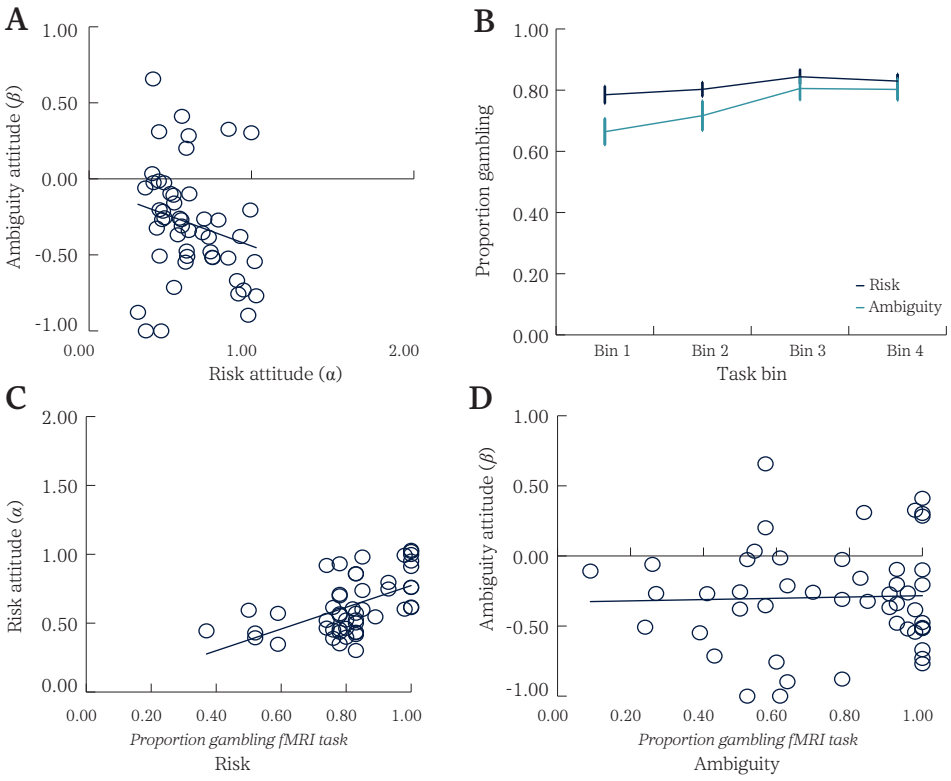


***Figure 2. A**. Relation between risk attitude (α; x-axis), and ambiguity attitude (β, y-axis), derived from the behavioral task. Higher values indicate more risk or ambiguity seeking. **B.** Proportion gambling (y-axis), across task bins for the risky and ambiguous conditions of the fMRI task. **C.** Relation between proportion gambling in the risky condition of the fMRI task (x-axis) and risk attitude derived from the behavioral task (α; x-axis). **D.** Relation between proportion gambling in the ambiguous condition of the fMRI task (x-axis) and ambiguity attitude derived from the behavioral task (β, y-axis).*

SD_{Ambig} = 281.95, M_{Risk} = 529.83, SD_{Risk} = 163.66), as well as the model with 50% probability trials only ($t(49) = 3.40$, $p = .001$, M_{Ambig} = 653.73, SD_{Ambig} = 281.95, M_{Risk50} = 547.84, SD_{Risk50} = 206.16). Thus, even though participants were encouraged to gamble in both conditions (by offering gambles with relatively high EVs), we still observed they chose the ambiguous gamble less frequently than the risky gamble, and responded slower in the ambiguous compared with risky condition, indicative of a general aversion to ambiguity (Ellsberg, 1961; Levy et al., 2010).

Next, to examine whether feedback influenced behavior in the scanner, we investigated changes in gambling behavior in the fMRI task across time. To this end, we divided behavior across four task bins (with 11 or 12 trials per bin) per condition (risk and ambiguity). A mixed ANOVA showed that in addition to a main effect of condition there was a significant bin X condition interaction, $F(3, 147) = 3.34$, $p = .021$, $\eta^2 = .064$) and a main effect of bin ($F(3,147) = 9.15$, $p < .001$, $\eta^2 = .157$). That is, gambling behavior overall increased slightly across time, specifically in the ambiguous condition (see Figure 2B). Similar effects were found when comparing the ambiguous condition to the 50% probability risk trials only (bin X condition interaction: $F(3, 147) = 3.27$, $p = .023$, $\eta^2 = .064$; main effect of bin: $F(3,147) = 8.57$, $p < .001$, $\eta^2 = .149$).

Finally, we correlated behavior from the fMRI task (proportion gambling in risk and ambiguity) with the model-based estimations of risk and ambiguity attitude (derived from the behavioral task outside the scanner). These analyses showed that risk attitude was positively correlated with proportion gambling in risk ($r_{all\ trials} = .453$, $p_{all\ trials} < .001$; $r_{50:50\ trials} = .317$, $p_{50:50\ trials} = .025$) and proportion gambling in ambiguity ($r = .465$, $p = .001$). However, ambiguity attitude was not correlated with behavior in the scanner (all *p's* > .7). This suggests that relatively more risk seeking, but not ambiguity seeking, attitudes were associated with a greater general tendency to gamble in the fMRI task (see Figures 2C and 2D).

fMRI results

Whole-brain contrasts

Risky and ambiguous gambling - First, to study which brain regions were more strongly activated during gambling under risk versus ambiguity, we calculated the whole-brain contrast Gamble Risk > Gamble Ambiguity, and the reversed contrast, based on all probability trials. The first revealed greater activation during gambling under risk in clusters including the right dorsolateral prefrontal cortex (PFC) and occipital cortex, extending into bilateral posterior parietal cortex (PPC) ($FWE_{cc} p < .05, k > 94$, Figure 3A; Table 1). The reversed contrast (Gamble Ambiguity > Gamble Risk), did not result in significant clusters of activation.

Conjunction analysis risky and ambiguous gambling - To check that regions important for complex decision-making were recruited during our task, we next examined the overlap in brain activation for risky and ambiguous gambling. To this end we performed a conjunction analysis in which we applied the 'Logical AND' strategy, which requires that all comparisons in the conjunction are individually significant (Nichols, Brett, Andersson, Wager, & Poline, 2005). These particular results are reported at FWE voxel correction ($p < .05$), because cluster correction resulted in one cluster of activation composed of almost the entire brain, impeding interpretation (Woo et al., 2014). As could be expected, the conjunction analysis

Table 1. MNI Coordinates Local Maxima Activated of clusters for the contrast Gamble Risk > Gamble Ambiguity.

Cluster of activation		MNI coordinates			Significance	Voxels
		x	y	z		
R	inferior temporal gyrus[1]	51	-58	-14	< .001	7235
R	middle occipital gyrus[1]	36	-88	10		
L	calcarine gyrus[1]	0	-88	-2		
R	calcarine gyrus[1]	12	-100	-2		
L	superior parietal lobule[1]	-27	-64	52		
L	middle occipital gyrus[1]	-30	-85	19		
L	superior parietal lobule[1]	-15	-73	55		
L	calcarine gyrus[1]	-12	-79	10		
R	calcarine gyrus[1]	12	-103	10		
L	superior occipital gyrus[1]	-15	-85	7		
L	middle occipital gyrus[1]	-39	-82	4		
R	middle frontal gyrus	48	44	16	< .001	94
R	inferior frontal gyrus	45	38	10		
R	middle frontal gyrus	45	41	25		

Note: L = Left; R = Right. [1]Coordinate remained present in the model with 50% probability trials only. Anatomical labels were acquired with automated anatomical labeling. Results were FWE cluster corrected (pFWE < .05, k > 94) with a primary voxel-wise threshold of p < .001 (uncorrected). Results of the reversed contrast (Gamble Ambiguity > Gamble Risk) did not result in significant brain activation.

revealed widespread overlapping activation for risky and ambiguous gambling in regions important for risky choice, such as the frontoparietal and parietal regions, including lateral PFC, PPC, anterior cingulate cortex (ACC), SMA, insula, and putamen (FWE $p < .05$; Table 2; Figure 3B).

Whole-brain regressions risk and ambiguity attitude

We next tested whether individual differences in risk and ambiguity attitude (derived from the behavioral task) were related to brain activation during risky and ambiguous gambling using whole-brain regressions[1]. Given the moderate correlation between risk and ambiguity attitude ($r = -.22$, $p = .124$), we controlled for ambiguity attitude in the regression with risk attitude, and for risk attitude in the regression with ambiguity attitude. Specifically, in the regression testing for associations between risk attitude and risky gambling, we entered ambiguity attitude as a covariate of no interest.

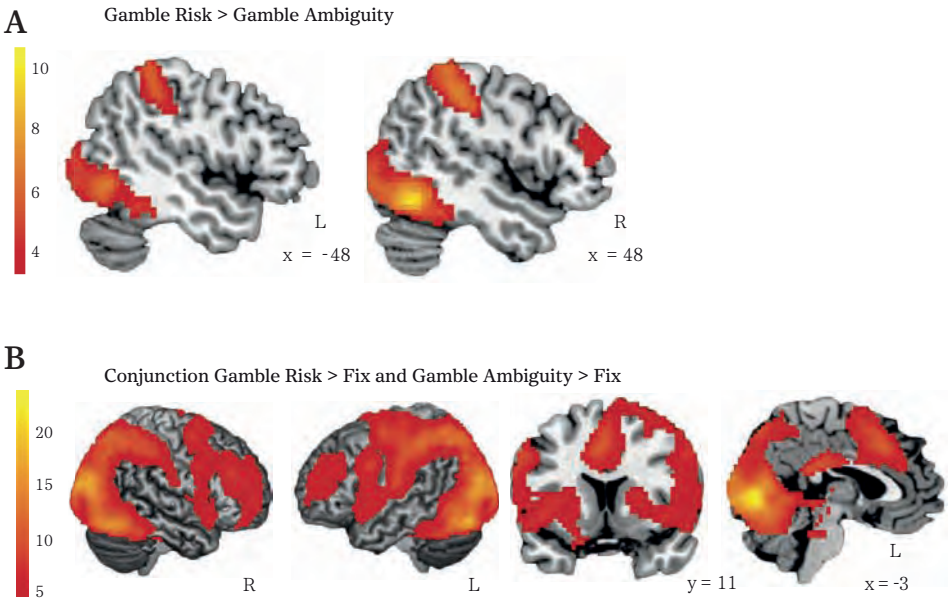


Figure 3. A. *Whole-brain contrasts for Gamble Risk > Gamble Ambiguity. Results were FWE cluster-corrected (pFWE < .05, k > 94) with a primary voxel-wise threshold of p < .001 (uncorrected). The reversed contrast (Gamble Ambiguity > Gamble Risk) yielded no significant activation.* ***B.*** *Conjunction of Gamble Risk > Fixation and Gamble Ambiguity > Fixation. Results were FWE voxel-wise corrected (p < .05) and are visualized with k > 10.*

Table 2. MNI Coordinates Local Maxima Activated for the conjunction analysis with Gamble Risk > Fixation and Gamble Ambiguity > Fixation.

Area of activation	MNI coordinates			T	Voxels
	x	y	z		
R fusiform gyrus[1]	24	-76	-11	24.04	21622
R superior occipital gyrus[1]	18	-94	16	23.44	
L lingual gyrus[1]	3	-79	1	23.24	
L middle occipital gyrus[1]	-30	-88	19	21.80	
L middle occipital gyrus[1]	-33	-88	13	21.26	
L fusiform gyrus[1]	-27	-79	-17	20.80	
R middle occipital gyrus[1]	33	-88	16	20.74	
L calcarine gyrus[1]	-6	-85	-5	20.70	
L lingual gyrus[1]	-12	-82	-8	20.66	
L fusiform gyrus[1]	-24	-70	-14	20.26	
L cerebellum[1]	-18	-82	-17	20.24	
L lingual gyrus[1]	-18	-79	-11	20.09	
L middle occipital gyrus[1]	-12	-100	1	19.33	
R calcarine gyrus[1]	12	-94	4	19.02	
L calcarine gyrus[1]	-12	-79	4	18.84	
L middle occipital gyrus[1]	-18	-97	10	18.37	
L middle frontal gyrus[1]	-45	38	31	9.72	383
L superior frontal gyrus[1]	-30	47	40	6.48	
L superior orbital gyrus[1]	-30	62	-2	5.65	
R middle frontal gyrus[2]	45	44	28	9.93	461
R middle orbital gyrus[2]	45	47	-17	6.12	
R superior frontal gyrus[2]	27	53	37	5.99	
R middle frontal gyrus[2]	42	59	4	5.94	
R middle orbital gyrus[2]	45	53	-5	5.86	

Note: L = Left; R = Right. [1]Local maximum remained present in the model with 50% probability risk trials only. [2]Local maximum was additionally present in the model with 50% probability risk trials only. Anatomical labels were acquired with automated anatomical labeling. Only areas of activation larger than 10 contiguous voxels are reported. Results were FWE voxel-wise corrected (p < .05).

Table 3. MNI Coordinates Local Maxima Activated of clusters for the contrast Gamble Risk > Fixation with risk attitude as a positive regressor.

Cluster of activation	MNI coordinates			Significance	Voxels
	x	y	z		
L middle orbital gyrus	-27	41	-11	.033	57
L middle orbital gyrus	-33	47	-14		
L middle orbital gyrus	-21	32	-20		
R olfactory cortex-caudate nucleus	3	17	-11	.013	71
L rectal gyrus	-9	17	-14		
L inferior frontal gyrus (pars orbitalis)	-18	23	-17		
L rectal gyrus	-12	26	-14		
R olfactory cortex	6	23	-5		
L olfactory cortex	-12	14	-17		

Note. L = Left; R= Right.

Results were FWE cluster corrected (pFWE < .05, k > 57) with a primary voxel- wise threshold of p < .001 (uncorrected). Anatomical labels were acquired with automated anatomical labeling.

Likewise, in the regression testing for associations between ambiguity attitude and ambiguous gambling, we entered risk attitude as a covariate of no interest.

First, we observed that a relatively more risk-seeking attitude was associated with increased activation during gambling under risk (Gamble Risk > Fixation) in the medial OFC-ventral ACC and in the le ft lateral OFC (FWE_{cc} $p < .05, k > 57$; Table 3; Figure 4A). With respect to gambling under ambiguity (Gamble Ambiguity > Fixation), a relatively more ambiguity-seeking attitude was related to increased activation in a cluster of right superior and middle temporal cortex (FWE_{cc} $p < .05$, $k > 88$; Table 4, Figure 4B). It should be noted that when testing brain-behavior associations restricted towards the activation observed in the main contrasts (Gamble Risk > Gamble Ambiguity and vice versa), no associations between risk and ambiguity attitudes and brain activation were observed.

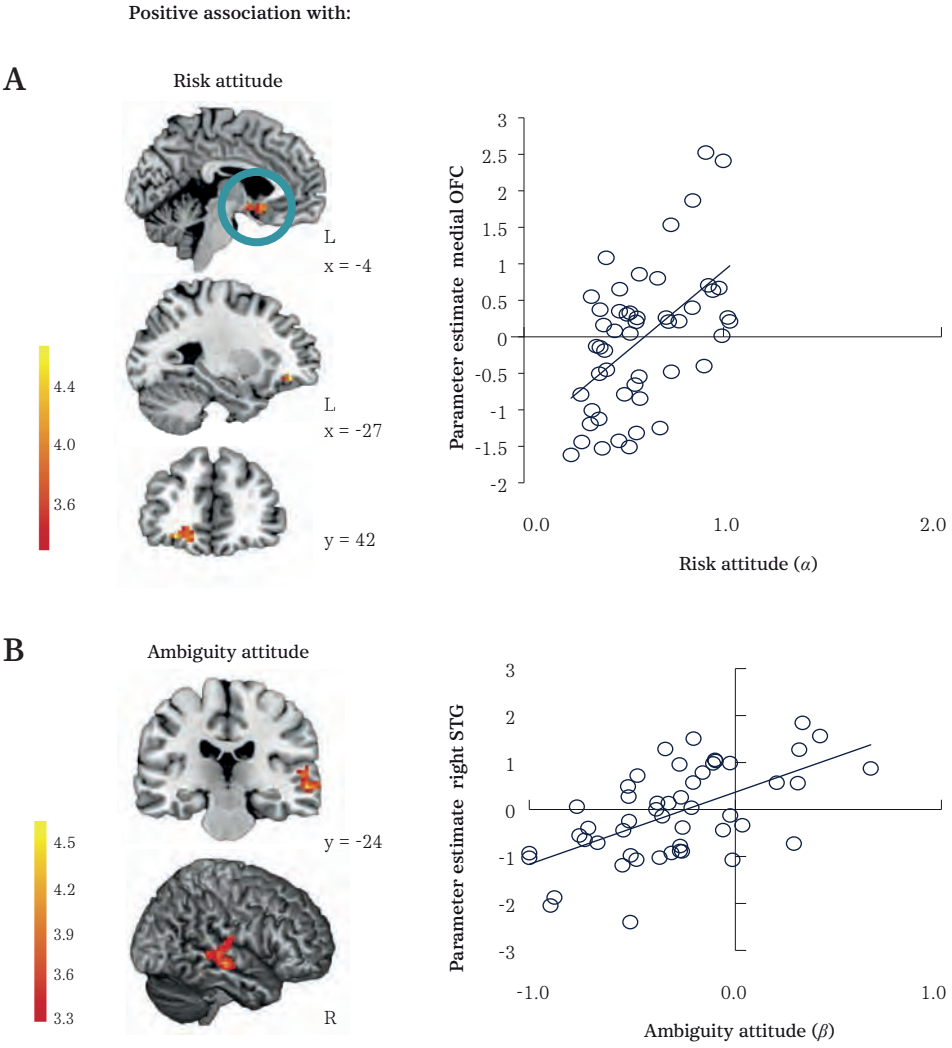


Figure 4. ***A.*** *The positive effect of risk attitude (α) on risky gambling (Gamble Risk > Fixation), controlled for ambiguity attitude. The right panel shows the positive relation between risk attitude (x-axis) on brain activation (y-axis) in the medial OFC. Results were FWE cluster-corrected (pFWE < .05, k > 57) with a primary voxel-wise threshold of p < .001 (uncorrected).* ***B.*** *The positive effect of ambiguity attitude (β) on ambiguous gambling (Gamble Ambiguity >Fixation), controlled for risk attitude. The right panel shows the positive relation between ambiguity attitude (x-axis) and brain activation (y-axis) in the right superior temporal gyrus. Results were FWE cluster-corrected (pFWE < .05, k > 88) with a primary voxel-wise threshold of p < .001 (uncorrected). The graphs are for illustrative purposes only. No statistical analyses were performed on the ROIs.*

Table 4. MNI Coordinates Local Maxima Activated of clusters the contrast Gamble Ambiguity > Fixation with ambiguity attitude as a positive regressor, for the model including all risk trials.

Cluster of activation	MNI coordinates			Significance	Voxels
	x	y	z		
R superior temporal gyrus	63	-22	-5	.008	88
R middle temporal gyrus	57	-28	1		
R middle temporal gyrus	57	-34	1		
R rolandic operculum	57	-16	16		

Note. L = Left; R= Right.

Anatomical labels were acquired with automated anatomical labeling.Results were FWE cluster corrected (pFWE < .05, k > 88) with a primary voxel-wise threshold of p < .001 (uncorrected).

Reward outcome after risky and ambiguous gambling

First we examined which areas contribute to gain versus no gain irrespective of risk and ambiguity by calculating the contrast Gain > No gain. These particular results are reported at FWE voxel correction ($p < .05$) because cluster correction resulted in one cluster of activation encompassing almost the entire brain, limiting interpretation (Woo et al., 2014). Here we observed activation in ventral striatum and middle cingulate cortex (FWE $p < .05$; Table 5, Figure 5A).

To compare reward processing (gain versus no gain) following an ambiguous or a risky gamble we ran a whole-brain repeated measures ANOVA with condition (Gain Risk>No Gain Risk; Gain Ambiguity>No Gain Ambiguity) as the within factor. Results of the ANOVA showed that reward processing following an ambiguous gamble, compared with a risky gamble, revealed increased activation in the dorsomedial PFC (MNI coordinates: x = 12, y = 29, z = 52, FWE_{cc} $p < .05$, $k = 52$; Figure 5B). The reversed effect ([Gain Risk>No Gain Risk] > [Gain Ambiguity>No Gain Ambiguity]) was not associated with significant brain activation.

Finally, no associations between risk and ambiguity attitude and brain activation during reward processing were observed.

Table 5. MNI Coordinates Local Maxima Activated for the contrast Gain > No gain, irrespective of risk and ambiguity.

Area of activation	MNI coordinates			T	Voxels
	x	y	z		
L putamen[1]	-15	8	-14	8.93	110
R putamen[1]	12	5	-17	7.57	76
R caudate nucleus[1]	9	11	-11	7.30	
L superior frontal gyrus[1]	-18	23	58	7.01	55
L precentral gyrus	-24	-23	58	6.96	
L middle frontal gyrus[1]	-21	26	55	6.68	
L superior frontal gyrus	-15	32	46	5.60	
R middle occipital gyrus[1]	51	-70	28	6.67	17
L inferior parietal lobe	-48	-40	49	6.45	21
L/R middle cingulate cortex	0	-40	43	6.24	25
R middle cingulate cortex	3	-34	40	5.74	
R middle cingulate cortex	3	-40	34	5.44	
R superior frontal gyrus	24	26	49	6.01	10
L rectal gyrus[2]	-3	41	-17	6.38	15
R/L middle orbital gyrus[2]	0	44	-14	5.96	
L superior frontal gyrus[2]	-21	41	40	6.08	17

Note: L = Left; R = Right.

[1]Local maximum remained present in the model with only 50% gain probability risk trials. [2]Local maximum was additionally present in the model with 50% probability risk trials only. Anatomical labels were acquired with automated anatomical labeling.

*Results were FWE voxel-wise corrected (**p** < .05). Only areas of activation larger than 10 contiguous voxels are reported.*

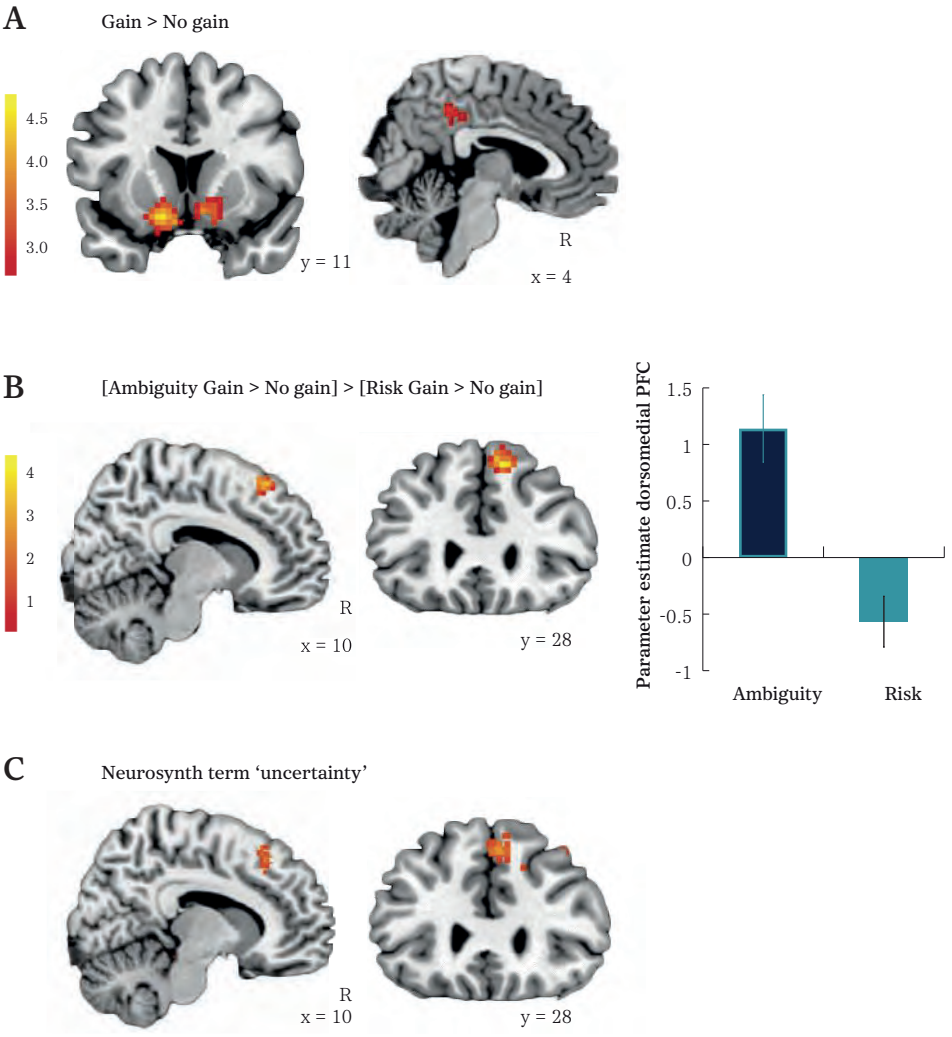


Figure 5. A. *Whole-brain contrast for Gain > No gain. Results were FWE voxel-wise corrected,* $p < .05$ *and visualized here with* $k > 10$. ***B.*** *Results of the whole-brain repeated measures ANOVA showing the contrast [Gain Ambiguity > No gain Ambiguity] > [Gain Risk > No gain Risk]. Results were FWE cluster corrected (*$p < .05$, $k > 52$*), with a primary voxel-wise threshold of* $p < .001$ *(uncorrected). The right panel shows the parameter estimate of the dorsomedial PFC, plotted for ambiguity and risk (for visual illustration only, no analyses were performed on the ROI).* ***C.*** *Neurosynth meta-analysis of fMRI activations associated with the search term 'uncertainty' (reverse inference, FDR-corrected 0.01) based on 98 studies.*

Discussion

This study aimed to elucidate specific neural systems underlying risk (known probabilities) and ambiguity (unknown probabilities) processing at the individual level. Specifically, we investigated the association between individuals' risk and ambiguity attitudes and brain activation during gambling; tested the role of risk and ambiguity within a choice at hand on subsequent neural reward processing; and explored associations between risk and ambiguity attitude and reward processing following a risky and ambiguous gamble. To these ends we combined an fMRI gambling paradigm with separately established model-based estimations of risk and ambiguity attitudes. Results showed that there was variability between individuals in risk and ambiguity attitudes, and that these attitudes were only moderately and non-significantly correlated. This allowed the investigation of risk and ambiguity attitudes as individual predictors of the neural processes underlying risky and ambiguous decision-making. The fMRI analyses resulted in a number of main findings. First, despite pronounced neural overlap between risky and ambiguous gambling in a network previously associated with risk taking and decision making (e.g., see Ernst et al., 2004; Eshel, Nelson, Blair, Pine, & Ernst, 2007; Huettel et al., 2005; Knutson et al., 2005; Kuhnen & Knutson, 2005; Levy, 2016; Platt & Huettel, 2008), individual differences in risk and ambiguity attitudes showed different neural substrates during risky and ambiguous gambling, respectively. That is, we observed that a relatively more risk-seeking attitude was associated with increased activation in medial and lateral OFC during risky gambling; and that a relatively more ambiguity-seeking attitude was related to increased activation in superior and middle temporal gyrus during ambiguous gambling. Second, processing rewards relative to no-rewards resulted in robust activity in the ventral striatum, irrespective of a previous risky or ambiguous gamble. However, processing rewards compared with no rewards after an ambiguous gamble, compared with after a risky gamble, resulted in increased dorsomedial PFC activation. Finally, risk and ambiguity attitude were not correlated with any neural activity during reward processing. The discussion is organized alongside these main findings.

The main question addressed in this study was whether risk and ambiguity processing relied on different neural substrates. Both risky and ambiguous gambling were associated with robust activity in ACC, PPC, lateral PFC, striatum (putamen), and insula, regions commonly observed in various risk taking paradigms (Ernst et al., 2004; Eshel et al., 2007; Huettel et al., 2005; Knutson et al., 2005; Kuhnen & Knutson, 2005; Levy, 2016; Platt & Huettel, 2008). The main comparisons between risk and ambiguity revealed little differences between risky and ambiguous gambling.

This was unexpected given that prior studies did observe differences between these conditions, although not all in consistent or overlapping directions (Hsu et al., 2005; Huettel et al., 2006; Levy et al., 2010). However, neural differences between risky and ambiguous gambling were observed when we related neural responses to individuals' attitudes towards risk and ambiguity. The use of model-based estimations have the advantage that they reflect a sensitive measure of an individual's preference for risk and ambiguity, and are derived from an integrative choice model that simultaneously estimates risk and ambiguity attitude (Blankenstein et al., 2016; Tymula et al., 2013).

From these analyses we observed that a relatively more risk-seeking attitude was related to increased activation in the medial and lateral OFC during risky gambling. Particularly the activation observed in the medial OFC coincides with prior studies that also used model-based estimations of risk attitudes, and observed that relatively less risk aversion (Tobler et al., 2007) or more risk seeking (Engelmann & Tamir, 2009) was associated with increased activation in the medial OFC. Possibly, this activation reflects the influence of individual differences in risk attitude in a region commonly associated with the coding of expected or subjective value (Levy & Glimcher, 2012; Tobler et al., 2007) and may suggest the enhanced recruitment of this area in individuals who exhibit relatively more risk-seeking behavior. With respect to ambiguity attitude we observed increased activation in superior and middle temporal gyrus with relatively more ambiguity-seeking attitudes. Together, these analyses suggest that despite the large overlap in the general network that was engaged when making risky and ambiguous gambles, the way these regions are engaged depends on individual differences in attitudes toward risk and ambiguity.

Not all findings that were reported in previous studies could be confirmed in the current study. Contrary to prior studies we did not find a relation between individuals' risk attitudes and activation fronto-parietal regions (e.g., inferior frontal gyrus, lateral PFC, PPC; Christopoulos et al., 2009; Fecteau et al., 2007; Gilaie-Dotan et al., 2014; Huettel et al., 2006). Unexpectedly we also did not observe a relation between ambiguity attitude and lateral PFC or OFC activation (Hsu et al., 2005; Huettel et al., 2006). In part this could be attributed to the use of model-free measures of risk behavior in some of these studies (e.g., behavior on the Balloon Analogue Risk Task; Fecteau et al., 2007; Knoch et al., 2006) which may be a different measure of someone's risk and ambiguity preferences. Furthermore, some of these abovementioned studies used transcranial magnetic/direct current stimulation or structural brain measures (i.e., gray matter volume), which may provide different but complementary information on risk and ambiguity processes (Fecteau et al., 2007; Gilaie-Dotan et al., 2014; Knoch et al., 2006). In addition, some of these studies offered choices between two gambles (with varying levels of risk) instead of offering

a choice between a gamble and a safe option, iteratively manipulated the value of the safe option based on participants' prior choices, or derived risk and ambiguity attitudes from different choice paradigms (Christopoulos et al., 2009; Hsu et al., 2005; Huettel et al., 2006). Finally, although our paradigm included variation in risk, it only included one level of ambiguity (see for a parametric approach Levy et al., 2010), leading to small(er) variations in subjective value of the latter. Together, the abovementioned elaborate manipulations are useful additions for future research. Alternatively, in the current study we examined neural correlates of each attitude while accounting for the other attitude. Thus, although our findings warrant replication, they may be more specific for individuals' risk and ambiguity attitudes.

A second question that we aimed to address was whether risk and ambiguity within a choice at hand influences the subsequent neural reward processing (gain versus no gain). We observed that reward processing irrespective of a prior risky or ambiguous gamble, and independent of risk or ambiguity attitude, resulted in a robust striatal response, replicating many prior studies (e.g., see Braams, Peters, Peper, Güroğlu, & Crone, 2014; Delgado, 2007; Knutson et al., 2005; Kuhnen & Knutson, 2005). This suggests that the striatum has a general reward signaling function and is not dependent on the nature of the gamble (i.e., known or unknown probabilities). A second finding was that reward processing after an ambiguous gamble compared with a risky gamble revealed increased activation in the dorsomedial PFC. This activity coincides with research on uncertainty processing in general. That is to say, a reversed inference search with the term 'uncertainty' in the Neurosynth data base (on online meta-analysis data base: www.neurosynth.org; Yarkoni et al., 2012) shows that the dorsomedial PFC is robustly documented in 98 studies on various forms of uncertainty processing (see Figure 5C), for instance with respect to risky decision-making (e.g., prediction uncertainty; Volz, Schubotz, & von Cramon, 2003, 2004), and even with respect to self-reported intolerance to uncertainty about possible future aversive events (Schienle et al., 2010). The fact that we observed this activation in our study during reward processing following an ambiguous gamble, fits well with the interpretation that this region represents a common neural substrate for uncertainty coding.

Finally, we explored whether individuals who differ in risk or ambiguity attitude also process outcomes of gambles differently, which has not yet been examined in prior research. No associations between risk or ambiguity attitude and brain activation during reward processing were observed. Possibly, individual differences in risk and ambiguity preferences are only reflected by the neural mechanisms underlying choices, and not the subsequent processing of outcomes. However, future research should further establish this finding.

A number of limitations need to be taken into consideration. First, although we observed *different* neural mechanisms underlying individuals' risk and ambiguity attitude during risky and ambiguous gambling, respectively, we stress that we did not observe a *dissociation*. That is, when investigating whether risk and ambiguity attitudes were associated with activation observed in the main contrasts (such as Risk > Ambiguity), no relations were found with risk or ambiguity attitudes. However, individual differences in risk and ambiguity attitude may not necessarily be reflected in the activation that is homogeneous for the group as a whole. Rather, individual differences in risk and ambiguity attitudes may be reflected in neural systems that show heterogeneity across subjects (e.g., see Gabrieli, Ghosh, & Whitfield-Gabrieli, 2014; van Duijvenvoorde et al., 2016). Nevertheless, future studies need to replicate these findings using larger sample sizes. Second, we used a task to define individuals' risk and ambiguity attitudes that differed on several aspects from the functional imaging task. That is, given our interest of neural processes underlying risky and ambiguous gambling, we manipulated the fMRI paradigm such that participants were more likely to gamble than to choose the safe option. That is, the expected value of the gamble option was considerably higher (i.e., between €7.75 and €25.5), than the safe option (€3). In addition, in the behavioral task participants did not observe direct outcomes and could not win any money, whereas in the fMRI task participants were told that they won the amount of three randomly chosen trials. Thus, we cannot know for certain whether participants considered the decisions in the behavioral task equally important as those in the fMRI task, and whether participants believed they were getting paid according to what was explained in the instructions in the fMRI task. Given that different behavioral and even brain patterns may emerge when using real versus hypothetical gambles (e.g., see Camerer & Mobbs, 2017), it is important to ensure that participants consider the gambles in both tasks equally important and that the payouts are believable. In future research this could be achieved by informing participants that three trials will be randomly played for real for each task, and preferably by letting the participants exert control over these randomly chosen trials (Levy et al., 2010). Furthermore, the behavioral task was always administered after the fMRI session, which may have affected the model-based estimations of risk and ambiguity attitude. Thus, when using a similar setup, future studies may benefit from counterbalancing the order of tasks to eliminate its effect. In addition, whereas risk attitude was positively related to gambling behavior in the fMRI task, we did not observe this between-task correlation for ambiguity attitude. Possibly, this is because we included only one level of ambiguity in the fMRI task, thereby limiting the variation in choice behavior. Whether the cognitive processes underlying both tasks are truly comparable is therefore difficult to establish, and thus

the brain-behavior associations observed in the current study need to be replicated in future research preferably with an fMRI task that allows the estimation of risk and ambiguity attitude from behavior in the scanner, while simultaneously enabling the investigation of reward processing after a risky and ambiguous gamble. Finally, the current study only focused on gambling in the gain frame. Future studies may benefit from also including a loss frame, for example, to study gain versus loss, or loss versus no loss, in risky and ambiguous conditions.

In conclusion, the current study aimed to provide a clear view of the neural substrates of risk and ambiguity processing at the individual level; the association between risk and ambiguity within a choice and subsequent reward processing; and associations between risk and ambiguity attitudes and reward processing. We show that despite the large overlap in the general network that was engaged during risky and ambiguous gambling, brain activation during gambling depends on individual differences in attitudes toward risk and ambiguity. Especially the neural correlates of risk attitudes during gambling under risk including medial OFC are consistent with a large body of literature suggesting that this valuation network drives risk taking (Delgado, 2007; Knutson et al., 2005; Kuhnen & Knutson, 2005; Levy & Glimcher, 2012; Platt & Huettel, 2008). The fact that we did not observe this pattern of brain activation with ambiguity attitude suggests that different neural correlates were associated with attitudes towards risk and towards ambiguity. Moreover, these findings highlight the importance of taking individual differences into account that may be masked by group effects. In addition, we found evidence that reward processing after an ambiguous, compared with risky, gamble is related to a heightened dorsomedial PFC response, indicative of a general signal of uncertainty coding. These insights may be applied to future research investigating individual differences in problematic decision-making behavior, such as pathological gambling, and adolescent risk taking, which is associated with a heightened sensitivity towards rewards (Braams, van Duijvenvoorde, Peper, & Crone, 2015; van Duijvenvoorde, Peters, Braams, & Crone, 2016).

Supplementary materials

[1]Note: Parametric results of subjective value under risk

A different approach to test for effects of individual differences in dealing with risk and ambiguity would be to probe for regions that correlate with subjective value modeled as a parametric modulator separately during risky decision-making and during ambiguous decision-making (cf. Levy et al., 2010). To investigate this we ran a model with the subjective values of the risky and ambiguous lotteries as parametric modulators. Specifically, we calculated the subjective value of each gambling option (which was either risky or ambiguous) in the fMRI task, for each individual separately, using the formula

$$EU(x,p,A) = (p - \beta * \frac{A}{2}) * x^{\alpha}$$

in which we entered the separately established model-based estimations of risk and ambiguity attitudes. The resulting individuals' subjective values were demeaned per subject. We next investigated the positive and negative effect of subjective value under risk (parametric) on risky gambling and subjective value under ambiguity (parametric) on ambiguous gambling. From these analyses we observed a significant positive (but no negative) effect of subjective value under risk in the right supramarginal gyrus (see Figure A1.A upper pannel, Table A1 below). Next, we next lowered the primary voxel-wise threshold to $p < .005$. With this more lenient threshold we did observe a significant negative effect in the anterior cingulate cortex/ dorsomedial PFC (Figure A1.B; Table A2), which is consistent with previous studies

Table A1. **Results of the parametric analyses showing the positive effect of subjective value under risk.**

	MNI coordinates				
Cluster of activation	x	y	z	Significance	Voxels
R supramarginal gyrus	63	-31	28	.026	54
	69	-28	19		
R superior temporal gyrus	63	-34	16		
	57	-31	16		

Note. L = Left; R= Right. Anatomical labels were acquired with automated anatomical labeling. Results were FWE cluster-corrected ($p < .05$, $k > 54$) with a primary voxel-wise threshold of $p < .001$ (uncorrected).

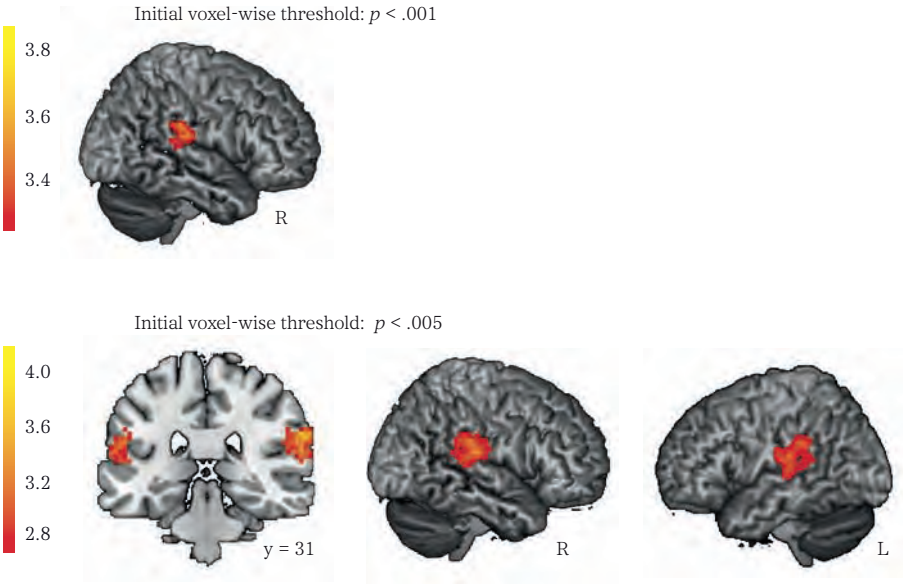
(Bartra et al., 2013). In addition, with this more lenient threshold, the positive effect of risk in the parietal lobe was now bilateral (Figure A1.A lower panel; Table A2). Because comparing subjective value under risk versus ambiguity was not the goal of the current study, and because no significant results were found for the ambiguous condition (not even with the more lenient threshold), this comparison between risk and ambiguity was not made.

Table A2. Results of the parametric analyses showing the positive effect of subjective value under risk.

		MNI coordinates				
	Cluster of activation	x	y	z	Significance	Voxels
Positive effect $k > 142$	L supramarginal gyrus	-48	-37	31	.014	142
	L supramarginal gyrus	-60	-28	22		
	L postcentral gyrus	-60	-22	22		
	L superior temporal gyrus	-57	-25	7		
	L superior temporal gyrus	-54	-28	13		
	L superior temporal gyrus	-63	-40	16		
	L supramarginal gyrus	-60	-37	25		
	L superior temporal gyrus	-63	-43	22		
	R supramarginal gyrus	63	-31	28	.007	162
	R superior temporal gyrus	69	-28	19		
	R superior temporal gyrus	63	-34	16		
	R superior temporal gyrus	57	-31	16		
	R supramarginal gyrus	54	-34	28		
Negative effect $k > 116$	L middle cingulate cortex	-12	26	34	.038	116
	L superior medial gyrus	0	20	43		
	R anterior cingulate cortex	12	35	22		
	R anterior cingulate cortex	6	38	25		
	L anterior cingulat cortex	-3	35	25		
	R superior frontal gyrus	18	44	28		

Note. L = Left; R= Right. Anatomical labels were acquired with automated anatomical labeling Results were FWE cluster-corrected ($p < .05$, $k > 142$ for positive and $k > 116$ for negative effect) with a primary voxel-wise threshold of $p < .005$ (uncorrected).

A Positive effect of risk (parametric)



B Negative effect of risk (parametric)

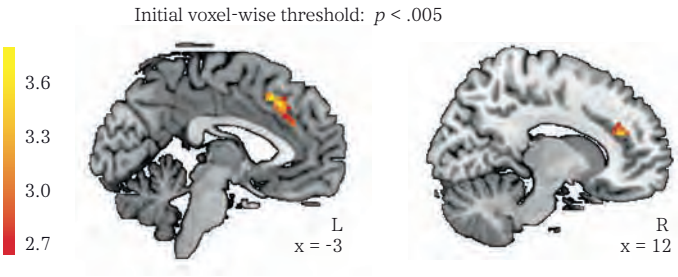


Figure A1. A. Upper panel: *Result of the parametric analyses showing a positive effect of subjective value under risk in the right supramarginal gyrus. Results were FWE cluster-corrected (p < .05, k > 54) with a primary voxel-wise threshold of p < .001 (uncorrected).* ***Lower panel:*** *The positive effect of subjective value under risk, FWE cluster-corrected (p < .05) with an initial voxel-wise threshold of p < .005 (k > 142).* ***B.*** *Negative effect of subjective value on the risky lotteries. Results are FWE cluster corrected (p < .05) with an initial voxel-wise threshold of p < .005 (k > 116).*

Chapter 4

Neural tracking of subjective value under risk and ambiguity in adolescence

This chapter is under review as: Blankenstein, N. E., & van Duijvenvoorde, A. C. K. Neural tracking of subjective value under risk and ambiguity in adolescence.

Abstract

Although many neuroimaging studies on adolescent risk taking focus on brain activation during outcome valuation, less attention is paid to the neural correlates of choice valuation. Subjective choice valuation may be particularly influenced by whether a choice presents risk (unknown outcomes with known probabilities) or ambiguity (unknown outcomes with unknown probabilities), which has rarely been studied in developmental samples. Therefore, we examined the neural tracking of subjective value during choice under risk and ambiguity in a large sample of adolescents (N = 188, 12-22 years). Specifically, we focused on whether risk and ambiguity were coded by activation in distinct or overlapping brain regions. A model-based approach to estimate individuals' risk and ambiguity attitude showed that there was prominent individual variation in individuals' aversion to risk and ambiguity. Furthermore, participants subjectively experienced the ambiguous options as riskier compared to the risky options. On the neural level we observed that subjective value tracking under risk was coded by activation in ventral striatum and superior parietal cortex. In contrast, subjective value tracking under ambiguity was coded by dorsolateral prefrontal cortex (PFC) and superior temporal gyrus activation. Finally, dorsomedial PFC activation reflected a common neural signal of subjective choice valuation, coding both risk and ambiguity. Together, this study indicates distinct and overlapping brain activation patterns for choice valuation under risk and ambiguity in an adolescent sample. Finally, we highlight the potential of combining behavioral modelling with fMRI for investigating choice valuation in adolescence, which may ultimately aid in understanding who takes risks and why.

Key words: adolescence, subjective value, risk, ambiguity, fMRI, parametric

Introduction

Adolescence encompasses the developmental phase from childhood to adulthood, and is often described as a period marked by increases in risk-taking tendencies such as reckless driving behavior and heightened levels of substance use (Crone & Dahl, 2012; Somerville, Jones, & Casey, 2010). To date, most research on adolescent risk taking has focused on relating reward processes under different conditions of risk, to task-based or real-life risk-taking behavior, and have observed meaningful relations. For instance, higher levels of real-life risk-taking have been associated with attenuated activation in lateral prefrontal regions during reward outcome processing, following decisions under risk (known probabilities) as well as ambiguity (unknown probabilities; Blankenstein, Schreuders, Peper, Crone, & van Duijvenvoorde, 2018). Surprisingly, fewer studies have focused on choice processes, and the development of choice valuation that may drive risk-taking behavior. In particular, classic economic theories posited that expected value, i.e., the product of the magnitude and the probability of the outcome, determines choice behavior, in which a higher objective value should be the more attractive choice. However, individuals' subjective evaluation of choice options rarely matches the objective expected value (Kahneman & Tversky, 1979). Therefore, subjective, rather than objective, choice valuation may be a more sensitive reflection of individual valuation processes (van den Bos, Bruckner, Nassar, Mata, & Eppinger, 2017). Moreover, subjective valuation of risk and ambiguity have been suggested to be sensitive to developmental change (Blankenstein, Crone, van den Bos, & van Duijvenvoorde, 2016; Tymula et al., 2012; van den Bos & Hertwig, 2017), but also shows large individual variation in adolescence (Blankenstein et al., 2016; Blankenstein et al., 2018). To date, few studies have explicitly focused on the behavioral and neural correlates of subjective, and expected, value tracking in adolescents, nor under conditions of risk and ambiguity. The current study therefore set out to investigate the behavioral and neural correlates of subjective value tracking under risk and ambiguity in a large sample of adolescents.

One common decision strategy suggested by influential behavioral economic theories such as prospect theory posits that when an individual is confronted with a decision between two alternatives, they first ascertain the subjective value of each available choice option, and then select the option with the highest subjective value (Kahneman & Tversky, 1979). A comprehensive meta-analysis of 206 studies examined the neural basis of subjective value in adults across a wide range of reward types (Bartra, McGuire, & Kable, 2013). This meta-analysis identified the anterior insula, dorsomedial prefrontal cortex (DMPFC), dorsal striatum, and

thalamus as key regions that have been found to code *both* positive and negative effects of subjective value on brain activation. That is, some studies have found activation increases in these regions with increasing subjective value, while others found activation increases in these regions with decreasing subjective value. This mixture of positive and negative effects was interpreted as a signal of salience or arousal (Bartra et al., 2013). Conversely, the ventral striatum (VS) and ventromedial prefrontal cortex (VMPFC) have been found to predominantly reflect positive effects of subjective value for different reward types (Bartra et al., 2013; Rangel & Clithero, 2014; Sescousse, Caldú, Segura, & Dreher, 2013).

Few studies have examined the neural signature of choice valuation in adolescents. Studies that focused on expected value coding during choice in children, adolescents, and adults (Barkley-Levenson & Galván, 2014; Van Duijvenvoorde et al., 2015), and showed that activation in VS, DMPFC, dorsolateral prefrontal cortex (DLPFC), and parts of the parietal cortex were positively related to increases in expected value. In addition, activation in VS was more pronounced with increasing expected value for adolescents compared with adults, highlighting that adolescents are more sensitive to these increases than adults, even when the adolescents were compared with adults who displayed similar gambling behavior (Barkley-Levenson & Galván, 2014). Importantly, these studies focused only on objective expected value scaling in adolescents. However, studies integrating the subjective evaluation of value are currently lacking and may be important because the expected value of a choice option may not exactly match an individual's subjective value of the choice at hand (van den Bos et al., 2017).

An important factor that contributes to individuals' (subjective) choice valuation is whether the choice alternatives reflect explicit risk or ambiguous risk. That is, in situations in which the decision outcomes are uncertain, explicit risk (henceforth referred to as risk) reflects decision environments in which the probabilities are known, whereas ambiguous risk (henceforth referred to as ambiguity) reflects decision environments in which the probabilities are unknown (Tversky & Kahneman, 1992). Not only are there considerable individual differences in the level of risk and ambiguity preferences (ranging from aversion to seeking), they may also vary across development, and are differentially related to overt risk-taking levels (Blankenstein et al., 2016; Tymula et al., 2012; van den Bos & Hertwig, 2017). On the neural level, deciding under conditions of risk and ambiguity have been found to be coded by different brain regions, particularly when considering individual differences in risk-taking levels under risk and ambiguity, in both adults and adolescents (Blankenstein, Peper, Crone, & Duijvenvoorde, 2017; Blankenstein et al., 2018). On the other hand, a key study comparing neural coding between risk and ambiguity in adults

showed that striatum, MPFC, PCC, and amygdala positively scaled with increases in subjective value under *both* risk and ambiguity. That is, in this study none of these brain regions conveyed unique information about subjective value under either risk or ambiguity. This suggests that at least in adults, subjective value tracking under risk and ambiguity is similarly represented in the brain, even though behavior under these conditions differs considerably (Levy, Snell, Nelson, Rustichini, & Glimcher, 2010). However, whether subjective value scaling under conditions of risk versus ambiguity differs or is similarly represented in adolescence, has yet to be examined.

Taken together, this follow-up study on Blankenstein et al. (2018) investigates subjective value tracking under risk and ambiguity, by combining an fMRI gambling task with separately estimated risk and ambiguity attitudes, in a large sample of adolescents (N = 188, 12-22 years). The goals of this study were threefold. First, we studied which regions code subjective value under risk and ambiguity, and investigated differences and similarities between these conditions. Second, we examined how these results compare to objective, rather than subjective, value coding. Finally, we explored whether there were age effects in subjective value coding. We hypothesized that activation in the VS, VMPFC, and parietal cortex in particular would increase with increasing subjective value (Barkley-Levenson & Galván, 2014; Van Duijvenvoorde et al., 2015). Given the mixed findings on DMPFC and insula, we expected that activation in DMPFC and insula could increase or decrease with increasing subjective value (Barkley-Levenson & Galván, 2014; Bartra et al., 2013). Specifically, to assess whether subjective value coding under risk and ambiguity relied on similar (Levy et al., 2010) or separate neural correlates in adolescence, we tested for unique activation patterns, as well as for overlap between conditions of risk and ambiguity. Although not necessarily within an adolescent age range, prior studies reported age differences in expected value tracking from adolescence into adulthood (Barkley-Levenson & Galván, 2014; Van Duijvenvoorde et al., 2015). Therefore, we explored linear and quadratic effects of age on the neural tracking of subjective value.

Methods

Participants

Two hundred and fourteen individuals (109 females, 105 males) between 12 and 22 years old participated in this study. Participants were part of a three-wave longitudinal study (Braintime; see for instance Peters & Crone, 2017, and Schreuders et al., 2018). Data of this sample has previously been reported in the cross-sectional study by Blankenstein et al. (2018). In this prior study, eighteen participants were

excluded because of psychiatric disorders, excessive head motion in the MRI scanner (> 3 mm), loss of data, and because of too few trials in which the gambling option was chosen in the fMRI task. For the goals of the current study we excluded ten additional participants because of violations of stochastic dominance in at least 50% of trials of the behavioral task (indicating a limited understanding of the task) and because of extreme outliers in risk attitude (i.e., > 3.5 *SD's* above the mean; in- or exclusion of these participants did not qualitatively affect our main behavioral or neural findings). The final sample therefore included 188 participants (100 female, 88 male, M_{Age} = 17.18, SD_{Age} = 2.59, range 12.02 – 22.02 years). An overview of the number of participants across age is provided in Figure S1A in the supplements. IQ was estimated in the first two waves, fell in the normal range, and did not correlate with age (see also Blankenstein et al., 2018; Peters & Crone, 2018; Schreuders et al., 2018).

The institutional review board of the University Medical Center approved this study. Written informed consent was given by adult participants, and by parents in the case of minors (minors provided written assent). All anatomical scans were cleared by a radiologist. Participants were screened for psychiatric or neurological disorders and MRI contra indications (none were observed).

Wheel of fortune task

fMRI task

Participants played a wheel-of-fortune task in the MRI scanner (see Figure 1; Blankenstein et al., 2017; Blankenstein et al., 2018). Here, participants were asked to make a series of decisions between a 'safe' wheel (presenting a consistent sure gain of €3) and a gambling wheel (presenting a chance of winning more money (€31-€34), but also a chance of winning nothing (€0)). The gambling wheel could either be risky (probabilities were known: 0.25, 0.50, or 0.75) or ambiguous (probabilities were hidden). After the decision, participants were presented with the outcome (gain or no gain). Behavioral results of the fMRI task are provided in the supplements (Figure S1B).

Ninety-two trials were presented: 46 ambiguous and 46 risky trials. Of the risky trials, 30 trials reflected a gamble with a 50% probability of winning, 8 trials reflected a gamble with a 75% probability of winning, and 8 trials reflected a gamble with a 25% probability of winning. The experiment was programmed such that these probabilities matched the actual probabilities of winning. Furthermore, one of the four possible amounts (€31, €32, €33, or €34) were randomly displayed (without replacement), on a trial-by-trial basis. Thus, although each participant was presented with the same distribution of probabilities, the amount varied per trial.

The task was presented in the scanner via E-prime (Psychology Software Tools).

Participants were presented with the pairs of wheels. Gamble and safe options were randomly displayed on the left or right side of the screen on a trial-by-trial basis, and the position of the blue and red parts of the risky wheels (left, right, bottom, and top of the wheel) were counterbalanced across trials. A gray square prompted the participants to give a response, which had to be given within a 3000 msec interval. A selection frame around the chosen wheel confirmed the response, and remained visible for the duration of the interval. The decision phase was separated from the outcome phase by a fixation cross of 2-4 seconds (jittered, with increments of 500 msec). Reward outcomes were presented for 1250 msec. The inter-trial-intervals and the optimal trial sequence were determined with OptSeq (Dale, 1999), with jittered intervals varying between 0 and 9350 msec. In addition, each trial was preceded by a 500 msec fixation cross, which was not part of the inter-trial-interval.

Behavioral task

Following the scan session, participants played a behavioral version of the wheel of fortune task (as validated previously, see Blankenstein et al., 2017; Blankenstein et al., 2016). This task includes more variation in probabilities (0.125, 0.25, 0.375, 0.50, 0.625, 0.75), amounts (€5, €8, €20, €50) and ambiguity level (0%, 25%, 50%,

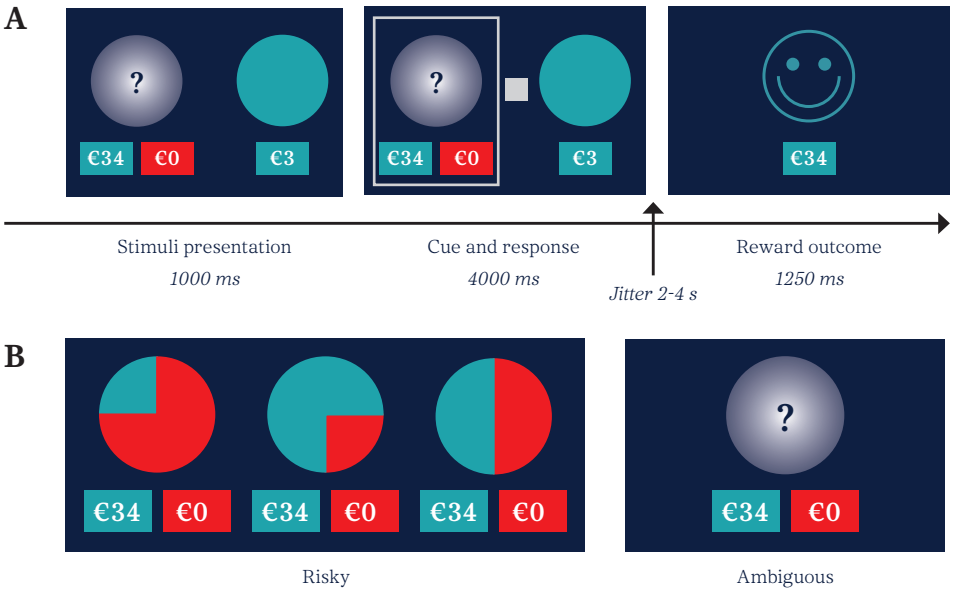


Figure 1. *Schematic representation of the fMRI task.* ***A.*** *Example of an ambiguous trial in which the outcome after choosing to gamble was gain.* ***B.*** *Risky and ambiguous stimuli.*

75%, 100%), allowing the model-based estimation of each individual's risk and ambiguity attitudes. No decision outcomes were provided in this task to ensure that the resulting risk and ambiguity attitudes could not be influenced by differences in the choice environment. The task included 24 unique risk trials (all probabilities combined with all amounts), and 16 unique risk trials (all ambiguity levels combined with all amounts). All trial types were presented twice, resulting in 80 trials used for the model-based estimations of risk and ambiguity attitudes.

Each trial started with a jittered fixation cross (500-1000 msec, with increments of 100 msec) followed by the wheels. A gray square in the center of the screen prompted the participants to respond (reaction time was self-paced), and a selection frame confirmed the participant's choice. The wheels (gamble, safe) were randomly displayed right and left on the screen, and the position of the blue and red portions of the risky wheels, and the position of the ambiguous lids (top or bottom) were counterbalanced across trials.

Risk and ambiguity attitude estimations

We estimated each participant's risk and ambiguity attitude from the behavioral task by modelling the expected utility (EU) of each choice option, using a power utility function with an additional term that takes into account ambiguity attitude (Blankenstein et al., 2016; Gilboa & Schmeidler, 1989; Levy et al., 2010; Tymula et al., 2012):

$$EU(x,p,A) = (p - \beta * \frac{A}{2}) * x^{\alpha} \qquad \textit{Equation 1.}$$

where x indicates the amount, p the probability, A the ambiguity level, α the risk attitude, and β the ambiguity attitude. A risk attitude of 1 indicates risk-neutrality, a risk attitude of < 1 indicates risk-aversion, and a risk attitude > 1 indicates risk-seeking. Relatedly, an ambiguity attitude of 0 indicates ambiguity-neutrality (meaning the participant is unaffected by the level of ambiguity), an ambiguity attitude > 0 indicates ambiguity-aversion (meaning the participants behaves as if the probability is less than the objective probability (50%), and an ambiguity attitude < 1 indicates ambiguity-seeking (meaning the participant behaves as if the probability is more than the objective probability).

For model fitting, the simplex algorithm of the general purpose optimization toolbox (optim) in R was used (R Core Team, 2015). To model trial by trial choices, a logistic choice rule was used to compute the probability of choosing to gamble (Pr(*ChoseGamble*) as a function of the difference in expected utility of the gamble (EU_{Gamble}) and the safe option (EU_{Safe}). Furthermore, the decisions of the participants

were modeled as susceptible to an error term (μ) to account for potential stochasticity in choice.

$$\Pr(ChoseGamble) = \frac{1}{1 + \exp(-(EU_{Gamble} - EU_{Safe}) / \mu)} \qquad \textit{Equation 2.}$$

This function was refitted with a grid search procedure to account for local minima in the estimated parameters. The resulting risk and ambiguity attitudes were used for behavioral analyses and to set up the parametric regressors for the whole-brain fMRI analyses (see 'General Linear Model'). In the supplementary materials we report the results of analyses on the raw choice behavior in the behavioral task (Figure S1C). In brief, these results show that participants were sensitive to the task parameters (amount, probability, ambiguity level), and thus that participants had a basic understanding of the behavioral task. Furthermore, on average, participants gambled an equal amount in the risky and ambiguous trials, but responded slower in the ambiguous than in the risky trials.

Exit questions subjective experience

To examine participants' subjective experience of the gambling wheels in the behavioral task, we presented participants with a number of exit questions following the behavioral task. Specifically, we presented participants with the different risky (0.125, 0.25, 0.375, 0.50, 0.625, 0.75 probabilities) and ambiguous (25%, 50%, 75%, 100%) wheels, without showing the amounts, and asked participants for each of these wheels how risky they found this wheel. Participants could indicate their perceived riskiness on a slider bar (0-100).

Procedure

The procedure was similar to Blankenstein et al. (2017; 2018). Participants were accustomed to the MRI environment using a mock scanner and received instructions on the wheel of fortune task in a quiet laboratory room. We explained participants that the ambiguous wheel could reflect a gamble of any of the risky probabilities (25%, 50%, 75%). Participants completed ten practice trials. In the scanner, participants responded to the task with their right hand using a button box, and head movements were restricted with foam padding. The fMRI task was followed by a high-definition structural scan.

After the MRI session, participants completed the behavioral version of the wheel of fortune task (see also Blankenstein et al., 2017), in which participants were given a hypothetical choice task and were instructed to choose which option they preferred. To explain the different ambiguity levels, we showed the different 'lids' that varied

in size and covered different proportions of the wheel, and showed the wheels that could lie underneath these lids. Participants practiced three trials beforehand.

Finally, participants completed the exit questions on their subjective experience of the wheels presented in the behavioral task, via Qualtrics (www.qualtrics.com). For other procedural details of the Braintime study that are not related to the current research goals, please see Blankenstein et al. (2018), Schreuders et al. (2018), and Peper & Crone (2018).

MRI data acquisition

We used a 3T Philips scanner (Philips Achieva TX) with a standard whole-head coil. Functional scans were acquired during two runs of 246 dynamics each, using T2* echo-planar imaging (EPI). Volumes covered the entire brain (repetition time (TR) = 2.2 s; echo time (TE) = 30 ms; sequential acquisition, 38 slices; voxel size 2.75 x 2.75 x 2.75 mm; field of view (FOV) = 220 x 220 x 114.68 mm). To allow for equilibration of T1 saturation effects we discarded the first two volumes. A high-resolution 3D T1 scan was obtained after the fMRI task for anatomical reference (TR = 9.76 msec, TE = 4.59 msec, 140 slices, voxel size = 0.875 mm, FOV = 224 × 177 × 168 mm).

MRI data analyses

Preprocessing

MRI preprocessing steps were identical to Blankenstein et al. (2018). Data was analyzed using SPM8 (Wellcome Department of Cognitive Neurology, London). Images were corrected for slice timing acquisition and rigid body motion. We spatially normalized functional volumes to T1 templates. Translational movement parameters never exceeded 3 mm (< 1 voxel) in any direction for any participant or scan. The normalization algorithm used a 12-parameter affine transform with a nonlinear transformation involving cosine basis function, and resampled the volumes to 3 mm^3 voxels. Templates were based on MNI305 stereotaxic space. The functional volumes were spatially smoothed using a 6 mm full width at half maximum (FWHM) isotropic Gaussian kernel.

General-Linear model

We used the general linear model (GLM) in SPM8 to perform statistical analyses on individual subjects' data. The fMRI time series were modeled as a series of two events: the decision phase and the outcome phase, convolved with a canonical hemodynamic response function (HRF). The onset of the decision phase was modeled with a duration of the participant's response (1000 msec + response time; see Figure 1), and the onset of the outcome phase (gain or no gain) was modeled with

zero duration. Events were modeled separately for risk and ambiguity. The GLM included the direct and parametrically modulated regressors of risk and ambiguity during the decision phase, and the direct regressors of gains and no gains during the outcome phase. In the current study, we were interested in the parametric tracking of subjective value under risk and ambiguity only, but in the supplements we show the main effects of choosing under risk and ambiguity (i.e., not parametrically modulated; Figure S2 A-B). Results of the main contrasts during the outcome phase are reported in Blankenstein et al. (2018).

Subjective value under risk and ambiguity were inferred by entering each individual's risk and ambiguity attitude, derived from the behavioral task, in Equation 1 for the trials in the fMRI task. That is, for each participant, we determined the subjective value of the wheel selected by the participant (gamble or safe) given the probability (0.25, 0.50, 0.75, or 1), amount (€3, €31, €32, €33, or €34), ambiguity level (0 or 1) of the selected wheel, and the participant's risk and ambiguity attitude derived from the behavioral task.

Trials on which participants did not respond were modeled separately as a regressor of no interest, and six motion parameters were included as nuisance regressors. The least-squares parameter estimates of the height of the best-fitting canonical HRF for each condition separately were used in pairwise contrasts. These pairwise comparisons resulted in individual-specific contrast images, which we used for the higher-level group analyses. All higher-level group analyses were conducted with Family Wise Error (FWE) cluster correction ($p < .05$, using a primary voxel-wise threshold of $p < .001$, uncorrected; Blankenstein et al., 2017; Woo, Krishnan, & Wager, 2014). We used the MarsBaR toolbox (Brett, Anton, Valabregue, & Poline, 2002; http://marsbar.sourceforge.net) to visualize patterns of activation in clusters identified in the whole-brain results. Coordinates of local maxima are reported in MNI space.

Results

Behavioral results

Risk and ambiguity attitude

First, we formally investigated the model-based estimations of risk and ambiguity attitude. To ease interpretation for these behavioral analyses, we recoded ambiguity attitude such that higher values indicate a relatively more seeking attitude. Figure 2A depicts box plots of risk and ambiguity attitude, with violin plots superimposed, which show the full distribution of the data. On average, participants were generally risk and ambiguity averse ($M_{risk} = .60$, $M_{ambig} = -.25$), although there were considerable

individual differences in these attitudes (SD_{risk} = .26, $range_{risk}$ =.11-1.52, SD_{ambig} = .36, $range_{ambig}$ = -1.00 – 1.00). Furthermore, participants did not differ in their degree of aversion to risk and ambiguity (p = .62, as indicated by a paired-samples t-test on z-transformed risk and ambiguity attitudes). Next, we tested for linear, quadratic, and cubic effects of age on risk and ambiguity attitudes using regression analyses. For risk attitude we observed a positive linear effect of age (R^2 = .02 , F(1, 186) = 4.29, b = .015, SE = .007, p = .04), indicating that risk-seekingness increased slightly across adolescence, while no effects of age were observed for ambiguity attitude (all *p's* > .1). Finally, a partial correlation showed that risk and ambiguity attitude, controlling for age, were not significantly correlated (*partial r* = -.083, p = .26).

Subjective experience behavioral task

To test the robustness of the behavioral estimates of risk and ambiguity attitudes, we examined participants' responses on the exit questions on perceived riskiness for each of the wheels in the behavioral task. First, a repeated measures ANOVA on the risky wheels with age linear and quadratic as covariates indeed showed that participants subjectively experienced the risky wheels as less risky with increasing gain probability (Figure 2B (left) main effect probability F(5, 920) = 154.99, p < .001, η_p^2 = .457; no effects of age (all p's > .25)). A similar finding was observed for the ambiguous wheels, in which participants subjectively experienced the ambiguous wheels as more risky with increasing ambiguity level (Figure 2B (right); main effect ambiguity level: F(3, 552) = 118.73, p < .001, η_p^2 = .392; no effects of age (all p's > .14)). On average, participants perceived the ambiguous wheels as riskier than the risky wheels (M_{ambig} = 62.75, SE_{ambig} = 1.22, M_{risk} = 52.52, SE_{risk} = .61, F(1, 184) = 54.50, p < .001, η_p^2 = .244, no effects of age (all p's > .16)).

Next we tested whether participants' average subjective experience was correlated with the behavioral estimations of risk and ambiguity attitude, while controlling for age. These partial correlations showed that risk attitude was negatively correlated with perceived riskiness of the risky wheels (*partial r* = -.21, p = .004, Figure 2C (left)), as well as of the ambiguous wheels (*partial r* = -.20 , p =.007, not depicted in a figure). Thus, a more risk-seeking attitude was correlated with perceiving these wheels as less risky. Finally, ambiguity attitude was correlated with the perceived riskiness of the ambiguous wheels (*partial r* = -.15, p = .043; Figure 2C (right)), such that a more seeking attitude was correlated with perceiving these wheels as less risky. This relation between ambiguity attitude and perceived riskiness of the risky wheels was not observed (*partial r* = .011, p = .88). Together, these findings show that the behavioral estimations of risk and ambiguity attitude also reflect participants' self-reported subjective experience of the gambles in the behavioral task

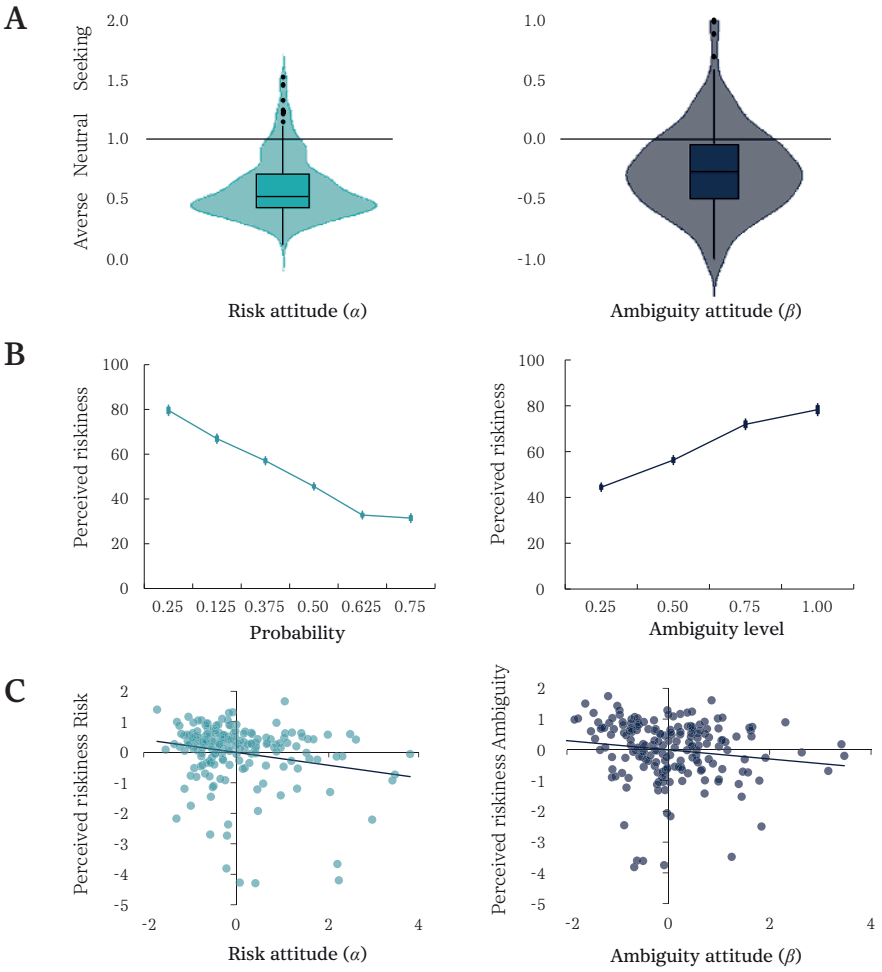


Figure 2. A. *Violin- and box-plots for risk attitude (left) and ambiguity attitude (right). The violin plots show the full distribution of the data. For risk attitude, 0 indicates risk aversion, 1 indicates risk neutrality, and 2 indicates risk seeking. For ambiguity attitude, -1 indicates ambiguity aversion, 0 indicates ambiguity neutrality, and 1 indicates ambiguity seeking. For both measures, participants were generally averse, although there were considerable individual differences.* ***B.*** *Average perceived riskiness for each of the risky wheels (left) and ambiguous wheels (right) presented in the behavioral task, controlled for age. Bars indicate standard errors.* ***C****. Partial correlations of risk attitude and the mean perceived riskiness of the risky wheels (left), and partial correlation of ambiguity attitude and the mean perceived riskiness of the ambiguous wheels (right), controlled for age. Risk attitude correlated with the perceived riskiness of both conditions, while ambiguity attitude only correlated with the perceived riskiness of ambiguity.*

fMRI results

Subjective valuation of risk and ambiguity

First, we examined the neural patterns of subjective value coding for risk and for ambiguity. To this end, we ran a whole-brain repeated measures ANOVA with condition (risk and ambiguity as parametric regressors) as within factor, and inspected the positive and negative *t*-contrasts for risk and ambiguity. For risk, we observed positive patterns of activation in bilateral VS, bilateral superior parietal cortex (SPL), postcentral gyrus, mid-cingulate cortex, and supplementary motor area, indicating that with increasing subjective value, activation in these regions increased. In addition, activation in DMPFC and right inferior parietal lobe (IPL) increased with decreasing subjective value (Figure 3A; Table 1).

For ambiguity, we observed subjective value coding also in DMPFC, but in addition in bilateral DLPFC, right superior temporal gyrus (STG), and bilateral inferior parietal lobe (IPL) (see Figure 3B, Table 1). In these regions decreasing subjective value was related to increasing neural activation. No positive activation patterns for ambiguity were observed.

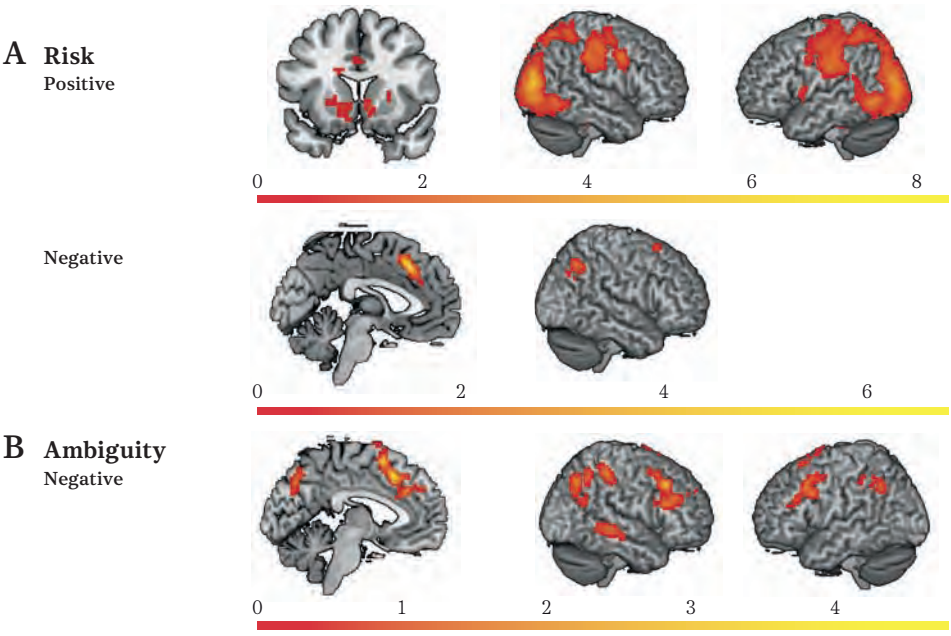


Figure 3. *Results of the whole-brain ANOVA, showing the unmasked T-contrasts for* ***A.*** *Risk positive (upper panel; y = 14; L; R); Risk negative (lower panel; x = -4; R)* ***B.*** *Ambiguity negative (x = -4; R; L). Results were FWE cluster-corrected (p < .05).*

Table 1. Results of unmasked *t*-contrasts for risk and ambiguity for subjective value.

Anatomical region	+/-	MNI coordinates x	y	x	T	*k*	*p*
Risk							
R middle occipital gyrus, including bilat. superior parietal lobe	+	30	-85	16	8,36	9610	< .001
R calcarine gyrus	+	15	-91	4	7,83		
R fusiform gyrus	+	30	-82	-8	7,68		
L insula lobe	+	-33	-4	16	5,18	1028	< .001
L putamen, including R and L caudate nucleus, L inferior frontal gyrus, L thalamus	+	-30	-10	-2	4,94		
R thalamus	+	21	-28	-2	5,05	299	< .001
R putamen, including R insula lobe	+	27	-10	7	4,92		
R middle cingulate cortex, including L middle cingulate cortex	+	12	5	43	4,17	269	< .001
R supplementary motor area	+	9	-1	58	4,08		
L supplementary motor area	+	-6	-1	52	3,54		
L superior medial gyrus	-	-6	23	40	6,86	324	< .001
R middle cingulate cortex	-	9	26	34	5,40		
R supplementary motor area, including R anterior cingulate cortex, R superior frontal gyrus	-	15	20	64	4,18		
Ambiguity							
R middle frontal gyrus	-	42	26	43	4,865	346	< .001
R inferior frontal gyrus	-	54	26	25	4,277		
R inferior frontal gyrus	-	42	32	28	4,102		
L supplementary motor area	-	-3	20	46	4,656	617	< .001
L supplementary motor area, including R supplementary motor area	-	-3	11	58	4,484		

Table 1. Continued

Anatomical region	+/-	MNI coordinates x	y	x	T	*k*	*p*
R anterior cingulate cortex, including L superior medial gyrus, L and R superior frontal gyrus, L anterior cingulate cortex	-	12	26	25	4,388		
R inferior parietal lobe	-	54	-37	55	4,48	394	< .001
R angular gyrus	-	36	-67	43	4,437		
R inferior parietal lobe	-	48	-55	52	4,12		
R middle temporal gyrus	-	66	-31	-2	4,247	146	.001
R middle temporal gyrus	-	63	-43	1	3,808		
L inferior frontal gyrus	-	-51	14	34	4,211	220	< .001
L middle frontal gyrus	-	-42	20	40	4,184		
L middle frontal gyrus	-	-42	14	49	3,949		
R precuneus	-	6	-67	40	3,959	156	.005
L precuneus, including L cuneus	-	-3	-73	37	3,844		
R cuneus, including L precuneus	-	9	-79	28	3,2		
L inferior parietal lobe	-	-48	-58	43	3,924	133	.011
L inferior parietal lobe	-	-45	-37	40	3,637		
L inferior parietal lobe, including L angular gyrus	-	-48	-40	52	3,387		

Note: L = left; R = right. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

Overlap risk and ambiguity

To formally test the overlap in the patterns of activation in risk and in ambiguity, we ran a conjunction analysis on the negative *t*-contrasts of risk and ambiguity from the whole-brain ANOVA (no positive activation patterns were observed for ambiguity, see above). To this end we used the 'Logical AND' technique, which requires that the contrasts included in the conjunction are individually significant (Nichols, Brett, Andersson, Wager, & Poline, 2005). The conjunction showed significant overlap in the DMPFC for the negative effects of risk and ambiguity (Figure 4A, Table 2), indicating that with decreasing subjective value, activation in this region increased, regardless of condition.

Unique effects of risk and ambiguity

Next, we investigated *unique* patterns of subjective value under risk and under ambiguity. That is, we tested for effects of risk restricted towards the voxels that were not activated under ambiguity (i.e., using exclusive masks), and vice versa. For risk, we observed unique patterns of positive activation in bilateral VS and bilateral SPL, and postcentral gyrus (Figure 4B, Table 2), indicating that with increasing subjective value under risk, activation in these regions increased. No unique patterns of negative activation were observed. For ambiguity, unique negative activation was found in bilateral DLPFC, right STG, and in right IPL (Figure 4C, Table 2), indicating that with decreasing subjective value under ambiguity, activation in these regions increased.

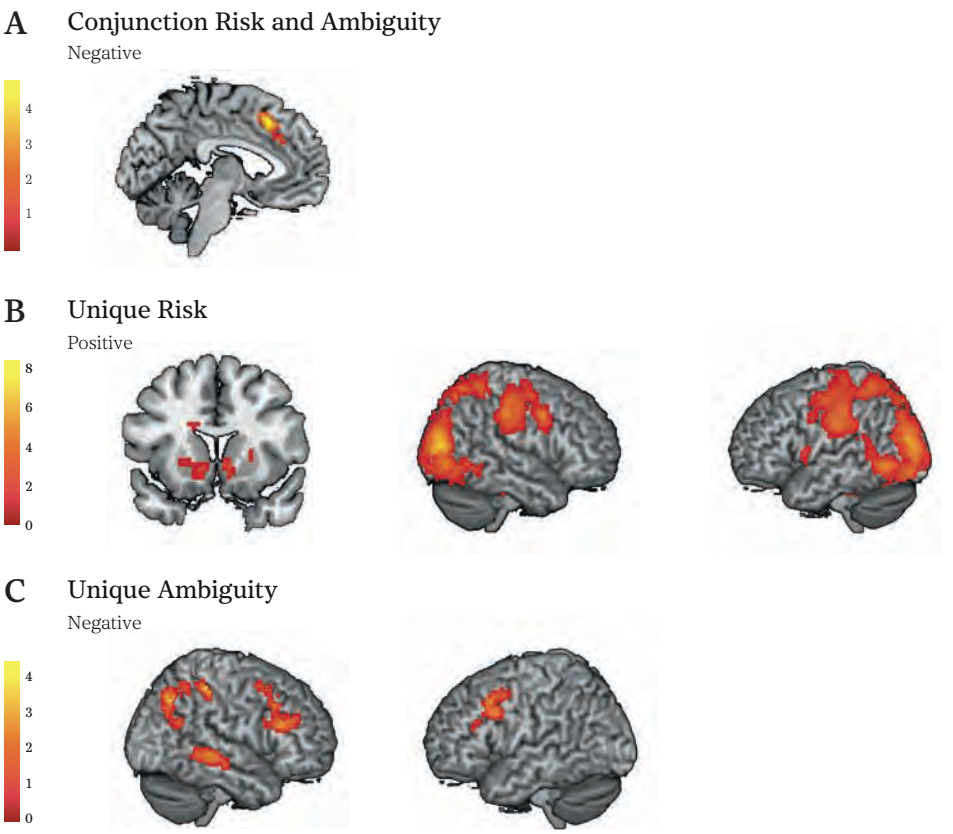


Figure 4. *Results of the whole-brain ANOVA, showing* ***A****. the conjunction between the negative effects of risk and ambiguity (x = -4)* ***B.*** *Risk positive, masked by Ambiguity (y = 14; L; R) and* ***C.*** *Ambiguity negative, masked by Risk (x = -4; R; L). Results were FWE cluster-corrected (p < .05).*

Table 2. Results of the whole-brain repeated measures ANOVA for subjective value.

		MNI coordinates					
Anatomical region	+/-	x	y	x	T	*k*	*p*
Conjunction risk and ambiguity							
L supplementary motor area	-	-3	20	46	4,66	168	.004
R anterior cingulate cortex	-	9	29	28	3,86		
L anterior cingulate cortex, including R middle cingulate cortex	-	-6	32	28	3,83		
Unique effect of risk							
R middle occipital gyrus, including bilat. superior parietal lobe	+	30	-85	16	8,36	7327	< .001
R calcarine gyrus	+	15	-91	4	7,83		
R fusiform gyrus	+	30	-82	-8	7,68		
R precentral gyrus	+	60	5	40	6,57	683	< .001
R postcentral gyrus, including R supramarginal gyrus	+	60	-19	52	6,18		
L insula lobe	+	-33	-4	16	5,18	995	< .001
L putamen, including R/L caudate nucleus, L thalamus, L inferior frontal gyrus	+	-30	-10	-2	4,94		
R thalamus	+	21	-28	-2	5,05	296	< .001
R putamen, including R insula lobe	+	27	-10	7	4,92		
Unique effect of ambiguity							
R inferior parietal lobe	-	54	-37	55	4,48	229	< .001
R angular gyrus	-	36	-67	43	4,44		
R angular gyrus	-	57	-58	25	3,81		
R inferior frontal gyrus (p. triangularis)	-	54	26	25	4,28	228	< .001
R middle frontal gyrus	-	42	20	40	4,10		
R inferior frontal gyrus (p. triangularis)	-	45	29	25	4,01		
R middle temporal gyrus	-	66	-31	-2	4,25	145	.007
L inferior frontal gyrus (p. opercularis)	-	-51	14	34	4,21	136	.01
L middle frontal gyrus	-	-42	17	43	4,06		
L inferior frontal gyrus (p. triangularis)	-	-54	29	28	3,50		
R precuneus	-	3	-67	37	3,64	149	.007
L precuneus	-	-3	-73	31	3,55		
R cuneus	-	9	-79	28	3,20		

Note: L = left; R = right. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

Expected versus subjective valuation of risk and ambiguity

Furthermore, we tested whether results from the conjunction, and the unique effects of risk and ambiguity, were also present in a model testing for expected value increases (i.e., probability * amount, not weighted by individuals' risk and ambiguity attitude). These results are reported in the supplementary materials (Figure S2 C-D; Table S1). In short, the conjunction observed in the model for subjective value was not present in the model for expected value. Furthermore, although results for risk were highly similar between models, results for ambiguity were less pronounced (i.e., activation in left DLPFC was no longer observed).

Effects of age

Finally, when including age (linear and quadratic) as a covariate on the *t*-contrasts of subjective, and expected, value under risk and ambiguity, we observed that these results remained the same, nor did we find any significant effects of age. This indicates that the parametric tracking of subjective and expected value under risk and ambiguity was independent of age in this adolescent sample.

Discussion

This study investigated the neural tracking of subjective value under risk and ambiguity in adolescence, by combining neural activation during an fMRI gambling task with separately estimated risk and ambiguity attitudes. We found pronounced differences in subjective value under risk (bilateral VS, SPL) and ambiguity (bilateral DLPFC, right STG), as well as overlapping activation between risk and ambiguity (DMPFC). These results were less pronounced when examining expected, rather than subjective, value, and were independent of age. Finally, behavioral risk and ambiguity attitudes showed limited developmental, but considerable individual indifferences, and echoed participants' self-reported perceived riskiness of the risky and ambiguous options. The following sections discuss these main findings in further detail.

Neural tracking of subjective value under risk and ambiguity

On the neural level, we observed that subjective value increases under risk were positively associated with increased activation in bilateral VS and SPL. Particularly the VS activation coincides with prior adult research on subjective value coding in general (Bartra et al., 2013), and has been suggested to predict risk-seeking choices (Engelmann & Tamir, 2009; Kuhnen & Knutson, 2005; Tobler, O'Doherty, Dolan, & Schultz, 2007). Interestingly, in a previous study we observed that greater

risk-seeking attitudes were associated with greater activation in neighboring, valuation, regions (medial and lateral orbitofrontal cortex) during risky gambles (in a separate sample of young adults (18-30 years) using the same experimental paradigms; Blankenstein et al., 2017). The current study extends this earlier work by using a parametric design in which subjective expected value was calculated on a trial-by-trial basis, indicating that neural coding of subjective valuation of risk is present in a similar set of regions in adolescence. Finally, the activation observed in parietal cortex fits well with prior adult research on assessing probabilities (Huettel, Song, & McCarthy, 2005) as well as with risk preference (both functionally (Huettel, Stowe, Gordon, Warner, & Platt, 2006) and structurally (Gilaie-Dotan et al., 2014)).

With respect to ambiguity, we observed that increased activation in superior temporal gyrus and bilateral DLPFC coincided with decreasing subjective value. In a separate sample of young adults (18-30 years) we observed that greater ambiguity-seeking attitudes were also associated with heightened superior temporal gyrus activation in a highly overlapping region (MNI coordinates: 63 -22 -5; Blankenstein et al., 2017). Thus, the superior temporal gyrus may be presented as a candidate region sensitive to individual differences in ambiguity valuation, although future studies may further investigate its specific direction of activation (increasing or decreasing with greater subjective valuation of ambiguity). Second, DLPFC activation has been suggested to foster exploration tendencies, and thus relates to more ambiguity-seeking attitudes (Huettel et al., 2006). Conversely, the DLPFC has also been associated with heightened cognitive control, and a reduced appetite for risk taking in tasks in which ambiguity can be reduced over time by experience (Fecteau et al., 2007; Knoch et al., 2006). The observation in the current study of heightened DLPFC activation with decreasing subjective valuation is in line with this latter interpretation (i.e., a reduced appetite for risk-taking). Together, the STG and DLPFC appear to play a key role in tracking individual differences in subjective valuation under ambiguity in adolescents.

Furthermore, we observed that activation in DMPFC coded both subjective value decreases under risk, as well as under ambiguity. The DMPFC (also commonly referred to dorsal anterior cingulate cortex) has been implicated in a majority of functions relation to motivation and cognitive control, and shifting decision strategies (Venkatraman, Payne, Bettman, Luce, & Huettel, 2009). The meta-analysis by Bartra et al. (2013) suggests that this region, which has been observed for both positive and negative effects of subjective value, plays a role in detecting arousal or saliency. In a similar vein, the Expected Value of Control theory (Shenhav, Botvinick, & Cohen, 2013) posits that activation in this region reflects general changes in task incentives or task difficulty. Suggestively, the negative coding of subjective value in the DMPFC

may be reflective of such changes in task incentives and task saliency, given that this region coded subjective value in both decision contexts, and thus did not differentiate between risk and ambiguity.

Subjective versus expected value coding under risk and ambiguity

In addition to testing subjective value under risk and ambiguity, we explored whether similar findings were observed in a model testing for objective expected value coding under risk and ambiguity (i.e., probability * amount, not weighted by individuals' risk and ambiguity attitude). Overall, we found similar, but less pronounced, results in this model (reported in the supplements). Specifically, similar to the model with subjective value, we found heightened activation in bilateral VS and SPL for increasing expected value under risk, but only right DLPFC and right IPL with decreasing expected value under ambiguity. Furthermore, we did not observe the common neural coding in DMPFC under risk and ambiguity in the model of expected value. On the one hand, these less pronounced findings may result from the fact that there was relatively little variation in the task parameters. That is, a limitation of the current fMRI task is that it includes no variation in ambiguity level, small variations in amounts, and only larger variations in probability level. Thus, not weighing expected value with individuals' risk and ambiguity attitude may have resulted in less variation in task parameters, and thus to fewer neural changes that could be detected. On the other hand, these findings may suggest that making use of subjective, rather than expected, valuation, is more meaningful when studying the neural underpinnings of (adolescent) choice valuation (Glimcher & Rustichini, 2004; van den Bos et al., 2017), and highlights the potential of this particular method. Nevertheless, future studies should replicate our findings, preferably by using a more elaborate task design.

Effects of age and individual differences in subjective valuation of risk and ambiguity

To assess individuals' preference towards risk and ambiguity, we made use of a behavioral task and a model-based approach. Concurring with previous findings, we observed that participants were generally risk- and ambiguity-averse, and responded slower in ambiguity compared with risk (Blankenstein et al., 2017). Furthermore, participants subjectively experienced the ambiguous wheels in the task as more risky, compared with the risky wheels. Moreover, we showed that behavioral risk aversion was associated with perceiving the risky and ambiguous wheels in the task as more risky, and ambiguity aversion with perceiving the ambiguous wheels as more risky. This latter finding in particular suggest that these model-based measures not only reflect behavioral tendencies under risk and ambiguity, but also reflect the

subjective experience of gambling behavior. In sum, these data suggest meaningful differences between individuals in subjective evaluation of risk under known (risk) and unknown (ambiguity) contexts. This inter-individual variability set the stage for testing our hypotheses on the neural tracking of subjective valuation under risk and ambiguity.

Behaviorally, we observed that risk-seeking slightly increased across adolescence, whereas no developmental change was observed for ambiguity attitudes. Previous findings observed heightened ambiguity tolerance in adolescents compared with adults (Blankenstein et al., 2016; Tymula et al., 2012) and for adolescents compared to children and adults (although in a loss frame only; van den Bos & Hertwig, 2017). Furthermore, risk attitudes have been found to either show no developmental trend (Blankenstein et al., 2016), show a quadratic peak in risk seeking in mid adolescents (van den Bos & Hertwig, 2017) or heightened risk aversion in adolescents compared with adults (Tymula et al., 2012). These previous studies included age ranges well into adulthood, or started in early childhood (Tymula et al.: 12-17 years and 30-50 years; van den Bos et al.: 8-22 years; Blankenstein et al.: 10-25 years). Together, the current findings indicate that a developmental window across adolescence and into young adulthood is suitable to test individual variation, but less meaningful to detect developmental change. An interesting next step would be to include young children (<8 years) and older adults (>25 years), to establish developmental differences in ambiguity and risk attitudes.

Finally, similar to the behavioral results, we did not observe any age effects (linear, nor quadratic) on neural patterns of activation. Prior studies have observed age differences in the neural tracking of expected value, specifically in VS (more pronounced in adolescents (13-17 years) compared with adults (25-30 years; Barkley-Levenson & Galván, 2014), and in VMPFC and parietal cortex (linear increases from childhood (8-11 years) to adolescence (16-19 years) to adulthood (25-34 years; Van Duijvenvoorde et al., 2015). However, in our previous study including the same participants, few age effects were observed on risk and ambiguity processing during gambling (Blankenstein et al., 2018). Furthermore, the fact that minimal age effects were observed behaviourally in the current study may further explain the absence of age effects on the neural coding of subjective and expected value. Again, including young children and older adults may prove valuable for future studies.

Conclusion

In this study, we aimed to extend previous research by explicitly investigating subjective value tracking under risk and ambiguity in a large sample of adolescents. Our findings suggest that the neural coding of subjective value under risk and ambiguity is reflected in both distinct and similar patterns of brain activation in adolescents. Moreover, these findings seem to suggest it is valuable to include subjective, rather than objective, measures of choice valuation in neuroimaging studies on adolescent risk taking. Indeed, behavioral estimations of risk and ambiguity preference showed considerable individual variation, which were reflected in individuals' self-reported perceived riskiness of the risky and ambiguous choice options. Furthermore, the limited age effects observed in the current study highlight the need for studying a wider age range to unravel these developmental differences with more certainty. Together, these findings help to gain insights into subjective valuation in adolescents, and suggest adolescence is an important developmental window in which differences between risky and ambiguous subjective value tracking may be more prominent than in adult samples. Finally, this study highlights the potential of combining model-based behavioral analyses with fMRI, which may ultimately aid in understanding who takes risks and why.

Supplementary Materials

Choice behavior fMRI task

In the fMRI task, participants gambled a considerable proportion of times in the risky and ambiguous condition, although these did not differ significantly (M_{risk} = .74, SE_{risk} = .015, M_{ambig} = .76, SE_{ambig} = .018, p = .13, no effects of age (linear or quadratic, all p's > .17)). Furthermore, there were considerable individual differences in gambling behavior (see Figure S1B). Finally, a repeated measures ANOVA with age (linear and quadratic) as a covariate showed that participants responded significantly slower in the ambiguous trials compared with the risky trials (M_{ambig} = 641.59 msec, SE_{ambig} = 14.26; M_{risk} = 597.06 msec, SE_{risk} = 12.89; $F(1, 185) = 8.79$, p = .003, η_p^2 = .045, no effects of age (linear or quadratic, all p's > .06)).

Choice behavior behavioral task

To investigate whether participants had a basic sensitivity to the parameters (amount, probability, ambiguity level) of the task outside the scanner, we examined raw choice behavior. Repeated measures ANOVAs with age group (12-16 years and 17-22 years, in line with Blankenstein et al., 2016) as a between-subjects factor showed that gambling behavior increased with increasing probability and amount, and decreased with increasing ambiguity level (see Figure S1C; main effect probability: $F(5, 930) = 570.91$, $p < .001$, η_p^2 = .754; age group * probability interaction effect: p = .498; main effect amount: $F(3, 558) = 915.59$, p = .83, η_p^2 = .831, age group * amount interaction effect: $F(3, 558) = 6.65$, $p < .001$, η_p^2 = .034; main effect ambiguity level: $F(3, 558) = 48.54$, $p < .001$, η_p^2 = .207, age group * ambiguity level interaction: p = .637). Thus, participants were sensitive to these parameters, indicating a general understanding of the task. Finally, paired-samples t-tests showed that on average, participants gambled an equal amount in the risky and ambiguous trials (p = .375, M_{risk} = .35, SE_{risk} = .007, M_{ambig} = .36, SE_{ambig} = .01), but that participants responded significantly slower in the ambiguous than in the risky trials ($t(187) = 3.462$, p = .001, M_{risk} = 470.75, SE_{risk} = 18.15, M_{ambig} = 495.11, SE_{ambig} = 18.96).

fMRI results for expected value

We tested whether the unique effects of risk and ambiguity, and the conjunction, were also present in a model testing for effects of objective expected value (i.e., product of probability and amount, not weighted by individuals' risk and ambiguity attitude). To this end we again ran a whole-brain repeated measures ANOVA with condition (risk and ambiguity as parametric regressors) as within factor, and we tested for effects of risk restricted towards the voxels that were not activated under ambiguity (i.e., using

exclusive masks), and vice versa. First, the positive effect of risk was highly similar in the expected value model, compared with the subjective value model, with activation in bilateral VS, SMA, and SPL (Table S1, Figure S2C). For ambiguity on the other hand, activation was less pronounced in right DLPFC and right IPL, and absent in left DLPFC (Table S1; Figure S2D). Moreover, in a conjunction analysis we observed that the activation in DMPFC observed for the negative effects of risk and ambiguity in subjective value, was not present in the model with expected value. Finally, as in the model with subjective value, all of these findings were independent of age.

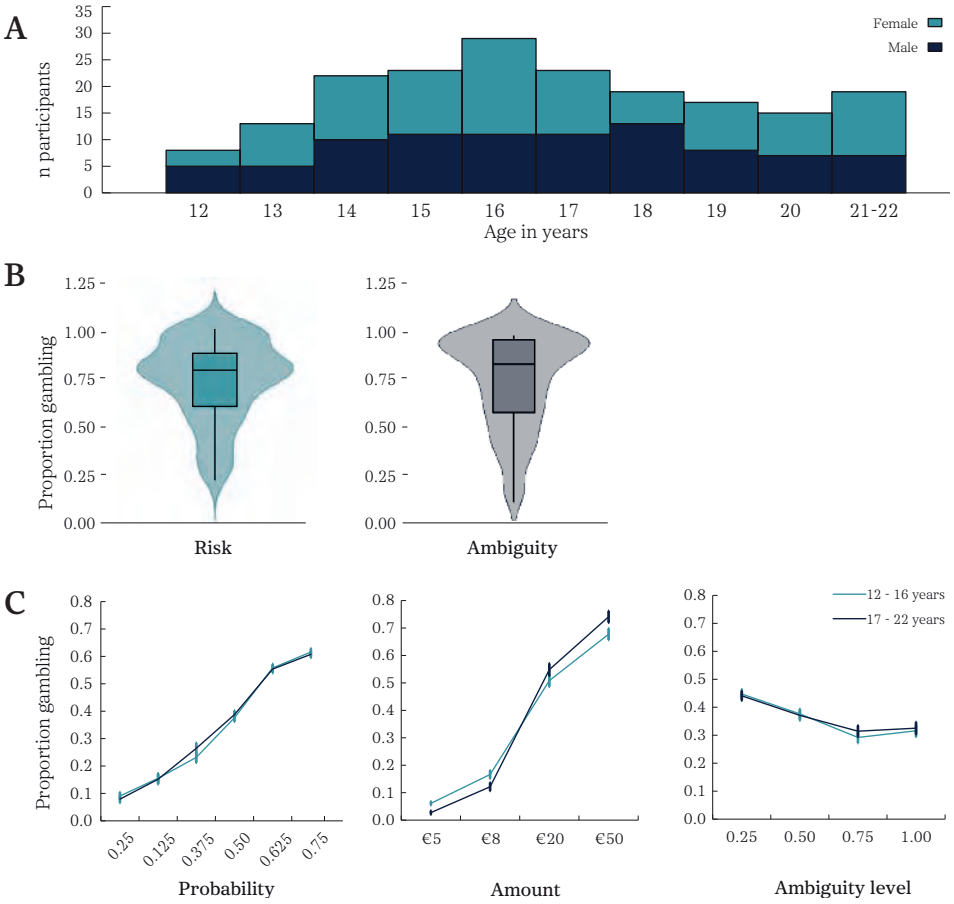


Figure S1. A. *Participant distribution across age.* ***B.*** *Violin- and box-plots of gambling under Risk (left) and Ambiguity (right).* ***C.*** *Proportion gambling for probability (left), amount (middle), and ambiguity level (right) per age group.*

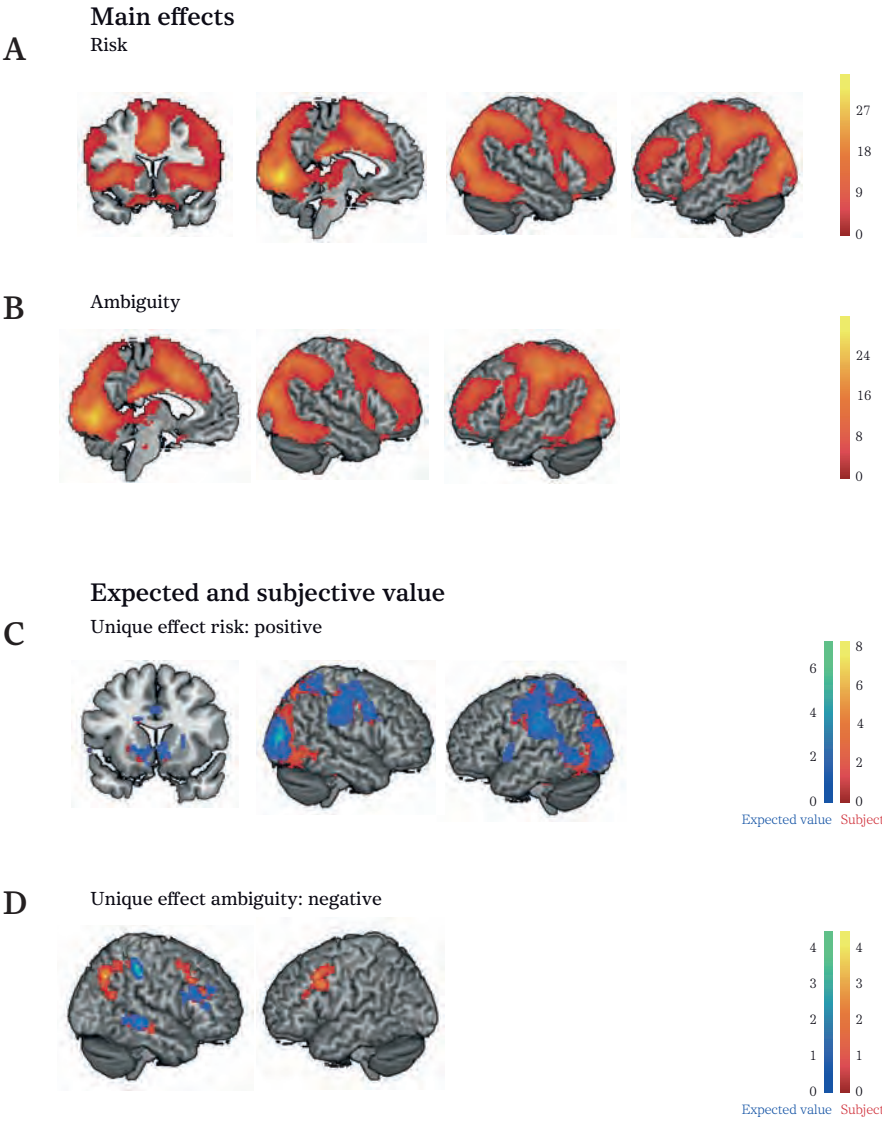


Figure S2. Upper panel: *Activation in the fMRI task during the decision-making phase (not parametrically modulated).* ***A.*** *Activation during risky decisions versus fixation (y = 14; x = -4; L; R).* ***B.*** *Activation during ambiguous decisions versus fixation (x = -4; L; R). Results were FWE voxel-corrected (p < .001).* ***Lower panel:*** *Expected and subjective value. Results of the unique effects of* ***C.*** *risk positive (y = 14; L; R). and* ***D.*** *ambiguity negative (R; L). Activation in blue represents activation for expected value, activation in red represents activation for subjective value. Results were FWE cluster-corrected (p < .05).*

Table S1. Results of the whole-brain repeated measures ANOVA for expected value.

Anatomical region	+/-	MNI coordinates x	y	z	T	*k*	*p*
Unique effect of risk							
R calcarine gyrus, including R superior occipital gyrus	+	15	-91	4	7,20	4446	< .001
R cuneus	+	18	-94	13	6,96		
R middle occipital gyrus, including L middle occipital gyrus, R lingual gyrus, R fusiform gyrus, L supramarginal gyrus	+	30	-91	10	6,95		
R postcentral gyrus	+	60	-19	52	5,90	631	< .001
R supramarginal gyrus, including R precentral gyrus, R superior frontal gyrus, R middle cingulate cortex	+	66	-28	40	5,81		
R caudate nucleus, including L caudate nucleus, L putamen	+	9	17	-5	5,19	295	< .001
R superior parietal lobe	+	27	-52	64	5,67	394	< .001
R precuneus	+	15	-58	61	5,14		
R paracentral lobe, including R inferior parietal lobe, R middle cingulate cortex	+	12	-31	52	4,06		
L inferior frontal gyrus (pars opercularis)	+	-57	8	7	4,59	97	.02
L temporal pole	+	-57	8	-2	3,98		
Unique effect of ambiguity							
R inferior parietal lobe	-	54	-37	52	4,48	88	.03
R middle temporal gyrus	-	69	-31	-2	4,12	89	.029
R middle temporal gyrus	-	60	-46	1	3,65		
R inferior frontal gyrus (pars triangularis)	-	54	23	28	3,95	143	.004
R inferior frontal gyrus (pars opercularis)	-	48	11	25	3,63		
R inferior frontal gyrus (pars triangularis), including R middle frontal gyrus	-	54	35	13	3,57		

Note: L = left; R = right. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

Chapter 5

Individual differences in risk-taking tendencies modulate the neural processing of risky and ambiguous decision-making in adolescence

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Abstract

Although many neuroimaging studies have investigated adolescent risk taking, few studies have dissociated between decision-making under risk (known probabilities) and ambiguity (unknown probabilities). Furthermore, which brain regions are sensitive to individual differences in task-related and self-reported risk taking remains elusive. We presented 198 adolescents (11-24 years, an age-range in which individual differences in risk taking are prominent) with an fMRI paradigm that separated decision-making (choosing to gamble or not) and reward outcome processing (gains, no gains) under risky and ambiguous conditions, and related this to task-related and self-reported risk taking. We observed distinct neural mechanisms underlying risky and ambiguous gambling, with risk more prominently associated with activation in parietal cortex, and ambiguity more prominently with dorsolateral prefrontal cortex (PFC), as well as medial PFC during outcome processing. Individual differences in task-related risk taking were positively associated with ventral striatum activation in the decision phase, specifically for risk, and negatively associated with insula and dorsomedial PFC activation, specifically for ambiguity. Moreover, dorsolateral PFC activation in the outcome phase seemed a prominent marker for individual differences in task-related risk taking under ambiguity as well as self-reported daily-life risk taking, in which greater risk taking was associated with reduced activation in dorsolateral PFC. Together, this study demonstrates the importance of considering

multiple risk-taking measures, and contextual moderators, in understanding the neural mechanisms underlying adolescent risk taking.

Keywords: individual differences, risk taking, ambiguity, adolescence, fMRI

Introduction

Adolescence, defined as the developmental phase between childhood and adulthood, is often described as a period marked by increases in risky behaviors such as excessive alcohol use and reckless driving, and a strong need for exploration (Crone & Dahl, 2012; Steinberg, 2008). Theoretical models have explained this rise in risk-taking behavior by long-lasting development of subcortical and cortical brain regions and their connections, in which regions involved in affective processing and reward sensitivity peak in reactivity during adolescence, whereas cortical brain regions supporting cognitive control undergo a more protracted development (Casey, Jones, & Hare, 2008; Somerville, Hare, & Casey, 2011; Crone & Dahl 2012; Casey 2015). Although a wealth of research has focused on the neural mechanisms underlying adolescent risk taking, few studies have systematically investigated the relation with actual risk-taking behavior either inside or outside the laboratory. These studies report conflicting findings, have relatively small sample sizes, or focus on only one or two brain regions-of-interest (for an excellent review, see Sherman, Steinberg, & Chein, 2017). Furthermore, although adolescence may be a period of heightened risk-taking tendencies on average, not all adolescents are risk takers (Bjork & Pardini, 2015), and risk-taking tendencies vary substantially between adolescents. Thus, including predictors of behavior on the individual level may be key in understanding what drives adolescent risk taking. In this study we investigated the neural mechanisms underlying individual differences in adolescent risk taking, using task-related and self-report measures of risk-taking tendencies in a large adolescent sample.

A number of brain regions have been associated with individual differences in risk-taking tendencies in adolescence (Sherman et al., 2017). For instance, a greater ventral striatum (VS) response when receiving monetary rewards has been associated with a greater self-reported drive to pursuit rewards, fun-seeking tendencies (Braams, van Duijvenvoorde, Peper, & Crone, 2015; Van Duijvenvoorde et al., 2014), the likelihood of engaging in real-life risky behaviors (Galvan, Hare, Voss, Glover, & Casey, 2007), and increased frequencies of illicit drug use, binge drinking, and sexual risky behaviors (Bjork & Pardini, 2015; Braams, Peper, van der Heide, Peters, & Crone, 2016). The ventromedial prefrontal cortex (VMPFC),

closely interacting with the VS, has been additionally related to measures of reward sensitivity in adolescents (Van Duijvenvoorde et al., 2015) as well as with greater risk preferences in adults (Blankenstein, Peper, Crone, & Duijvenvoorde, 2017; Engelmann & Tamir, 2009). Conversely, reduced risk-taking tendencies in laboratory choice tasks have been related to increased anterior insula and dorsomedial prefrontal cortex (DMPFC) activation, regions that are typically related to conflict and uncertainty in decision making, and to the integration of cognitive and affective neural signals (Smith, Steinberg, & Chein, 2014; Van Duijvenvoorde et al., 2015; Van Leijenhorst et al., 2010). Finally, reduced activation in the lateral prefrontal cortex (LPFC), a key region involved in self-control (Dixon, 2015), has been associated with greater laboratory risk taking in young adults (Gianotti et al., 2009). In contrast, studies with adolescents have shown that longitudinal declines in LPFC activation were associated with declines in self-reported frequency of real-life risky behaviors (such as getting high or drunk at parties; Qu, Galvan, Fuligni, Lieberman, & Telzer, 2015). Taken together, these studies highlight candidate regions sensitive to individual differences in risk-taking tendencies, yet none of these studies have included a substantial adolescent sample size, nor provided a comprehensive overview of task-related, and self-reported, measures of risk taking.

Importantly, the majority of these studies used fMRI paradigms that present explicit risky (e.g., the Columbia Card Task; Van Duijvenvoorde et al., 2015), rather than ambiguous risky, choice contexts. That is, while explicit risk presents known probabilities (such as in a coin toss, in which the chance of 'tails' is known: 50%), ambiguity presents unknown probabilities (such as texting while driving: the chance of causing an accident, for example, is unknown; Tversky & Kahneman, 1992). However, the majority of risky situations in daily life presents ambiguous risk. Indeed, in adolescence, the tendency to gamble under ambiguity, but not risk, has been associated with individual differences in real-life risk-taking behavior, such that a higher 'tolerance' to ambiguity was related to higher levels of reckless behavior such as speeding and having unprotected sex (Blankenstein, Crone, van den Bos, & van Duijvenvoorde, 2016; Tymula et al., 2012), and rebellious behavior such as staying out late (van den Bos & Hertwig, 2017). This may suggest that behavior under ambiguity is a better reflection of adolescent risk taking in real life (Blankenstein et al., 2016; Tymula et al., 2012; van den Bos & Hertwig, 2017). Possibly, a tolerance to ambiguity in adolescence is important for accomplishing important goals prominent in adolescence, such as exploring new environments, and gathering information about the world (e.g., Crone & Dahl, 2012; Hartley, & Somerville, 2015). Consequently, distinguishing the mechanisms underlying risk and ambiguity coding in adolescence is pivotal given that these may have different relations with observed risk-taking

behavior in adolescence. To date, the neural mechanisms underlying risky versus ambiguous decision-making have not been investigated in adolescence, nor have these been related to individual differences in risk-taking tendencies in adolescence.

Taken together, we aimed to elucidate individual differences in task-related and self-reported risk-taking behavior in relation to brain activation in risky and ambiguous decision contexts, in 198 adolescents aged 11 to 24 years, an age range in which individual differences in daily-life risk taking are most prominent (Bjork & Pardini, 2015; Willoughby, Good, Adachi, Hamza, & Tavernier, 2013). We applied the same paradigm as has been previously reported in a different sample of young adults (Blankenstein et al., 2017), which allows to study choice (choosing to gamble or not) and reward processing (gains versus no gains) under risk and ambiguity. In line with this prior study with adults, we expected few overall differences between risky and ambiguous gambling (Blankenstein et al., 2017, but see Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005; Huettel, Stowe, Gordon, Warner, & Platt, 2006), although we expected that the DMPFC would particularly distinguish between risky and ambiguous outcomes (Blankenstein et al., 2017). Particularly, we expected that individual differences in risk-taking tendencies would be positively associated with activation in VS and VMPFC, and negatively with DMPFC, insula, and LPFC. Given the mixed findings on the LPFC, this relation could also be reversed (i.e., enhanced activation with greater risk taking; Qu et al., 2015; Telzer, Fuligni, Lieberman, & Galván, 2013). Second, given that behavior under ambiguity, but not risk, has been related to real-life risk-taking tendencies (Blankenstein et al., 2016; Tymula et al., 2012; van den Bos & Hertwig, 2017), we expected these brain-behavior associations to be more pronounced under conditions of ambiguity than risk.

Methods

Participants

Two hundred and sixteen right-handed individuals (110 females, 106 males) between 11 and 24 years old participated in this study. Participants were part of a longitudinal study ('Braintime', which included three time points each separated by a two-year interval), and were recruited through schools and local advertisements. The data of the current study were collected at the third time point, and this was the first time the current task was presented. Eighteen participants were excluded from analyses because they were either diagnosed with a psychiatric disorder (n = 5), exceeded movement in the MRI scanner with more than 3 mm (n = 1), loss of data (n = 3), or because of too few trials in which the gambling option was chosen

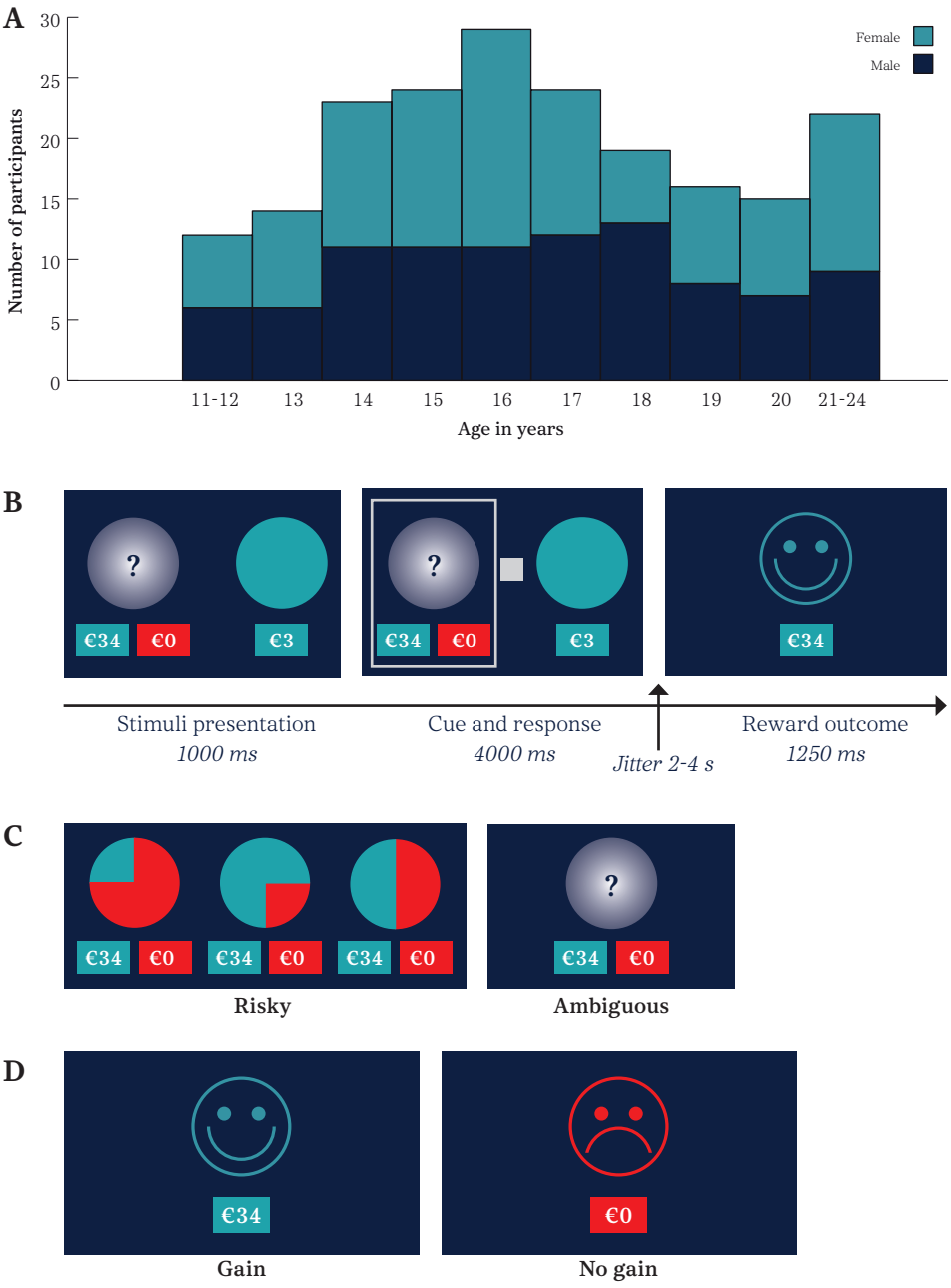


Figure 1. A. *Number of participants across age per gender.* ***B.*** *Example trial of the wheel of fortune task showing an ambiguous trial with gain as reward outcome.* ***C.*** *The different gambling wheels.* ***D.*** *Gain and no gain outcomes.*

(i.e., fewer than five gambles in either the risky or ambiguous condition, n = 9; see 'Wheel of fortune task'). The final sample therefore included 198 healthy participants (94 female, 104 male, M_{Age} = 17.15, SD_{Age} = 2.75, range 11.94 – 24.68 years, see Figure 1A). IQ fell in the normal range, as estimated on previous time points of the longitudinal Braintime study (T1: M = 110.08, SD = 9.54; T2: M = 107.84, SD = 10.17), using subtests of the WISC-III (participants 8- to 15-years old) or WAIS-III (participants 16 and older), and did not correlate with age (see also Braams et al., 2015; Peters, Van Duijvenvoorde, Koolschijn, & Crone, 2016).

This study was approved by the institutional review board of the University Medical Center. Adult participants and parents of underage participants provided written informed consent, and underage participants provided written assent. All anatomical scans were cleared by a radiologist and no abnormalities were reported. Participants were screened for MRI contra indications and psychiatric or neurological disorders and had normal or corrected-to-normal vision.

Wheel of fortune task

Participants played a child-friendly wheel of fortune task (see Figure 1 and Blankenstein et al., 2017). Participants made a series of choices between pairs of wheels. One wheel represented a safe option (i.e., a 100% chance of winning 3 Euro), whereas the other option represented a gambling option which could yield more money (i.e., €31, €32, €33, or €34) but could also yield nothing (€0). The gambling option could either be risky (probabilities were known) or ambiguous (probabilities were unknown), and the safe option was a sure gain of €3 on every trial. In the risky wheels, gain probabilities were presented as the portions of the wheels in blue, whereas no gain probabilities were presented as the portions of the wheel in red. Of the risky trials, 30 trials reflected a gamble with a 50% gain probability, 8 trials reflected a gamble with a 75% gain probability, and 8 trials reflected a gamble with a 25% gain probability (Figure 1C). In the ambiguous trials, the wheel was covered with a grey lid showing a question mark (Figure 1C). Participants played 46 ambiguous trials and 46 risky trials, which were presented inter-mixed.

After the choice, participants were presented with the reward outcome (Figure 1D; gain, no gain). The task was programmed such that the probabilities presented in the wheels (25%, 50%, and 75%) matched the actual probabilities of winning when choosing the gambling option. That is, when presented with a 75% risky trial, there was a 75% chance of winning when choosing to gamble. Furthermore, the order of gains and no gains was randomized for each participant, and the computer randomly (without replacement) selected one of the four possible amounts (€31, €32, €33, or €34) to present on a trial-by-trial basis. The outcome for gains was

presented with the amount in blue over a smiley face, and the outcome for no gains was presented with €0 in red over a sad face. Finally, the expected value (i.e., the probability*amount) of the gambling options was much higher than the safe option (which was consistently €3). This was done to encourage gambling behavior, so that participants had a sufficient number of trials for the comparisons of brain activation of gambling under risk and under ambiguity, their corresponding reward outcomes, and associations with individual differences in risk-taking tendencies.

The task was presented in the scanner via E-prime (Psychology Software Tools). Participants were presented with the pairs of wheels presenting a gamble and safe option. Gamble and safe options were randomly displayed on the left or right side of the screen on a trial-by-trial basis. After 1000 msec a grey square appeared in the center of the screen, prompting the participants to respond. A response had to be given within a 3000 msec interval. Participants responded with their right index finger (to select the wheel on the left) and right middle finger (to select the wheel on the right). A grey selection frame around the chosen wheel confirmed the response, and remained visible for the duration of the 3000 msec interval. If participants failed to respond within 3000 msec, the words 'TOO LATE' appeared in the center of the screen for 1250 ms, after which the next trial began. On average, 0.99% of the trials did not include a response, and these trials were excluded from all analyses. The choice phase was separated from the outcome phase by a fixation cross of 2-4 seconds (jittered, with increments of 500 msec). The reward outcomes (gain, no gain, or safe gain) were presented for 1250 msec. The inter-trial-intervals and the optimal trial sequence were determined with OptSeq (Dale, 1999), with jittered intervals varying between 0 and 9350 ms. In addition, each trial was preceded by a 500 ms fixation cross, which was not part of the inter-trial-interval.

Questionnaires

To test for associations between brain activation during decision-making under risk and ambiguity and indices of real-life risk taking, 192 participants completed the Adolescent Risk-Taking Questionnaire (ARQ; Gullone, Moore, Moss, & Boyd, 2000). In particular, we focused on the *behavior* scale of this questionnaire, which assesses the frequency of engaging in risky activities in real life with four subscales: Thrill-seeking (Cronbach's α = .205), Rebellious (α = .888), Reckless (α = .497), and Antisocial behavior (α = .508). Participants indicated on a 5-point Likert scale how often they engaged in risky activities (with 1 indicating *never* and 5 indicating *very often*). Examples include 'Snow skiing' (Thrill-seeking), 'Staying out late' (Rebellious), 'Having unprotected sex' (Reckless), and 'Cheating' (Antisocial).

To test for associations with self-reported reward approach and avoidant

behavior, 182 participants completed the Behavioral Inhibition System/Behavioral Activation System questionnaire (BIS/BAS; Carver & White, 1994). The BIS/BAS questionnaire is comprised of four subscales: BAS Drive (a measure of persistence in the pursuit of goals, α = .750), BAS Fun seeking (a measure of desire for rewards and the willingness to approach rewards, α = .512), BAS Reward Responsiveness (a measure of responses to rewards and reward anticipation, α = .659), and BIS (a measure of punishment sensitivity, α = .779). Participants indicated on a 4-point Likert scale the degree to which statements were applicable to them with (with 1 indicating *very true* and 4 indicating *very false*). Examples include 'When I want something I usually go all-out to get it' (BAS Drive), 'I'm always willing to try something new if I think it will be fun' (BAS Fun seeking), 'When I get something I want, I feel excited and energized' (BAS Reward responsiveness), and 'I worry about making mistakes' (BIS). Items were recoded such that higher scores indicates more approach (BAS) or avoidant (BIS) behavior.

Procedure

Participants received instructions about the MRI session in a quiet laboratory room, and were accustomed to the MRI environment with a mock scanner. Next participants received instructions about the wheel of fortune task, and practiced ten trials on a laptop. We explained to the participants that the ambiguous wheel could reflect a gamble of any of the risky probabilities (i.e., 25%, 50%, 75%). In addition, we explained that the computer would randomly select the outcomes of three trials, of which the average amount was paid out in addition to the standard payout fee. Eventually, the computer selectively drew a gain, a no gain, and a safe gain outcome (or a gain and two no gain outcomes if the participant never chose the safe option). This draw amounted to an additional rounded payout of €11 or €12 for each participant.

The wheel of fortune task lasted approximately 18 minutes, in two runs of 9 minutes each, win a short break in between. Participants could respond with their right index and middle fingers using a button box that was attached to the participant's leg. The task was followed by a high-definition structural scan, which lasted approximately five minutes.

Participants completed the ARQ and BIS/BAS questionnaire at home, online via Qualtrics (www.qualtrics.com), before the scan date. Adult participants received €60 and underage participants received €30 for their participation, in addition to their winnings in the wheel of fortune task (€11 or €12), and small presents.

MRI data acquisition

We used a 3T Philips scanner (Philips Achieva TX) with a standard whole-head coil. Functional scans were acquired during two runs of 246 dynamics each, using T2* echo-planar imaging (EPI). The volumes covered the whole brain (repetition time (TR) = 2.2 s; echo time (TE) = 30 ms; sequential acquisition, 38 slices; voxel size 2.75 x 2.75 x 2.75 mm; field of view (FOV) = 220 x 220 x 114.68 mm). The first two volumes were discarded to allow for equilibration of T1 saturation effects. A high-resolution 3D T1 scan for anatomical reference was obtained after the wheel of fortune task (TR = 9.76 msec, TE = 4.59 msec, 140 slices, voxel size = 0.875 mm, FOV = 224 × 177 × 168 mm).

MRI data analyses

Preprocessing

We analyzed the data with SPM8 (Wellcome Department of Cognitive Neurology, London). Images were corrected for slice timing acquisition and rigid body motion. Functional volumes were spatially normalized to T1 templates. Translational movement parameters never exceeded 3 mm (< 1 voxel) in any direction for any participant or scan (movement range: 0.31 – 0.19 mm, M = 0.065, SD = 0.028). The normalization algorithm used a 12-parameter affine transform with a nonlinear transformation involving cosine basis function, and resampled the volumes to 3 mm^3 voxels. Templates were based on MNI305 stereotaxic space. The functional volumes were spatially smoothed using a 6 mm full width at half maximum (FWHM) isotropic Gaussian kernel.

General-Linear model

We used the general linear model (GLM) in SPM8 to perform statistical analyses on individual participants' data. The fMRI time series were modeled as a series of two events convolved with a canonical hemodynamic response function (HRF): the choice phase and the outcome phase. First, the onset of the choice phase was modeled with a duration of response (1000 msec + response time; see Figure 1). Events were modeled separately for gambling under risk and gambling under ambiguity, and for choosing the safe option under risk and choosing the safe option under ambiguity, which resulted in four conditions: Risk Gamble, Ambiguity Gamble, Risk Safe, and Ambiguity Safe. Second, the onset of the outcome phase was modeled with zero duration. We modeled the outcomes (gain, no gain, and safe gain) following a risky or ambiguous gamble, or safe choice, which resulted in six conditions in the outcome phase: Risk Gain, Risk No Gain, Ambiguity Gain, Ambiguity No Gain, Risk Gain Safe, and Ambiguity Gain Safe. In the current study we were particularly interested

in brain activation during gambling, and brain activation during reward processing following a gamble.

Trials on which participants did not respond were modeled separately as a covariate of no interest. In addition, we included six motion parameters as noise regressors. The least-squares parameter estimates of the height of the best-fitting canonical HRF for each condition separately were used in pairwise contrasts. These pairwise comparisons resulted in subject-specific contrast images, which were used for the second-level group analyses. We conducted all second-level group and regression analyses with Family Wise Error (FWE) cluster correction ($p < .05$, using a primary voxel-wise threshold of $p < .001$, uncorrected; Blankenstein et al., 2017; Woo, Krishnan, & Wager, 2014). We used the MarsBaR toolbox (Brett, Anton, Valabregue, & Poline, 2002; http://marsbar.sourceforge.net) to visualize patterns of activation in clusters identified in the whole-brain regressions. Finally, the coordinates of local maxima are reported in MNI space.

Analyses with individual differences

First, we included a GLM to test for associations between brain activation and individual differences in gambling behavior in the wheel of fortune task (i.e., task-related risk-taking tendencies). A second model was included to test for associations with ARQ and BIS/BAS scores (i.e., self-reported risk-taking tendencies). Task-related risky and ambiguous gambling were both included in the first model so that when testing for unique effects of risky gambling, we controlled for ambiguous gambling (i.e., this was a covariate of no interest), and vice versa. The same approach was used for the ARQ and BIS/BAS questionnaire, in which we entered all subscales of both questionnaires in one model. Due to the absence of correlations between task behavior and self-report measures, including all individual-difference measures in one GLM did not change any of the reported findings. Finally, although age was not included as a regressor of interest in our primary models, we ran our models with and without age (linear) as a covariate, and report in the text which results remain significant when controlling for age. In addition, we exploratively report effects of age in the corresponding tables.

Results

Behavioral results

Table 1 summarizes the correlations between the behavioral measures (wheel of fortune task, ARQ, and BIS/BAS). In the wheel of fortune task (n = 198), a paired samples t-test showed that participants gambled a comparable proportion of times under risk and under ambiguity ($t(197)$ = -.158, p = .116, M_{risk} = .74, SD_{risk} = .21, $range_{risk}$ = .22 – 1.00, M_{ambig} = .76, SD_{ambig} = .25, $range_{ambig}$ = .11– 1.00), although there were individual differences in gambling behavior (see Figure 2A). A correlation analysis showed that gambling under risk and ambiguity were correlated (r = .686, p < .001; Table 1). Furthermore, a paired samples t-test on reaction times showed that when choosing to gamble, participants responded significantly slower in ambiguous than in risky trials ($t(197)$ = -5.41, p < .001, M_{risk} = 585.81, SD_{risk} = 193.51, M_{ambig} = 645.36, SD_{ambig} = 213.63). Finally, given the presence of outcome feedback in the task, we tested for changes in behavior under risk and ambiguity across time. To this end, we divided gambling behavior across four task bins of 11 or 12 trials per bin, per condition (risk and ambiguity). A within (task bin) * between (risk vs ambiguity) subjects ANOVA with age as a covariate showed a significant interaction effect between condition and task bin ($F(3, 576)$ = 5.84, p < .001, η^2 = .03; Figure 2B), in which gambling increased slightly across task bins in the ambiguous ($F(3, 579)$ = 18.83, p < .001, η_p^2 = .09) but not in the risky condition ($F(3, 579)$ = 1.11, p = .35).

Correlation analyses on the ARQ questionnaire (n= 192) showed that the subscales were all moderately correlated, with the exception of Thrill-seeking and Rebellious behavior (Table 1). With respect to the BIS/BAS questionnaire (n = 182), we observed that BAS Drive, BAS Fun seeking, and BAS Reward responsiveness were moderately correlated, and that BAS Reward responsiveness was additionally correlated with BIS. Furthermore, correlation analyses between the ARQ and BIS/BAS scores (n = 179) showed that ARQ Rebellious was correlated with BAS Drive and BAS Fun seeking, and that ARQ Reckless and ARQ Antisocial were both correlated with all BAS subscales. Finally, task behavior was not related to any of the self-report measures (Table 1). Age effects on all behavioral measures are reported in the supplementary materials (Appendix A1).

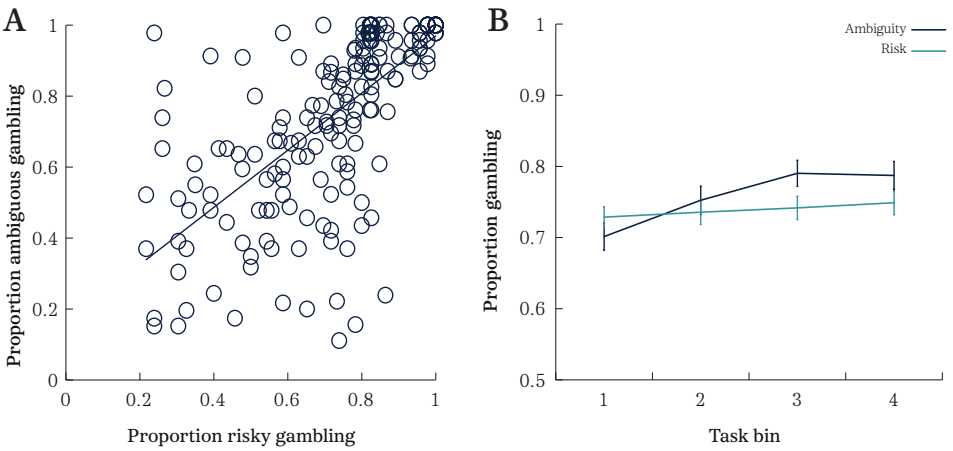


Figure 2. A. *Correlation between proportion gambling under risk and proportion gambling under ambiguity in the wheel of fortune task.* ***B.*** *Proportion gambling across time (task bins) for the ambiguous (black line) and risky (grey line) conditions. The y-axis is displayed from 0.5 to 1 to more clearly illustrate the interaction effect.*

Table 1. Correlation matrix of the behavioral measures, showing Pearson's *r*.

		1	2	3	4	5	6	7	8	9	10
1	Risky gambling	–									
2	Ambiguous gambling	**.686**$^{***\circ}$	–								
3	ARQ Thrill-seeking	-.050	-.006	–							
4	ARQ Rebellious	.115	.043	.092	–						
5	ARQ Reckless	.114	.064	**.144***	**.486**$^{***\circ}$	–					
6	ARQ Antisocial	.064	-.019	**.206****	**.479**$^{***\circ}$	**.275**$^{***\circ}$	–				
7	BAS Drive	.079	.094	.090	**.206****	**.185***	**.197****	–			
8	BAS Fun seeking	.069	.132	.171*	**.383**$^{***\circ}$	**.240****	**.259**$^{***\circ}$	**.485**$^{***\circ}$	–		
9	BAS Reward responsiveness	.002	.064	.086	.122	**.180***	**.163***	**.414****	**.415**$^{***\circ}$	–	
10	BIS	.069	-.008	-.135	.048	-.050	.086	-.008	-.103	**.270**$^{***\circ}$	–

*Note. Risky and ambiguous gambling: n = 198, ARQ: n = 192, BIS/BAS: n = 182, ARQ and BIS/BAS: n = 179. ° Correlation is significant with Bonferroni correction for multiple comparisons ***Correlation is significant at p < .001 (two-tailed, uncorrected for multiple comparisons). **Correlation is significant at p < .01 (two-tailed, uncorrected for multiple comparisons). *Correlation is significant at p < .05 (two-tailed, uncorrected for multiple comparisons).*

fMRI results

Whole-brain contrasts

Choice phase - First, we investigated which brain regions showed greater activation during gambling under risk versus ambiguity. The contrast Risk Gamble > Ambiguity Gamble revealed greater activation for risk compared to ambiguity in the bilateral precentral gyrus, right VLPFC, and posterior parietal cortex (PPC; Figure 3A, Table 2). The reversed contrast (Ambiguity Gamble > Risk Gamble) resulted in left DLPFC, bilateral temporal lobe, inferior parietal cortex (angular gyrus) and precuneus activation (Figure 3B, Table 2). When exploratively testing for effects of age, only activation in the superior parietal lobe increased with age for gambling under ambiguity compared with risk (see Table A1; Figure A1.E).

Although in the current study we were interested in contrasting risky and ambiguous gambling, an additional interesting analysis may be to compare gambling versus choosing safe across risk and ambiguity. We report the results of this analysis in the supplementary materials (Appendix A2; Table A2; Figure A1.A-D).

Outcome phase - To test which regions coded reward outcomes, we first calculated the contrast Gain > No Gain. This contrast resulted in robust activation in bilateral striatum, VMPFC, PPC, and angular gyrus (Figure 3C, Table 4). When exploring age effects on this contrast, we observed greater superior parietal and motor cortex activation for younger ages (Table A3; Figure A1.F).

To more specifically examine which regions differentially coded reward outcomes following a risky versus ambiguous gamble, we ran a whole-brain condition (risk, ambiguity) * reward outcome (gain, no gain) ANOVA. This resulted in a significant interaction effect in the MPFC (Figure 3D; Table 4). To understand the direction of this interaction effect, we plotted the parameter estimates of this region for risk and ambiguity, and gain and no gain, separately (Figure 3D, right panel). From this plot it can be seen that this interaction is particularly driven by reward outcomes following an ambiguous gamble. That is, the difference in brain activation in the MPFC between gain and no gain following an ambiguous gamble is larger than this difference following a risky gamble. We also tested whether the effects observed in the whole-brain ANOVA on reward outcomes in the MPFC were associated with age, by extracting the parameter estimates of this ROI for the difference scores and correlating these with age. No significant relations were observed (all *p's* > .1).

Table 2. MNI coordinates of Local Maxima Activated for the contrasts Risk Gamble > Ambiguity Gamble, and the reversed contrast.

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
Risk Gamble > Ambiguity Gamble						
R middle occipital gyrus, including bilateral parietal lobe, bilat. temporal gyrus, bilat. postcentral gyrus	33	-85	16	17.32	< .001	9196
L calcarine gyrus	0	-85	1	15.43		
R calcarine gyrus	12	-91	4	14.65		
R precental gyrus	48	5	31	8.96	< .001	302
R middle frontal gyrus	27	-4	52	7.22	< .001	217
R superior frontal gyrus	24	2	70	3.32		
R inferior frontal gyrus (pars triangularis)	51	38	13	6.04	< .001	235
R inferior frontal gyrus (pars triangularis)	45	41	1	4.21		
Ambiguity Gamble > Risk Gamble						
R angular gyrus	57	-67	34	7.25	< .001	307
L angular gyrus	-42	-64	31	4.09	< .001	346
R rolandic operculum, including R superior temporal gyrus, R postcentral gyrus, R posterior insula	54	-19	16	5.00	< .001	206
R rolandic operculum	45	-19	16	4.85		
R superior temporal gyrus	60	-10	-5	4.00		
R precuneus	3	-55	34	4.89	< .001	202
L middle cingulate cortex	-12	-49	37	4.67		
L middle temporal gyrus	-69	-40	-2	4.33	.025	81
L middle temporal gyrus	-63	-28	-2	3.84		
L middle frontal gyrus, including L superior frontal gyrus	-30	20	49	4.47	< .001	177
	-36	11	58	3.90		
	-21	29	52	3.60		

Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

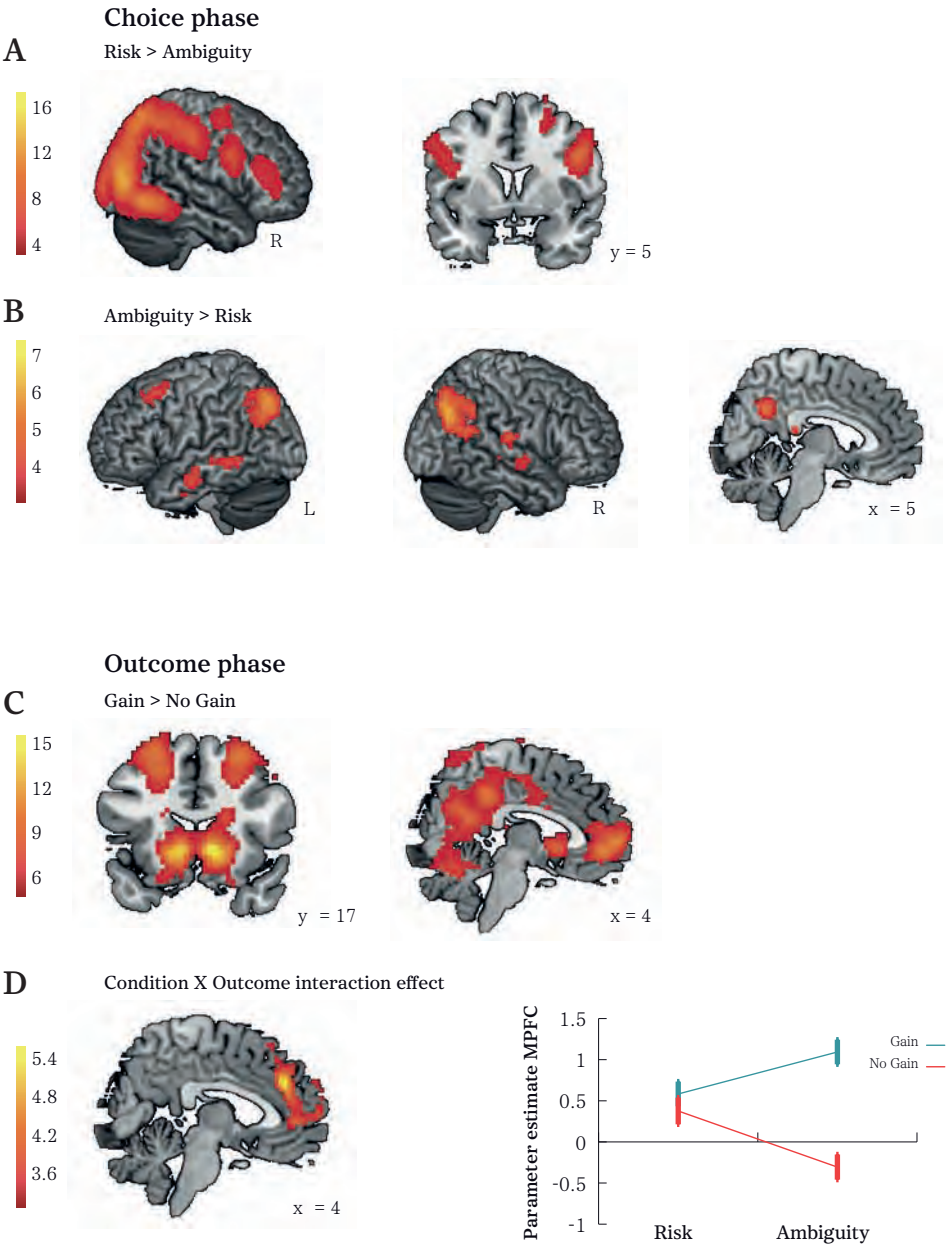


Figure 3. *Activation during the contrasts* ***A.*** *Risk Gamble > Ambiguity Gamble,* ***B.*** *Ambiguity Gamble > Risk Gamble,* ***C.*** *Gain > No Gain.* ***D.*** *Activation from the Condition * Outcome interaction effect. The graph is for illustrative purposes only.*

Table 4. MNI coordinates of Local Maxima Activated for the contrast Gain > No Gain , irrespective of risk and ambiguity

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
Gain > No Gain, voxel-corrected						
R caudate nucleus	12	17	-5	15.51	< .001	11259
L caudate nucleus	-9	17	-5	13.73		
L anterior cingulate cortex, including bilat. superior medial gyrus, R mid orbital gyrus, bilat. middle frontal gyrus, bilat. precuneus	-6	44	1	10.83		
L inferior gyrus, including L superior temporal gyrus	-54	-49	-11	7.68	< .001	664
L middle temporal gyrus	-63	-7	-17	6.96		
L inferior temporal gyrus	-60	-58	-11	6.75		
R angular gyrus	42	-73	40	7.12	< .001	230
R angular gyrus	39	-67	55	5.82		
R superior parietal lobe	33	-76	52	5.30		
R superior temporal gyrus, including R fusiform gyrus	63	-4	1	7.02	< .001	556
R middle temporal gyrus	63	-4	-23	6.92		
R superior temporal gyrus	66	-4	-8	6.74		
R putamen	30	-13	7	5.97	< .001	58
L precentral gyrus	-48	2	22	5.55	.001	24
*Interaction effect Condition * Outcome, cluster-corrected*						
L superior medial gyrus, including R superior medial gyrus, R superior frontal gyrus, R anterior cingulate cortex	3	38	31	5.59	< .001	536
R superior frontal gyrus	18	50	40	4.38		
R middle frontal gyrus	21	59	28	4.19		
R inferior parietal lobule	45	-52	46	4.43	.001	115

*Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. (FWE voxel-corrected, p < .05 and presented here with k >10) and the interaction effect of condition (risk, ambiguity) * reward outcome (Gain, No Gain; FWE cluster-corrected, p < .05).*

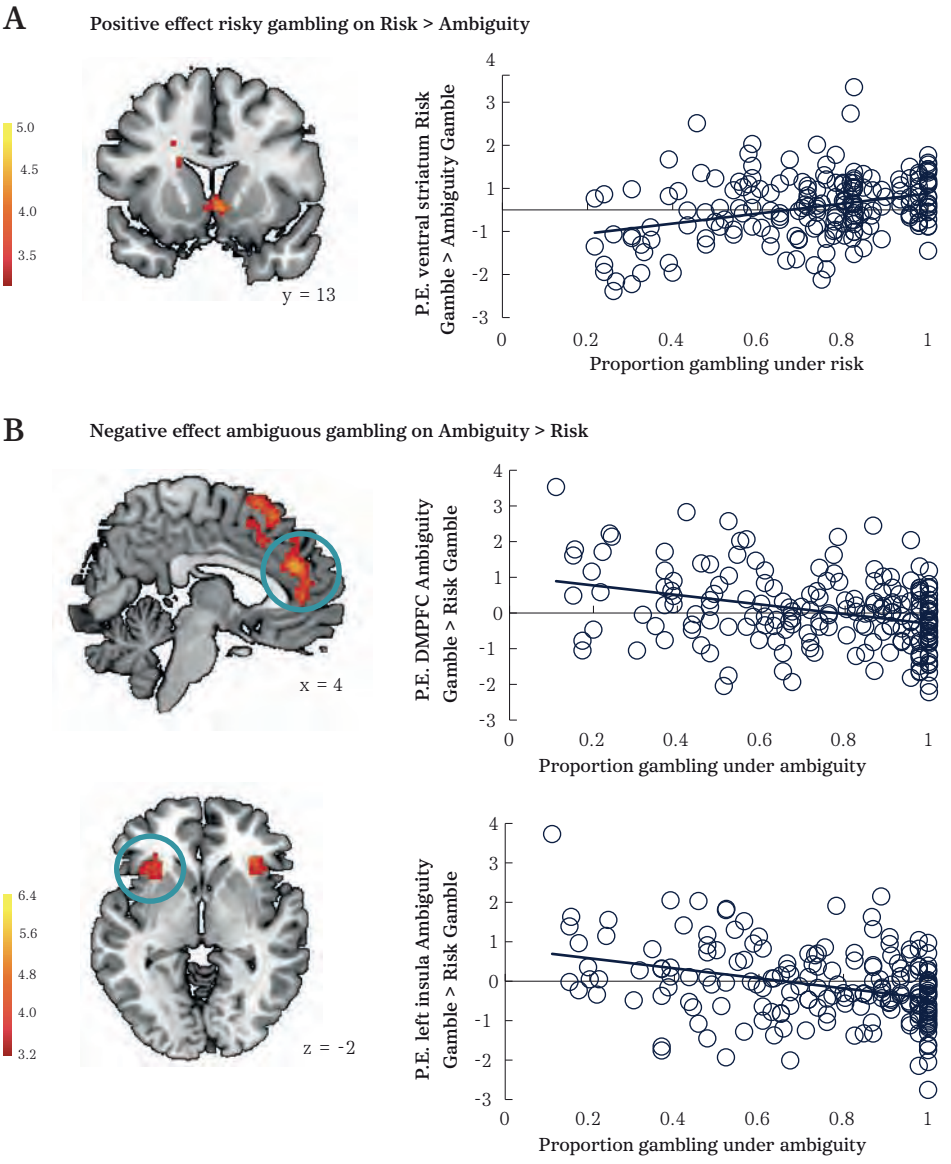


Figure 4. A. *The positive effect of risky gambling on Risk Gamble > Ambiguity Gamble in the ventral striatum. A higher frequency of gambling under risk was associated with increased ventral striatum activation during Risk Gamble > Ambiguity Gamble.* ***B.*** *The negative effect of ambiguous gambling on Ambiguity Gamble > Risk Gamble. Increased gambling behavior under ambiguity was associated with an attenuated DMPFC and bilateral insula response. The graphs are for illustrative purposes only. P.E. = parameter estimate.*

Table 5. MNI coordinates of Local Maxima Activated for the results of regressions with gambling behavior on Risk Gamble > Ambiguity Gamble and the reversed contrast.

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
Positive effect of risky gambling on Risk Gamble > Ambiguity Gamble						
L caudate nucleus	-15	2	25	4.86	< .001	170
R caudate nucleus	6	14	-5	4.15	.008	105
Negative effect of ambiguous gambling on Ambiguity Gamble > Risk Gamble						
L anterior cingulate cortex	-9	35	19	6.44	< .001	429
R anterior cingulate cortex	6	38	25	5.38		
L superior medial gyrus	-9	32	31	5.06		
L supplementary motor area, including R supplementary motor area, bilat. superior medial gyrus, bilat. superior frontal gyrus, R middle cingulate cortex	-9	11	52	5.13	< .001	392
	-3	26	52	5.11		
	0	17	64	4.56		
L insula lobe	-27	26	4	4.88	.005	116
L insula lobe	-30	11	-14	4.49		
L insula lobe	-30	20	-11	4.32		
L inferior frontal gyrus (pars orbitalis)	-36	26	-5	3.53		
R insula lobe	33	29	-2	4.62	.005	117
R inferior frontal gyrus (pars orbitalis)	39	20	-20	3.93		
R inferior frontal gyrus (pars orbitalis)	42	29	-17	3.46		

Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

Associations with individual-differences measures

Regressions with task behavior: Choice phase - Our main interest was to examine relations between brain activation during risky and ambiguous decision-making and individual differences in risk-taking tendencies. First we examined whether individual differences in gambling behavior in the wheel of fortune task were associated with different activation patterns during risky and ambiguous gambling, respectively. We observed a positive effect of risky gambling on the Risk Gamble > Ambiguity Gamble contrast in the VS (Figure 4A, Table 5). That is, participants

who gambled more frequently on risky trials (controlling for gambling in ambiguous trials) showed greater activation in this region during risk compared with ambiguity (Figure 4A, right panel).

In the reversed contrast (Ambiguity Gamble > Risk Gamble), we observed a negative effect of ambiguous gambling (controlled for risky gambling) in bilateral insula, DMPFC, and dorsal ACC/SMA (Figure 4B, Table 5). Specifically, these analyses show that participants who gambled less frequently on ambiguous trials in general, showed greater activation in these regions for Ambiguity Gamble > Risk Gamble when choosing to gamble (Figure 4B, right panel).

When we included age as an additional covariate in these analyses, these effects remained the same.

Table 6. MNI coordinates of Local Maxima Activated for the negative effect of ambiguous gambling on Gain > No Gain.

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
L superior temporal gyrus, L posterior insula	-54	-19	13	4.74	< .001	531
L postcentral gyrus	-54	-13	40	4.44		
R superior frontal gyrus	24	20	58	5.67	.007	102
R middle frontal gyrus	45	26	37	3.82		
R middle frontal gyrus	42	35	43	3.65		
R precentral gyrus, including R supplementary motor area, R postcentral gyrus	39	-19	58	4.73	< .001	505
R paracentral lobule	3	-31	58	4.33		
R posterior insula lobe, including R superior temporal gyrus, R precentral gyrus, R postcentral gyrus, R inferior frontal gyrus (pars opercularis).	36	-7	13	4.26	< .001	244
R rolandic operculum	45	-7	19	4.25		
R rolandic operculum	48	-16	13	4.17		

Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

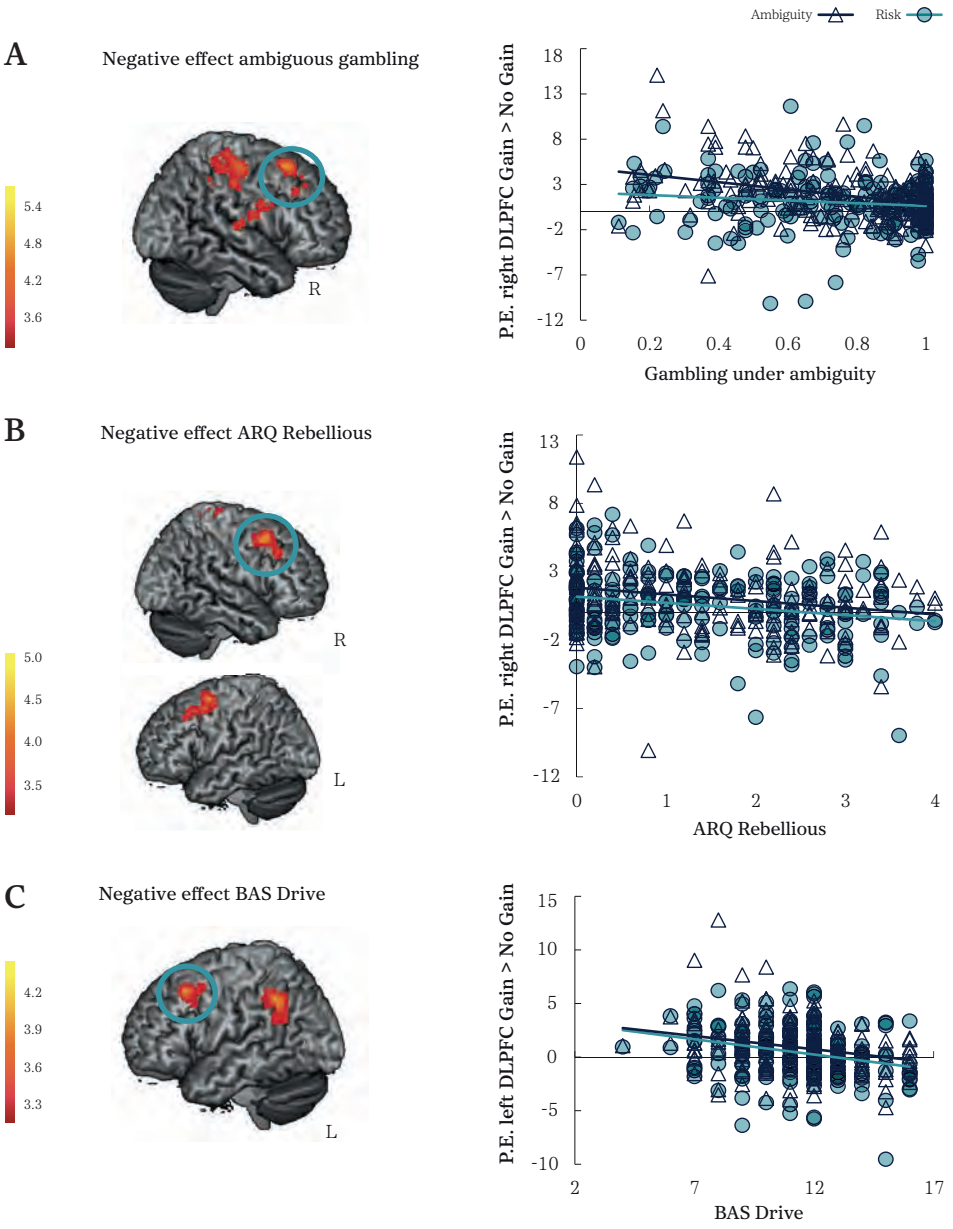


Figure 5. A. *The negative effect of gambling under ambiguity on Gain > No Gain.* ***B.*** *The negative effect of ARQ Rebellious behavior on Gain > No Gain.* ***C.*** *The negative effect of BAS Drive on Gain > No Gain. Activation was similar for both conditions (see graphs, right panels). P.E. = parameter estimate.*

Regressions with task behavior: Outcome phase - Similarly, as for the choice phase, we investigated effects of gambling in the wheel of fortune task on the reward outcome phase (Gain > No Gain, collapsed across risky and ambiguous conditions). A whole-brain regression with risky and ambiguous gambling behavior as predictors showed a specific negative effect of ambiguous gambling in the right DLPFC and right superior temporal gyrus (extending into the posterior insula; Figure 5A, Table 6). These effects remain the same when including age as an additional covariate.

We used an ROI approach to test whether the DLPFC activation differed between reward outcome processing following a risky or an ambiguous gamble. This was not the case: the partial correlations between ambiguous gambling (controlling for risky gambling) and DLPFC did not differ significantly between reward processing following risk or ambiguity (Fisher's Z = 1.35, p = .17; Ambiguity Gain > Ambiguity No Gain: r = -.302, p < .001; Risk Gain > Risk No Gain: r = -.183, p = .01). This result indicates that those participants who gambled less frequently in the ambiguous trials showed greater activation in this region when processing rewards, but this was not driven by processing rewards after risk or ambiguity (Figure 5A, right panel).

Regressions with self-reported risk-taking behavior: Choice phase - To test which regions were associated with self-reported risk-taking measures, we included ARQ and BIS/BAS subscales in a whole-brain regression. No activation in hypothesized

Table 7. MNI coordinates of Local Maxima Activated for the results of regressions with ARQ and BIS/BAS subscales on Ambiguity Gamble > Risk Gamble.

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
Positive effect of BAS Drive on Ambiguity Gamble > Risk Gamble						
R inferior parietal lobe	54	-52	46	4.18	.02	70
Positive effect of BAS Fun Seeking on Ambiguity Gamble > Risk Gamble						
R supramarginal gyrus, including R postcentral gyrus	63	-28	49	3.87	.048	56
R supramarginal gyrus	51	-31	40	3.58		
R supramarginal gyrus	54	-34	49	3.51		

Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

regions was observed during the choice phase (Risk Gamble > Ambiguity Gamble or vice versa). The only clusters that survived thresholding was a positive relation with BAS Drive and BAS Fun Seeking in parietal and motor brain regions during Ambiguity Gamble > Risk Gamble (summarized in Table 7). When including age as an additional covariate, only the effect of BAS Drive survived cluster correction.

Regressions with self-reported risk-taking behavior: Outcome phase - A similar regression was performed testing for effects of ARQ and BIS/BAS subscales on the general contrast Gain > No Gain. First, we observed a negative effect of ARQ Rebellious behavior in the bilateral DLPFC (Figure 5B; Table 8). Specifically, this

Table 8. MNI coordinates of Local Maxima Activated for the results of the regression with ARQ and BIS/BAS subscales on Gain > No Gain.

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
Negative effect of ARQ Rebellious on Gain > No Gain						
R middle frontal gyrus	39	14	52	5.02	.006	112
R middle fro ntal gyrus	39	26	37	3.93		
L precental gyrus	-36	2	61	4.41	.001	148
L middle frontal gyrus	-36	5	52	4.25		
L middle frontal gyrus	-27	14	43	3.89		
R paracentral lobule	6	-34	73	4.06	.025	80
R precuneus	6	-46	67	3.82		
R precentral gyrus	15	-22	64	3.56		
Negative effect of BAS Drive on Gain > No Gain						
L inferior parietal lobule	-57	-52	40	4.45	.006	110
L angular gyrus	-42	-55	25	3.62		
L supramarginal gyrus	-60	-52	28	3.56		
L middle frontal gyrus	-42	23	49	4.43	.022	83
L middle frontal gyrus	-39	11	49	3.47		
L middle frontal gyrus	-33	20	43	3.46		

Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected ($p < .05$).

indicates that those participants who show more rebellious behavior in daily life, showed significantly less activation in the DLPFC when processing reward outcomes. Similar, but less pronounced, results were observed when including age as a covariate.

We tested whether this activation pattern was driven by outcome processing in the risky or ambiguous condition. When comparing the partial correlations between Rebellious behavior (controlling for the other ARQ and BIS/BAS subscales) and DLPFC activation in the risky, with the ambiguous condition, we observed no significant differences between these conditions (left DLPFC: Fisher's $Z = .72$, $p = .47$, right DLPFC: $Z = .06$, $p = .95$; ambiguity: left DLPFC $r = -.307$, $p < .001$, right DLPFC: $r = -.258$, $p = .001$, risk: left DLPFC: $r = -.239$, $p = .002$, right DLPFC: $r = -.252$, $p = .001$; Figure 5B, right panel). This shows that the negative association between rebellious behavior and reward outcome processing did not depend on whether the reward was preceded by a risky or ambiguous gamble.

With respect to BAS Drive, a greater tendency to work for rewards was also associated with an attenuated left DLPFC response when processing rewards (Figure 5C, Table 8). These effects remained the same when including age as an additional covariate.

Again we tested whether this activation pattern was driven by outcome processing in the risky or ambiguous condition. Similar to the association with Rebellious behavior, we observed that the association with BAS Drive did not differ ($Z = -.104$ $p = .92$) between rewards following a risky ($r = -.243$, $p = .001$) and ambiguous gamble ($r = -.233$, $p = .002$, Figure 5C, right panel).

Discussion

This study investigated the neural mechanisms underlying individual differences in risk-taking tendencies during risky and ambiguous decision-making in a large adolescent sample with a wide age range (11-24 years). We specifically focused on two indices of risk taking: task-related (gambling under risk and ambiguity) and self-reported indices of risk taking (the frequency of engaging in real-life risky behaviors and trait reward sensitivity). The analyses resulted in a number of main findings. First, we discovered that risky versus ambiguous gambling are reflected in different patterns of brain activation. Second, individual differences in task-related risk taking recruited different regions depending on whether the context was risky or ambiguous. Finally, individual differences in self-reported risk taking were primarily reflected in activation during reward outcome processing. The discussion is organized alongside these main findings.

Neural mechanisms underlying risky and ambiguous decision-making

First, we investigated the neural correlates of gambling and reward processing under risk and ambiguity, using a previously validated fMRI gambling paradigm (Blankenstein et al., 2017). Previous neuroimaging studies in adults have questioned whether risk and ambiguity are reflected by the same underlying neural mechanisms, given that risk and ambiguity preferences may separately influence risk taking (Tversky & Kahneman, 1992). Although some have predominantly observed overlap in the neural correlates underlying valuation under risk and ambiguity (Blankenstein et al., 2017; Levy, Snell, Nelson, Rustichini, & Glimcher, 2010), others have observed distinct neural patterns between these decision contexts (Hsu et al., 2005; Huettel et al., 2006), which may particularly arise when including individuals' preferences for risk and ambiguity (Blankenstein et al., 2017). When contrasting risky and ambiguous gambling, we observed that risk resulted in greater activation in the right ventral LPFC, bilateral precentral gyrus, and parietal cortex, whereas ambiguity resulted in greater activation in left dorsal LPFC and temporal lobe. Activation in the former set of regions may possibly serve the executive processing of explicit probabilities presented during risky trials as found in prior studies with adults (Blankenstein et al., 2017; Huettel, Song, & McCarthy, 2005; Huettel et al., 2006), but do not concur with adult findings of risk preferences in the striatum or OFC (Blankenstein et al., 2017; Engelmann & Tamir, 2009; Hsu et al., 2005). The regions that were particularly activated during gambling under ambiguity fit well with earlier findings of ambiguity coding in the LPFC in adults (Huettel et al., 2006).

We further addressed whether outcomes were processed differently after gambling in a risky or ambiguous context. Although VS and MPFC were generally activated in response to rewards irrespective of a risky or ambiguous decision context, a more dorsal region of the MPFC was particularly activated during rewards following ambiguous, compared with risky, gambles. A similar pattern has been observed in prior work with adults (although slightly more dorsal; Blankenstein et al., 2017), and was interpreted as a general signal of uncertainty coding, being particularly present in ambiguous contexts (based on a search in NeuroSynth, an online meta-analysis database; Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011). Alternatively, the MPFC has been implicated in performance monitoring and feedback integration following risky decisions (McCormick & Telzer, 2017a; van Noordt & Segalowitz, 2012; Xue et al., 2009), which would concur with a learning signal over time that is greater in ambiguous compared to risky contexts. Although behavior did not change profoundly in both decision contexts, gambling increased slightly over time for ambiguous trials. Future studies may therefore further investigate the role of the MPFC in learning (e.g., behavioral adjustment) versus

resolving outcome uncertainty under risky and ambiguous conditions, for instance by using a paradigm in which outcomes influence subsequent decisions in a learning context, and using varying levels of ambiguity.

Relations with task-related and self-reported risk taking

Our main interest was to relate individual differences in risk-taking tendencies to brain activation during risky and ambiguous decision-making during adolescence, given that this is a time marked by a rise in risk taking (Steinberg, 2008). To this end we included participants from a wide age range, in which individual differences in risk-taking tendencies are most prominent (Bjork & Pardini, 2015; Willoughby et al., 2013). Although participants were encouraged to gamble by presenting gambling options higher in expected value than the safe option, there was substantial variability in risky and ambiguous gambling behavior, allowing the investigation of these individual-difference measures in relation to brain activity.

First, during the choice phase, a higher frequency of gambling under risk (but not ambiguity) was associated with increased activation in the VS in the risky condition only, whereas a greater tendency to gamble under ambiguity (but not risk) was related to reduced DMPFC and insula activation in the ambiguous condition only. Generally, we replicated prior research showing that enhanced risk taking is associated with greater striatum activation (Galvan et al., 2007), and reduced DMPFC and insula activation (Van Duijvenvoorde et al., 2015; Van Leijenhorst et al., 2010). However, we now show that these neural correlates differed across task conditions. Speculatively, these findings may relate to the difference in subjective evaluation of the decisions at hand, in which the tendency to engage in risky gambles may be triggered by a greater reward valuation, whereas the tendency to engage in ambiguous gambles is mainly driven by an aversion to uncertainty. Previous research has related insula and DMPFC activation in the context of risky decision-making as an affective and cognitive component (respectively) of uncertainty processing (Mohr, Biele, & Heekeren, 2010; Van Duijvenvoorde et al., 2015). That is, activation in the insula may reflect the increased experienced negative affect when encountering uncertainty (Van Duijvenvoorde et al., 2015), which may be more pronounced under ambiguity than risk. Simultaneously, activation in the DMPFC may function as a cognitive warning signal to prevent risky behavior and has been related to participants' subjective experience of uncertainty (Xue et al., 2009). This interpretation fits well with the finding that insula activation was heightened for those individuals who gambled less frequently in this condition.

A new direction in this study is that we related individual differences in risk-taking tendencies not only to choice, but also to outcome processing. We observed

that a greater tendency to gamble under ambiguity was associated with decreased right DLPFC activation during reward processing. In addition, greater self-reported rebellious behavior, and a greater drive for rewards, were also associated with a reduced DLPFC response when processing rewards. This contradicts prior research on adolescent individual differences in real-life risk taking and brain activation, which showed the opposite relation (a greater DLPFC response with increased risk taking; Qu et al., 2015), but is in line with prior research in young adults (Gianotti et al., 2009) and with studies that relate lower impulsivity to strengthened connectivity between the striatum and DLPFC (Achterberg, Peper, van Duijvenvoorde, Mandl, & Crone, 2016; Dixon, 2015; van den Bos, Rodriguez, Schweitzer, & McClure, 2014). These findings point towards an important role for the LPFC in individuals' risk preferences, and concurs with the idea that lower self-control in response to rewards may lead adolescents to engage in greater risk taking. However, it should be noted that in the current task, risk taking could be seen as advantageous (i.e., the gamble presented a higher expected value), thus leading to more monetary gains. Similarly, it may be adaptive to display certain levels of reward motivation or rebellious behavior, particularly in this age range (Romer, Reyna, & Satterthwaite, 2017). The adaptive nature of risk taking should be further examined, considering adolescence as a period of opportunities, and not only of risk (Crone, Duijvenvoorde, & Peper, 2016).

Limitations and future directions

A number of limitations need to be considered. First, although the current study included a wide age range across adolescence (11-24 years, an age range in which individual differences in daily-life risk taking are prominent; Bjork & Pardini, 2015; Willoughby, Good, Adachi, Hamza, & Tavernier, 2013), the majority of our findings were independent of age, except for the results on self-report measures. That is, ARQ and BAS subscales increased with age and/or peaked in adolescence, which is consistent with prior reports on these measures which is consistent with prior reports on these measures (Blankenstein et al., 2016; Urošević, Collins, Muetzel, Lim, & Luciana, 2012) and with previous reports of this sample (regarding the BAS scales, Braams et al. 2015; Schreuders et al., 2018). While in the current study we focused particularly on individual differences in an adolescent sample, it is surprising that we did not find effects of age on our neural results. Prior studies reported heightened activation in dorsal ACC in early adolescence (Van Leijenhorst et al., 2010) and in DMPFC, anterior insula, and subcallosal cortex in mid-adolescence with increasing risk processing (Van Duijvenvoorde et al., 2015; Van Leijenhorst et al., 2010) and adolescent peaks in striatum activity (Braams et al., 2015; Van Leijenhorst et al., 2010; Silverman, Jedd, & Luciana, 2015). Others reported a monotonic increase from

childhood to adulthood in MPFC during reward processing (Van Duijvenvoorde et al., 2015). Importantly, these studies included participants from late childhood/early adolescence (8-10 years), whereas our youngest participants were 11-12 years old. Indeed, in a recent review it was argued that information from childhood is needed to fully understand developmental patterns and underlying factors of risk taking across adolescence (Li, 2017). Furthermore, developmental effects are often not observed when the risky option is obviously advantageous (Defoe, Dubas, Figner, & Van Aken, 2015; Li, 2017), as in the current study. An opportunity for future research may therefore be to determine age effects in risk and ambiguity sensitivity, a question that may be tackled with paradigms including a non-safe alternative (e.g., Defoe et al., 2015) as well as including multiple levels of risk and ambiguity (Blankenstein et al., 2016) in a broad age range starting in late childhood and extending into adulthood.

Second, task behavior was not correlated to any of our measures on real-life risk taking. Studies using both task-related and self-report measures of risk taking often do not find significant correlations, which have been suggested to be caused by underpowered studies (for a review, see Sherman et al., 2017). However, the current study, and others (e.g., Mamerow, Frey, & Mata, 2016) with relatively large sample sizes also did not find associations between task-related and self-reported risk taking. Recently, a large comprehensive study with adults used a psychometric approach to examine the multidimensionality of risk taking (Frey, et al., 2017). This study showed that risk propensity measures (i.e., self-report measures on for instance sensation-seeking and impulsivity) and risk frequency measures (i.e., real-life risk behaviors such as smoking) were only weakly correlated with behavioral measures (i.e., revealed preferences: task-based risk measures such as behavior on the Balloon Analogue Risk Task and the Columbia Card Task). That is, the authors discovered that a general factor of risk preference emerged from the propensity measures and frequency measures, which did not share variance with behavioral measures (revealed preferences). Possibly, in the current study, task-related risk taking (a behavioral measure) and self-reported risk taking as measured with the BIS/BAS subscales (a propensity measure), and the ARQ subscales (a frequency measure) also reflect different behavioral manifestations of risk behavior in our adolescent sample. Although the psychometric properties of risk preferences in adolescence warrants further study, this echoes the need for and potential of including multidimensional measures of risk taking (i.e., behavior, propensity, and real-life frequencies) in adolescence.

Third, task behavior was heavily tuned towards gambling, by presenting participants with gambles much higher in expected value than the safe option. To derive a more sensitive measure of individuals' preferences for risk and ambiguity, future research may benefit from including an additional task that presents multiple

levels of risk and ambiguity (Blankenstein et al., 2017; Engelmann & Tamir, 2009).

Fourth, participants' gambling frequency determined the number of gain and no gain trials included in the analyses. That is, those participants who gambled more frequently experienced more reward outcomes than those participants who chose the safe option more frequently, which may have biased our results in the reward outcome phase. However, a loss of power due to fewer trials is unlikely to drive our main results, given that less gambling actually led to greater activation during choice and outcome.

Finally, indices of real-life risk taking were based on retrospective, self-report questionnaires. An opportunity for future research is to more explicitly measure day-to-day risk taking, for instance by using ecological momentary assessments, in which participants are asked to answer questions multiple times each day for an extended period of time, making it possible to collect rich, real-time data on individuals' risk-taking behavior (Shiffman, Stone, & Hufford, 2008; Turner, Mermelstein, & Flay, 2004).

Conclusion

This study is the first to examine individual differences in risk taking in adolescence in relation to the neural mechanisms underlying decision-making under risk and ambiguity. Using a previously established fMRI gambling paradigm, we were able to study gambling and reward processing under risk and ambiguity in a large adolescent sample spanning a wide age range (11-24 years). We demonstrate that risky and ambiguous gambling is reflected in different patterns of brain activation, and that the MPFC appears key in processing reward outcomes following ambiguity. In addition, individual differences in task-related and self-reported risk-taking tendencies were associated with activation in the VS, LPFC, insula and DMPFC, regions previously associated, respectively, with reward processing, cognitive control, and cognitive-affective integration. Moreover, we found that the neural mechanisms underlying task-related risk taking were differentially recruited depending on whether the choice context was risky or ambiguous. Finally, reward valuation in the LPFC seems key for individual differences in risk-taking tendencies in this adolescent sample. Together, this study demonstrates the importance of considering multiple measures of risk taking, and contextual moderators, in unraveling the neural mechanisms underlying risk taking in adolescents.

Supplementary materials

A1. Behavioral age effects

We explored linear, quadratic, and cubic changes with age (with age as a polynomial predictor) on the behavioral risk-taking measures using hierarchical multiple regression models. These regressions indicated that gambling under risk increased slightly with age (i.e., linearly: $R^2 = .03$, $F(1, 196) = 6.35$, $b_{age} = .014$, $p = .013$), whereas gambling under ambiguity did not ($b_{age} = .010$. $p = .126$). For the ARQ subscales, we observed no age effects for Thrill-seeking behavior ($p = .614$), a quadratic age effect for Rebellious behavior ($R^2 = .40$, $\Delta F(2, 189) = 6.73$, $\Delta p = .010$, $b_{age^2} = -.021$, $p_{age^2} = .019$), and positive linear age effects for Reckless ($R^2 = .26$, $F(1, 190) = 66.23$, $b_{age} = .099$, $p < .001$) and Antisocial behavior ($R^2 = .085$, $F(1, 190) = 17.67$, $b_{age} = .059$, $p < .001$). Finally, we observed a positive linear age effect for BAS Drive ($R^2 = .022$, $F(1, 180) = 3.98$, $b_{age} = .129$, $p = .048$), a quadratic age effect for BAS Fun seeking (peaking around 18-20 years, $R^2 = .06$, $\Delta F(2, 179) = 6.33$, $\Delta p = .013$, $b_{age^2} = -.039$, $p_{age^2} = .018$), no significant age-related change for BAS Reward responsiveness ($p = .182$), and a positive linear age effect for BIS ($R^2 = .023$, $F(1, 180) = 4.15$, $b_{age} = .211$, $p = .043$).

Table A1. MNI coordinates of Local Maxima Activated for the positive effect of age (linear) on Ambiguity Gamble > Risk Gamble.

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
R superior parietal lobule	18	-58	49	4.77	.002	139
	15	-67	64	4.24		
	15	-61	58	4.14		

Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

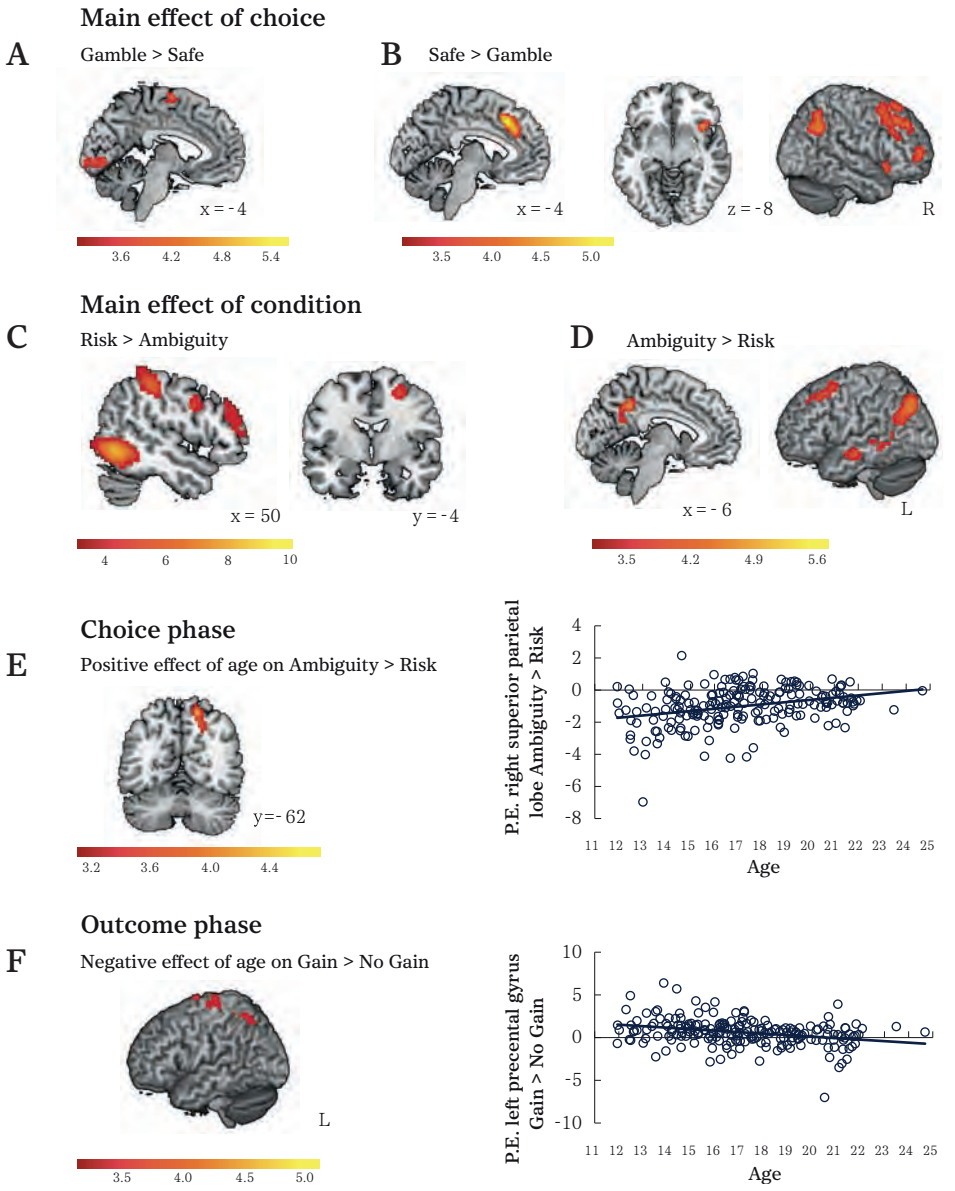


Figure A1. *Supplementary whole-brain results, FWE cluster-corrected ($p < .05$).* ***A-D.*** *Results of the choice (gamble, safe) * condition (risk, ambiguity) whole-brain ANOVA, showing the main effect of choice (**A.** Gamble > Safe and **B.** Safe > Gamble) and the main effect of condition (**C.** Risk > Ambiguity and **D.** Ambiguity > Risk). There was no interaction effect.* ***E.*** *The positive effect of age on Ambiguity Gamble > Risk Gamble.* ***F.*** *The negative effect of age on Gain > No Gain.*

A2. Gambling versus choosing safe across risk and ambiguity

Although not the main focus of the current study, we tested whether gambling versus choosing safe was coded differently for risk versus ambiguity. To this end we conducted a whole-brain choice (gamble, safe) * condition (risk, ambiguity) ANOVA. This analysis, including 152 participants (i.e., participants who chose the gamble and safe option in each condition), resulted in a main effect of choice, and a main effect of condition, but no interaction effect. This indicates that gambling versus choosing safe (and vice versa) was coded similarly for risk and ambiguity. The results of the main effects are shown in Table A2 and Figure A2 and described below.

The main effect of choice showed increased activation in the supplementary motor are for Gamble > Safe, and increased activation in anterior cingulate cortex, right ventrolateral and dorsolateral PFC, and right anterior insula for Safe > Gamble. With respect to the main effect of condition we observed heightened right lateralized DLPFC activation for Risk > Ambiguity (irrespective of the type of choice), and left lateralized DLPFC, and precuneus, activation for Ambiguity > Risk.

Table A2. MNI coordinates of Local Maxima Activated Clusters for results of the choice (gamble safe) * condition (risk, ambiguity) ANOVA.

		MNI coordinates					
Effect	Area of activation	x	y	z	T	pFWE	Volume
Gamble > Safe	L occipital middle gyrus	-15	-97	7	5.50	< .001	727
	R cuneus	21	-94	10	4.78		
	L supplementary motor area	-3	-7	67	4.08		85
Safe > Gamble	L superior medial gyrus	-3	23	43	5.19	< .001	262
	R anterior cingulate cortex	12	29	25	4.44		
	R superior frontal gyrus, including R superior medial gyrus	21	41	37	4.50	< .001	477
	R middle frontal gyrus	27	29	46	4.39		
	R middle frontal gyrus	42	26	34	4.13		
	R inferior parietal lobe	51	-58	46	4.45	< .001	211
	R angular gyrus	51	-61	37	4.45		
	L inferior parietal lobe	-48	-61	52	4.34	.014	78

Table A2. Continued

Effect	Area of activation	MNI coordinates			T	pFWE	Volume
		x	y	z			
Safe > Gamble (continued)	L inferior parietal lobe	-45	-58	43	3.85		
	R insula lobe	36	17	-8	4.31	.03	65
	R middle frontal gyrus	30	53	4	4.23	.003	106
	R superior frontal gyrus	18	62	7	3.44		
Risk > Ambiguity	R middle occipital gyrus	33	-85	10	10.08	< .001	5534
	R superior parietal lobe	21	-67	58	9.55		
	R inferior temporal gyrus	45	-67	-5	9.52		
	R precentral gyrus	48	5	31	5.16	.016	76
	R superior frontal gyrus	27	-4	55	4.82	.047	58
	R inferior frontal gyrus (pars Triangularis)	54	35	28	4.35	.019	73
	R middle frontal gyrus	54	41	19	3.95		
Ambiguity > Risk	L inferior parietal lobe	-45	-76	37	5.05	< .001	334
	L inferior parietal lobe	-39	-76	46	4.81		
	L angular gyrus	-51	-70	34	4.50		
	L middle frontal gyrus	-24	20	46	4.92	< .001	246
	L middle frontal gyrus	-33	11	58	3.93		
	L superior frontal gyrus	-18	38	28	3.92		
	R angular gyrus	57	-67	31	4.83	< .001	166
	R angular gyrus	63	-58	25	4.45		
	L precuneus	-9	-49	40	4.59	.001	127
	L precuneus	-3	-55	25	3.63		
	R precuneus	6	-55	22	3.33		
	L middle temporal gyrus	-51	-19	-14	4.21	.008	88
	L middle temporal gyrus	-57	-13	-8	4.15		

Note: L = left; R = right. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected ($p < .05$).

Table A3. MNI coordinates of Local Maxima Activated for the negative effect of age (linear) on Gain > No Gain.

	MNI coordinates					
Area of activation	x	y	z	T	pFWE	Volume
Negative effect of age on Gain> No Gain, cluster-corrected						
L precentral gyrus, including L superior parietal lobe, L supplementary motor area, L precuneus	-21	-25	58	5.11	< .001	368
	-21	-25	67	4.73		
L postcentral gyrus	-21	-49	55	4.47		
R precentral gyrus, including R supplementary motor area	18	-25	67	4.63	< .001	167
R paracentral lobule	15	-28	58	4.38		
R superior frontal gyrus	15	-1	73	4.02		
R superior frontal gyrus	18	-7	70	3.87		

Note: L = left; R = right; bilat = bilateral. Anatomical labels are based on the Automated Anatomical Labeling (AAL) atlas. Results were FWE cluster-corrected (p < .05).

Chapter 6

Behavioral and neural pathways supporting the development of prosocial and risk-taking behavior across adolescence

This chapter is under review as: Blankenstein, N. E., Telzer, E. H., Do, K. T., van Duijvenvoorde, A. C. K., & Crone, E. A. Behavioral and neural pathways supporting the development of prosocial and risk-taking behavior across adolescence.

Abstract

This study tested the pathways supporting adolescent development of prosocial and rebellious behavior. Self-report and structural brain development data were obtained in a three-wave, longitudinal neuroimaging study (8-29 years, N = 210 at wave three). First, prosocial and rebellious behavior assessed at wave three were positively correlated. Perspective taking and empathy uniquely predicted prosocial behavior, whereas fun seeking (current levels and longitudinal changes) predicted both prosocial and rebellious behaviors. These changes were accompanied by developmental declines in nucleus accumbens and medial prefrontal cortex (MPFC) volumes, but only faster decline of MPFC (faster maturity) was related to less rebellious behavior. These findings point towards a possible differential susceptibility marker, fun seeking, as a predictor of both prosocial and rebellious developmental outcomes.

Key words: prosocial, risk-taking, brain, adolescence, longitudinal

Introduction

Adolescence is often described as the most important transition period for developing into an adult with social competence and mature social goals (Blakemore & Mills, 2014; Crone & Dahl, 2012). Yet, there are many paradoxes when describing typical adolescent behavior. For instance, adolescents are described as notorious risk takers, with a preferred focus on short-term rewards rather than long-term consequences of their decisions (Dahl, 2004; Hall, 1904; Steinberg, 2008). Experimental and self-report studies have confirmed this adolescent rise in risk taking (Burnett, Bault, Coricelli, & Blakemore, 2010; Defoe, Dubas, Figner, & van Aken, 2015), which is more pronounced in social contexts, such as in the presence of friends (Gardner & Steinberg, 2005; Knoll, Magis-Weinberg, Speekenbrink, & Blakemore, 2015). However, in parallel, most individuals also develop social competence during adolescence, with rises in perspective taking and in considering the needs of others (Blakemore & Mills, 2014). Indeed, adolescents show increases in prosocial behaviors, especially towards their friends (Guroglu, van den Bos, & Crone, 2014), and show increases in social perspective taking (Dumontheil, Apperly, & Blakemore, 2010). Adolescence has therefore been described as a developmental period of both risks and opportunities (Crone & Dahl, 2012; Do, Guassi Moreira, & Telzer, 2017). While it is key to our understanding of how these behaviors develop in tandem in adolescence, the relation between risk-taking and prosocial tendencies in adolescence has been overlooked (Telzer, Fuligni, Lieberman, & Galvan, 2013). Therefore, a critical question concerns whether risk-taking and prosocial tendencies are related constructs over adolescent development, and which processes predict these seemingly paradoxical behaviors. Understanding the mechanisms that underlie or differentiate these two seemingly disparate behaviors may help to identify pathways for reducing risks and/or promoting opportunities often inherent in adolescence (Crone & Dahl, 2012).

One possible mechanism that may account for increases in the occurrences of both risk-taking and prosocial tendencies is elevated reward sensitivity (Crone & Dahl, 2012; Telzer, 2016; van Duijvenvoorde, Peters, Braams, & Crone, 2016). It has been well conceptualized that reward sensitivity is correlated with risk-taking behavior such as alcohol consumption, and functional neuroimaging work has shown that heightened activation of the ventral striatum (a subcortical region that plays a primary role in reward sensitivity) during receipt of reward correlates with alcohol use (Braams, Peper, van der Heide, Peters, & Crone, 2016). To date, it remains unclear whether sensitivity to rewards also drives prosocial tendencies, although prior functional neuroimaging studies have established that heightened

ventral striatum activation is also observed during positive, other-oriented behavior such as giving to others (Telzer, 2016; Telzer, Masten, Berkman, Lieberman, & Fuligni, 2010). Furthermore, gaining for others also results in activity in the ventral striatum (Varnum, Shi, Chen, Qiu, & Han, 2014), and this activity is heightened in adolescents when gaining for close family members (Braams & Crone, 2017). If sensitivity to rewards is related to both risk-taking and prosocial tendencies, then an important question concerns whether adolescence is a window for stronger reward reactivity that may, in some instances, lead adolescents to develop stronger risk-taking tendencies, whereas in other instances, lead adolescents to develop stronger prosocial tendencies, also referred to as differential susceptibility (Schriber & Guyer, 2015). Alternatively, the same window of reward sensitivity may also result in a subgroup of adolescents who show *both* risk-taking behavior as well as prosocial tendencies, also referred to as 'prosocial risk takers' (Do et al., 2017). Thus, in this study we address whether the development of behavioral reward sensitivity underlies risk-taking and/or prosocial tendencies, as well as a combination of these traits.

Two other processes that have previously been related to prosocial behavior are social perspective taking and empathic concern (Overgaauw, Rieffe, Broekhof, Crone, & Guroglu, 2017). First, the development of perspective taking has been well described, such that perspective-taking abilities increase across adolescence (Humphrey & Dumontheil, 2016), and adolescents who show better perspective-taking skills report more prosocial behavior (Tamnes et al., 2017). In addition, in adolescence, activation in the medial prefrontal cortex (a region part of the 'social brain network', involved in social cognitive processing and mentalizing; Mills, Lalonde, Clasen, Giedd, & Blakemore, 2014), has been found to be heightened during prosocial behavior in the presence of peers (Van Hoorn, Van Dijk, Güroğlu, & Crone, 2016). Second, empathy increases across age (10-15 years) in girls, and declines in boys, and specifically the empathic intention to comfort others has been related to lower levels of bullying behavior (Overgaauw et al., 2017). Thus, the development of perspective-taking abilities and the intention to comfort others has been shown to promote prosocial behavior, and may also have a buffering effect against antisocial tendencies (Overgaauw et al., 2017). However, it is not yet known if perspective taking and empathy also relate to risk-taking behavior. Therefore, an additional question concerns whether individuals' development of perspective taking and the intention to comfort others are related to prosocial and/or risk-taking behaviors in adolescents.

Finally, in addition to the development of reward sensitivity and social skills, the development of brain structures that may accompany the development of these behaviors is relatively understudied. Structural brain development, which follows

the most consistent within-individual patterns of change, has been associated with a number of developmental outcomes such as identity formation (Becht et al., 2018) but how structural development relates to prosocial and/or risk-taking behaviors is less well known. In two recent studies, the nucleus accumbens, a region of the ventral striatum involved in reward sensitivity (Sescousse, Caldú, Segura, & Dreher, 2013), decreased in volume during the course of adolescent development (Herting et al., 2018; Wierenga et al., 2018). A separate study showed that this volume decrease was correlated with greater behavioral reward sensitivity (Urosevic, Collins, Muetzel, Lim, & Luciana, 2012). However, the relation between this structural decrease and risk-taking tendencies is not yet known. In addition, the medial prefrontal cortex (MPFC) has consistently been linked to social perspective taking (Blakemore & Mills, 2014) and prosocial behavior (Thijssen et al., 2015; Wildeboer et al., 2017). Alternatively, functional MRI studies have consistently linked this region to choice valuation and reward outcome processing of risky decisions in adolescence (Blankenstein, Schreuders, Peper, Crone, & van Duijvenvoorde, 2018; van Duijvenvoorde et al., 2015), but the relation between the structural development of MPFC and risk taking is less well understood. Taken together, in addition to reward sensitivity, social perspective taking, and empathy, the structural development of brain regions related to these processes (NACC and MPFC) may provide additional insights into developmental outcomes, namely risk-taking and prosocial tendencies.

The current study

This study set out to test four questions in the Braintime sample, a large longitudinal neuroimaging study with three biannual measurement waves. First, we examined the occurrence of two important developmental outcomes in adolescence, risk-taking behavior and prosocial behavior, and how they are related in adolescents and young adults between ages 12 and 30 years at the final measurement wave. We made use of self-report findings because previous studies have shown that these are most trait-like and take into account the history of individuals (Peper, Braams, Blankenstein, Bos, & Crone, 2018). We were especially interested in the question whether risk-taking behavior and prosocial behaviors were positively related (reflecting a subgroup of 'prosocial risk takers'; Do et al., 2017); negatively related (those who are risky are less prosocial and vice versa); or not related (indicating they do not covary meaningfully within individuals). A frequency measure of rebellious behavior was used as an index of risk taking (Gullone, Moore, Moss, & Boyd, 2000), given that these types of behaviors were most related to risk-taking tendencies in real life, such as alcohol consumption and smoking. In addition, a frequency measure of prosocial actions was used as an index of prosocial tendencies, as this measure

examined occurrences of actual prosocial behaviors. Given that both traits have previously been related to age and gender, these factors were included and controlled for in the analyses, given that the focus in this study was on individual differences in trajectories of change.

A second question in this study concerned whether reward sensitivity related to rebellious behavior and prosocial behavior using the BAS-subscales of the BIS/BAS questionnaires (drive, fun seeking, reward responsiveness; Carver & White, 1994). In addition to reward sensitivity, we examined the contributions of perspective taking, as assessed with the perspective taking subscale of the interpersonal reactivity index (Davis, 1983), and the intention to comfort others, as assessed with the empathic concern questionnaire for children and adolescents (Overgaauw et al., 2017). We hypothesized that reward sensitivity, perspective taking, and intention to comfort would be related to prosocial behavior, and that reward sensitivity would also be related to rebellious behavior. Furthermore, we explored associations between perspective taking, intention to comfort, and rebellious behavior.

Third, we examined in the same individuals whether the developmental trajectory of reward sensitivity and perspective taking across the three measurement waves, would predict the outcome measures rebellious behavior and prosocial behavior at the final wave. In previous research, it was demonstrated that not only the initial levels (intercepts), but also the trajectory of change (slopes) is informative for predicting developmental outcomes. Therefore, longitudinal measurements are crucial to examine whether trajectories of change are predictive for developmental outcome measures. Because our variable of empathy was only available at the final wave, this question was not addressed for this measure.

Finally, we examined whether the development of volumes of the nucleus accumbens and medial prefrontal cortex predicted the outcomes of prosocial and rebellious behavior. Again, for brain measures the trajectory of change is presumed to be more informative than the mean levels, and therefore we determined both mean levels (intercepts) as well as trajectories of change (slopes), to use as predictors for risk-taking and prosocial outcomes above the behavioral indices (Foulkes & Blakemore, 2018).

Methods

Participants

Participants were part of the Braintime study, a longitudinal study conducted in the Netherlands in 2011 (time point 1: T1), 2013 (T2), and 2015 (T3). At T1, data from 299 participants were collected (153 female, 8-25 years), at T2 287 participants (149 female, 10-27 years), and at T3 275 participants (143 female, 12-29 years). In total, across all time points, there were 15 participants (5%) who reported they currently used medicine for a neuropsychiatric disorder (such as anxiety, depression, or AD(H)D). To include as many participants in our analyses as possible, these participants were included in the current study (excluding these participants did not qualitatively affect our results). Table 1 depicts an overview of the number of observations per measure on each time point.

Self-report measures

Outcome measures

Rebellious behavior - To measure participants' risk-taking behavior at T3 (age range 11.94-28.72 years), we examined the Rebellious subscale of the Adolescent Risk-Taking Questionnaire (Gullone et al., 2000). This scale assesses the frequency with which individuals displayed risky behaviors such as 'Staying out late', and 'Getting drunk, with 5 items (α = .880), on a scale ranging from 1 ('Never') to 5 ('Very often'). Data of this subscale have previously been reported in Blankenstein et al. (2018) in a subset of the current sample.

Prosocial behavior - We assessed participants' prosocial behavior at T3 (age range 11.94-28.72 years) with 27 items (α = .924) assessing the frequency of prosocial actions towards friends and peers within the last few months. Example items include 'Sacrifice your own goals to help a friend or peer with theirs', 'Helped a friend find a solution to their problem', and 'Gave money to a friend or peer because they really needed it'. The items covered a broad range of prosocial actions such as helping, giving, altruistic tendencies, and providing emotional support. Participants indicated how often they displayed these behaviors, ranging from 1 ('Not something I do') to 6 ('Very often').

Predictor variables

Behavioral Inhibition / Behavioral Approach Questionnaire - We used the BAS scales of the Behavioral Inhibition / Behavioral Activation questionnaire (BIS/BAS; Carver & White, 1994) to obtain indices of participants' approach behavior. BAS

Table 1. Number of observations per time point, and intraclass correlations (ICC) with 95% confidence intervals (CI).

	N (female)			ICC T1, T2, T3 (95% CI)
Variable	T1	T2	T3	
Prosocial behavior	-	-	263 (142)	-
Rebellious behavior	-	-	226 (116)	-
EMQ Intention to Comfort	-	-	274 (143)	-
IRI Perspective Taking	31 (16)	286 (148)	262 (141)	.76 (.54-.89)
BAS Drive	277 (145)	286 (148)	262 (141)	.60 (.50-.68)
BAS Fun Seeking	277 (145)	286 (148)	262 (141)	.58 (.48-.66)
BAS Reward Responsiveness	277 (145)	286 (148)	262 (141)	.60 (.50-.68
Nucleus Accumbens	238 (129)	226 (119)	219 (120)	.94 (.92-.96)
Medial Prefrontal Cortex	238 (129)	226 (119)	219 (120)	.96 (.77-.99)

scales were available at each time point (age ranges: T1: 8.01-25.95; T2: 9.92-26.6; T3: 11.94-28.72 years). The BAS subscales are Drive (the tendency to persist in pursuit of goals, α_{T3} = .725; four items), Fun seeking (the desire for rewards and the willingness to approach rewards; α_{T3} = .546; four items), and Reward Responsiveness (the response to rewards and reward anticipation; α_{T3} = .609; five items). Participants indicated on a four-point scale the degree to which statements applied to them, ranging from 1 ('Very true') to 4 ('Very false'). Example items include 'When I want something I usually go all-out to get it' (Drive), 'I'm always willing to try something new if I think it will be fun' (Fun seeking), and 'When I get something I want, I feel excited and energized' (Reward Responsiveness). We recoded the items such that higher scores indicate more approach behavior. T3 data of a subset of the current sample are reported in Blankenstein et al. (2018), and longitudinal trajectories of these subscales are reported in Schreuders et al. (2018).

Interpersonal Reactivity Index: Perspective Taking - At T1, we presented participants aged 18 and older (range 18.44-25.95 years) with the Perspective Taking subscale of the Interpersonal Reactivity Index (Davis, 1983). At T2 and T3, we administered this scale to all participants (age ranges: T2: 9.92-26.6; T3: 11.94-28.72 years). The Perspective Taking subscale measures the spontaneous tendency to adopt another person's point of view in daily life, with seven items

(α_{T3} = .775). Example items include 'I sometimes try to understand my friends better by imagining how things look from their perspective' and 'When two peers disagree, I try to see both sides'. Participants gave their responses on a scale ranging from 1 ('Does not describe me well') to 5 ('Describes me very well').

Empathy Questionnaire for Children and Adolescents: Intention to Comfort scale - At T3 (age range: 11.94-28.72 years), we introduced the Intention to Comfort subscale of the Empathy Questionnaire for Children and Adolescents (EmQue-CA; (Overgaauw et al., 2017). This subscale includes five items (α = .599) and measures the extent to which someone feels inclined to actually help or support a person in need. Participants were asked to rate to what extent the description was true for them on a three-point scale: 1 ('Not true'), 2 ('Somewhat true'), and 3 ('True'). Examples include 'If a friend is sad, I like to comfort him', and 'I want everyone to feel good'.

Brain imaging

We used a 3T Philips Achieva MRI scanner for structural neuroimaging. All images were visually inspected after processing (using the longitudinal pipeline) for accuracy (e.g., Mills & Tamnes, 2014; Becht et al., 2018). Scans of poor quality were excluded, and high quality scans were reprocessed though the longitudinal pipeline (single time points were also processed longitudinally). This procedure of quality control was repeated until only acceptable scans were included. See Table 1 for the number of scans included per time point (age ranges: T1: 8.01-25.95; T2: 9.92-26.6; T3: 11.94-28.72 years). Scan acquisition parameters and a detailed description of the structural analyses are described in (Bos, Peters, van de Kamp, Crone, & Tamnes, 2018; Wierenga et al., 2018)

Regions of interest

We derived the measure of gray matter volume for the NACC using the volumetric segmentation procedure. We used the average of left and right NACC in our analyses. Gray matter volume was obtained using the surface-based reconstructed image. We defined the MPFC by combining the following subregions: superior frontal, rostral anterior cingulate, and caudal anterior cingulate of the Desikan-Killiany-Tourville atlas (Klein & Tourville, 2012).

Individual estimations intercepts and slopes from longitudinal measures

From the longitudinal measures (IRI Perspective Taking, BAS scales, brain structure) we estimated starting points and rates of change (i.e., intercepts and slopes) for each

participant. To do so, we ran regression analyses for each participant individually, in which we predicted the longitudinal variables across time points, from age at T1 (or the first time point for which data was available). This resulted in an estimation of an intercept and a linear slope for each participant (except for participants who had data on only one time point, for which slopes could not be estimated). Because there were only three waves, only linear slopes were estimated (Becht et al., 2018). These estimates of individual intercepts and linear slopes were used in subsequent analyses predicting the outcome variables Prosocial and Rebellious behavior.

Note that in the supplements we report which developmental trajectories best described the longitudinal measures (i.e., Perspective Taking, BAS scales, and brain structures), on a group level. Developmental trajectories of BAS scales and NACC volume are already described in Schreuders et al. (2018) and Wierenga et al. (2018), respectively, while the longitudinal development of IRI Perspective Taking and MPFC have not yet been reported. In brief, IRI Perspective Taking followed a cubic developmental pattern across age, described best as an adolescent-emergent pattern of Perspective Taking increasing into adulthood, and higher levels of Perspective Taking in girls than in boys (see also Figure 1A below). MPFC volume was best described by a declining cubic effect of age, and greater volumes in boys than in girls (Figure 1B). In the supplementary materials an elaborate description of these results is provided.

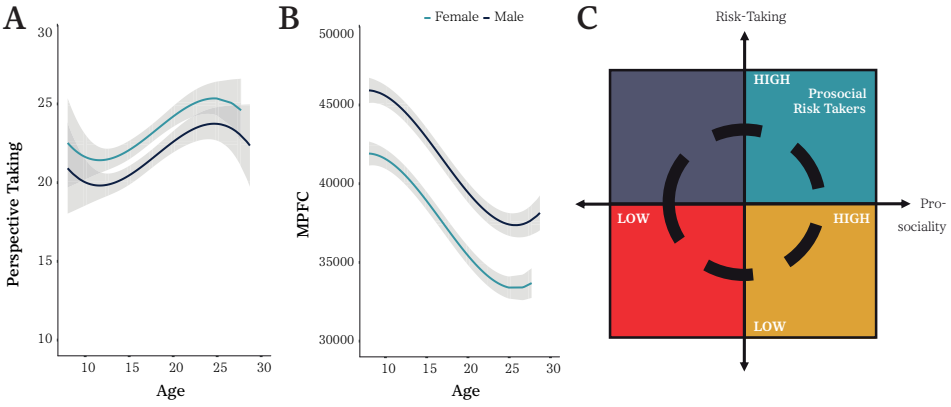


Figure 1. *Developmental trajectories of Perspective Taking* ***(A)*** *and Medial prefrontal cortex* ***(B),*** *in cubic millimeters. Light blue lines indicate females, dark blue lines indicate males, and grey areas mark the 95% confidence interval. Developmental trajectories of BAS scales and NACC are described in Schreuders et al. (2018) and Wierenga et al. (2018), respectively.* ***C.*** *Theoretical model depicting the intersection between risk-taking and prosocial tendencies. Adapted (with permission) from Do et al., 2017.*

Analysis plan

First, to address whether prosocial and rebellious behavior were negatively related, positively related, or not related, we ran a partial correlation analysis on these measures, controlling for age and gender. Second, in our cross-sectional analyses (data from the final wave), we tested which predictors (i.e., empathy, perspective taking, BAS scales) best described prosocial behavior and which predictors best described rebellious behavior (controlling for age and gender). We also tested to which extent these predictors were specific for prosociality, controlling for rebelliousness (i.e., patterns of behavior in the upper right and lower right quadrants of the conceptual model by Do et al. 2017; see Figure 1C) and vice versa (i.e., upper left and lower left quadrant). In addition, to test if and which predictors best described a combination of prosocial and rebellious behavior we created a combined interaction variable of these traits. Here we tested which predictors best described a combination of high levels of rebelliousness and prosociality (upper right quadrant, also referred to as 'prosocial risk takers'; Do et al., 2017). Next, in our longitudinal analyses, we tested whether longitudinal change (i.e., linear slopes) predicted additional variance above initial levels (i.e., intercepts) of our behavioral predictors on prosocial and rebellious behavior, and on their interaction (similar to the cross-sectional analyses). Finally, we tested if structural brain development (i.e., intercepts and slopes) of NACC and MPFC predicted additional variance above the behavioral indices (i.e., above their intercepts and slopes).

Results

Cross-sectional relations among behavioral measures at the final wave

First, we tested the association between the outcome measures Rebellious and Prosocial behavior, controlling for age and gender. A partial correlation showed that these outcome measures were positively correlated (*partial r* = .259, $p < .001$; see Figure 2). Next, we predicted the outcome measures from the other behavioral measures at T3 (BAS scales, Perspective Taking, and Intention to Comfort), while controlling for age and gender. To explore which behavioral predictors best described the dependent variables, we used stepwise regressions. Age and Gender were always included in the model to control for their effects. Table 2 depicts the correlations between the outcome measures (rebellious and prosocial behavior) and the behavioral predictors at T3, controlled for age and gender.

Table 2. Partial correlations between behavioral variables at T3, controlled for age (linear) and gender.

		1	2	3	4	5	6	7
1	Rebellious behavior	-						
2	Prosocial behavior	.259***	-					
3	BAS Drive	.119	.115	-				
4	BAS Fun Seeking	.318***	.175**	.468***	-			
5	BAS Reward Responsiveness	.084	.133*	.378***	.321***	-		
6	IRI Perspective Taking	.097	.261***	.037	.050	.097	-	
7	EMQ Intention to Comfort	.086	.234***	.070	.170**	.078	.237***	-

** p < .05, ** p < .01, *** p < .001*

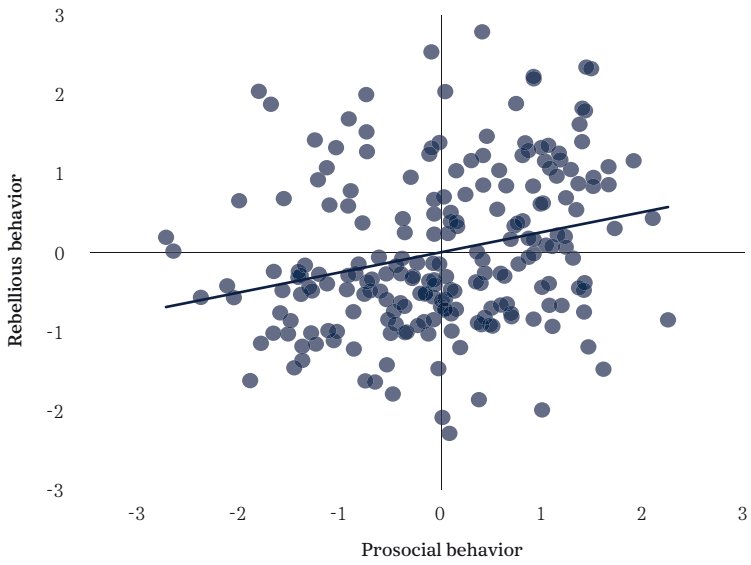


Figure 2. *The positive association between prosocial and rebellious behavior, controlled for age and gender.*

Table 3. Coefficient statistics for the cross-sectional stepwise regressions.

	Prosocial			Rebellious			Prosocial * Rebellious		
Predictor	b	SE	β	b	SE	β	b	SE	β
(Constant)	1.66**	.58	-	-3.70***	.504	-	.106	.523	-
Age	-.03	.01	-.115	.18***	.019	.535	-.044*	.019	-.156
Gender	-.43***	.10	-.264	-.05	.129	-.022	-.130	.134	-.066
Fun Seeking	.06*	.02	.137	.17***	.035	.265	.078*	.036	.147
Perspective Taking	.05***	.01	.219	-	-	-	-	-	-
Empathy	.45*	.18	.156	-	-	-	-	-	-

*$p < .05$, **$p < .01$, ***$p < .001$.

Prosocial behavior

Prosocial behavior was best explained by IRI Perspective Taking, EMQ Intention to Comfort, and BAS Fun Seeking ($R^2 = .228$, $F(5, 250) = 14.798$, $p < .001$, $\Delta R^2 = .018$, $\Delta F(1, 250) = 5.855$, $\Delta p = .016$; Intention to Comfort: $b = .452$, SE = .177, $p = .011$; Perspective Taking: $b = .045$, SE = .013, $p < .001$, Fun Seeking: $b = .059$, SE = .024, $p = .016$; see Table 3). All regression coefficients were positive, indicating that higher levels of the predictor variables were related to higher levels of Prosocial behavior. Note that when adding ARQ Rebellious behavior to the model (after trimming the model from the non-significant predictors Drive and Reward Responsiveness) the effects of BAS Fun Seeking and Perspective Taking remained significant (Fun Seeking: $b = .056$, SE = .028, $\beta = .126$, $p = .049$; Perspective Taking: $b = .053$, SE = .014, $\beta = .257$, $p < .001$) while this was not the case for Intention to comfort ($p = .13$).

Rebellious behavior

Next, we predicted Rebellious behavior from the independent variables. Rebellious behavior was best explained by BAS Fun Seeking, in which higher levels of Fun Seeking were related to higher levels of Rebellious behavior ($R^2 = .38$, $F(3, 209) = 43.39$, $p < .001$, $\Delta R^2 = .07$, $\Delta F(1, 209) = 23.58$, $p < .001$; $b = .169$, SE = .035, $p < .001$; see Table 3). When adding Prosocial behavior to the model, this effect of BAS Fun Seeking remained significant ($b = .147$, SE = .035, $\beta = .230$, $p < .001$).

*Prosocial * Rebellious behavior*

Finally we predicted the combined effect of Prosocial and Rebellious behavior from the other behavioral predictors. This combined variable was creating by Z-transforming Rebellious and Prosocial behavior and then multiplying them, thus creating an

Table 4. Coefficient statistics for the regressions with longitudinal predictors.

	Prosocial			Rebellious		
Predictor	b	SE	β	b	SE	β
(Constant)	2.595***	.481	-	-3.913***	.688	-
Age	-.028*	.013	-.126	.178***	.019	.523
Gender	-.481***	.095	-.295	-.060	.134	-.025
Fun Seeking intercept	.068*	.032	.155	.179***	.045	.291
Fun Seeking slope	.078**	.028	.192	.727***	.144	.372
Perspective Taking intercept	.059***	.014	.290	.007	.020	.025
Perspective Taking slope	.078**	.028	.179	.057	.040	.089

**p < .05, **p < .01, ***p < .001.*

*No significant findings were observed for the interaction variable Prosocial * Rebellious.*

interaction variable (Prosocial * Rebellious). Higher values indicate relatively more rebellious, as well as more prosocial behavior ('prosocial risk-takers'), while lower values indicate relatively lower rebellious and prosocial behavior. This interaction variable was predicted by BAS Fun Seeking only (R^2 = .045, $F(3, 209) = 3.29$, p = .022, ΔR^2 = .021, $\Delta F(1, 209) = 4.69$, Δp = .032; b = .078, SE = .036, p = .032; Table 3), with higher levels of Fun Seeking related to higher values of this combined variable.

Together, these cross-sectional findings set the stage for testing our hypotheses on longitudinal associations between these behavioral measures and Prosocial and Rebellious behavior. From these analyses, IRI Perspective Taking and BAS Fun Seeking appeared consistent predictors for both prosocial and rebellious behavior. We therefore aimed to investigate whether these variables had longitudinal predictive value as well. Hence, we proceeded with these variables in the subsequent analyses.

Longitudinal predictions of Prosocial and Rebellious behavior

Next, we predicted Prosocial behavior, Rebellious behavior, and the interaction variable Prosocial * Rebellious from the longitudinal Perspective Taking and BAS Fun Seeking data. That is, we tested whether initial levels of Perspective Taking and BAS Fun Seeking (i.e., intercepts; see Methods for further specification) predicted variance above age and gender. Next, we tested whether the rate of change in these variables (i.e., linear slopes) predicted additional variance above intercepts and age and gender. Coefficients and significance levels of the predictors are presented in Table 4.

Prosocial behavior

For prosocial behavior, we observed that BAS Fun Seeking intercept and Perspective Taking intercept predicted additional variance above age and gender, and additionally, that the slopes predicted additional variance above intercepts (R^2= .22, $F(6,252) = 11.56$ $p < .001$, ΔR^2= .05, $\Delta F(2, 252) = 7.56$, $\Delta p = .001$; Perspective Taking intercept: $b = .06$, SE = .014, $p < .001$, Fun Seeking intercept: b = .07, SE = .032, p = .038, Perspective Taking slope: b = .08, SE = .027, p = .006, Fun Seeking slope b = .262, SE = .102, p = .011). That is, greater longitudinal increases in BAS Fun Seeking and Perspective Taking predicted higher levels of prosocial behavior at T3, above initial levels of BAS Fun Seeking and Perspective Taking. When including Rebellious behavior in the model, the effects of BAS Fun Seeking intercept and slope were no longer significant (intercept: p = .27, slope: p = .099).

Rebellious behavior

For Rebellious behavior, we observed that greater increases in BAS Fun Seeking was related to higher levels of Rebellious behavior at T3, above initial levels of BAS Fun Seeking and age and gender (R^2= .40, $F(6, 203) = 22.79$, $p < .001$, $\Delta R^2 = .083$, $\Delta F(2, 203) = 14.09$, $\Delta p < .001$, intercept: b = .179, SE = .045, $p < .001$, slope: b = .727, SE = .144, $p < .001$). No effects of Perspective Taking were observed. When including Prosocial behavior in the model these findings remained significant.

*Prosocial * Rebellious behavior*

Finally, we tested whether the intercepts and slopes of Fun Seeking and Perspective Taking predicted the interaction variable Prosocial * Rebellious. Here, no significant findings were observed.

Longitudinal predictions of Prosocial and Rebellious behavior: behavior and brain

Finally, we tested whether development of brain structures predicted Prosocial and Rebellious behavior at T3. That is, we reran the behavioral longitudinal analyses on Prosocial and Rebellious behavior, and added intercepts and slopes of NACC and MPFC above the behavioral predictors. Only for Rebellious behavior did we observe a small but significant effect of MPFC slope above the behavioral predictors (R^2= .46, $F(12, 169) = 11.99$, $p < .001$, $\Delta R^2 = .05$, $\Delta F(2, 169) = 8.06$, $\Delta p < .001$; b = -.001, SE = .000, β = -.253, p = .025), indicating that greater reductions in MPFC volume were associated with lower levels of Rebellious behavior at T3. When including Prosocial behavior in the regression model, this effect remained significant. Finally, the regressions on Prosocial behavior and the interaction variable yielded no significant findings.

Discussion

This study set out to test the behavioral and neural predictors leading to prosocial and risk-taking behaviors in adolescents and young adults using a three-wave longitudinal design. The results showed three main conclusions. First, prosocial and rebellious behavior were positively correlated. Second, perspective taking and empathy uniquely predicted more prosocial behavior. However, current levels, as well as longitudinal change, in fun seeking behavior were positive predictors of both prosocial and rebellious behavior. Finally, these findings co-occurred with pronounced decreases in volumes of the nucleus accumbens and medial prefrontal cortex, of which greater declines in medial prefrontal cortex predicted less rebellious behavior. These findings are interpreted in the context of current conceptualizations of adolescent development as a period of both risks and opportunities (Crone & Dahl, 2012; Do et al., 2017), and the need to better understand individual differences in developmental trajectories in behavioral and brain development to predict developmental outcomes (Foulkes & Blakemore, 2018).

Developmental trajectories

What predicts who will become prosocially oriented and who will show rebellious behavior? In this study we tested this question using occurrences of prosocial and rebellious behaviors as outcome measures, and we aimed to gain a better understanding of subtypes of individuals, rather than using the dichotomy of separable outcomes. This approach was driven by the observation that the seemingly paradoxical measures prosocial and rebellious behavior were in fact positively correlated, suggesting that the same developmental processes may result in both types of behaviors (Schriber & Guyer, 2015). Indeed, cross-sectionally, we observed that higher levels of fun seeking were related to both prosocial and rebellious behaviors, as well as their interaction. Previous studies already reported relations between approach tendencies and risk taking (Steinberg, 2007), but the current study demonstrated that the same fun seeking tendencies may also be related to prosocial tendencies, and the combination of prosocial and rebellious behaviors. These findings fit with the hypothesis that adolescent development may be a tipping point for how interacting social-affective systems may influence trajectories of development (Crone & Dahl, 2012; Schriber & Guyer, 2015). Furthermore, consistent with prior studies, high levels of empathy and social perspective taking uniquely predicted prosocial behavior, but these measures were not related to rebellious behavior. The relations between empathy, perspective taking, and prosocial behaviors have been well documented (Eisenberg, 2000; Overgaauw, Guroglu, Rieffe, & Crone, 2014; Tamnes

et al., 2018), and previous studies also reported relations between emotionality and prosocial behavior (Eisenberg et al., 1994).

From our longitudinal analyses, we observed that prosocial and rebellious behavior were not only predicted by initial levels of perspective taking and fun seeking (i.e., intercepts), but also the change over time (i.e., linear slopes). Consistent with previous longitudinal studies, we observed that IRI perspective taking and BAS Fun Seeking emerged in adolescence, following a cubic increasing developmental slope (Hawk et al., 2013; Urosevic et al., 2012; see also Schreuders et al., 2018). In particular, those individuals who showed the greatest increase in perspective taking and fun seeking during adolescent development showed more prosocial behavior at the final measurement. In addition, individuals who showed the largest increase in fun seeking during adolescent development showed more rebellious behavior at the final measurement. The common contribution of fun seeking to both prosocial and rebellious behavior suggests that developmental increases in this fun seeking tendency may be a differential susceptibility marker in adolescence that may contribute to different types of behaviors (Do et al., 2017; Schriber & Guyer, 2015; Telzer, 2016). That is, specifically the tendency to approach a possibly rewarding event in the spur of the moment, may lead individuals to develop prosocial behaviors in some instances, whereas in other instances it may lead individuals to develop rebellious behaviors. Finally, these findings are consistent with the suggestion that change measures are informative for detecting development (Crone & Elzinga, 2015).

An important question was the extent to which these predictors were specific for subgroups of prosocial or rebellious individuals. Previous studies have mainly focused on the development of either prosocial development or risk-taking development, but this may have led to an oversight of individuals who develop these behaviors in parallel. The analyses that examined rebellious behavior controlling for prosocial behaviors showed that fun seeking was a consistent factor in predicting rebellious outcomes. However, when examining the relation between prosocial behavior while controlling for rebellious behavior, the relation with fun seeking was no longer significant, suggesting that some of this variation was driven by rebellious individuals. Finally, change in fun seeking was not related to a combined variable of high prosocial and high rebellious behavior, suggesting that this particular change may not be predictive for a specific subgroup of 'prosocial risk takers'. Together, these findings tentatively support the view of a differential susceptibility marker (fun seeking) that may predict developmental outcomes in the domains of prosocial and rebellious behaviors (Do et al., 2017), although more research is needed to confirm these findings.

Brain development and the relation with developmental outcomes

Prior studies have consistently reported that brain regions important for approach behaviors and social functioning show pronounced changes in gray matter (Mills, Goddings, Clasen, Giedd, & Blakemore, 2014; Mills et al., 2014). We previously reported a developmental decline in NACC volume in participants included in the current data set (Wierenga et al., 2018). The current study further confirmed a similar decline in volume of MPFC, consistent with prior work(Mills et al., 2014), and extended this to three subregions in the MPFC (superior frontal, rostral anterior cingulate, and caudal anterior cingulate, see supplement). Previous studies have demonstrated the importance to distinguish between subregions in the MPFC (Pfeifer & Peake, 2012). Here, we demonstrated that all three subregions of the MPFC showed cubic developmental patterns with relatively rapid declines during mid to late adolescence. The results are comparable to prior work that has demonstrated gray matter volume declines in prefrontal and parietal cortex across several adolescent samples from multiple sites (including the current sample; Tamnes et al., 2017).

The question of how individual patterns of brain development predicted occurrences of prosocial and rebellious behaviors was addressed by adding NACC and MPFC volume intercepts and slopes to the regression models. Only MPFC slope was related to the behavioral outcome measures, such that greater decreases in MPFC were negatively related to rebellious behavior. More specifically, stronger declines in volume, or faster maturation, was related to lower levels of rebellious behavior at the final wave. This finding fits well with prior functional neuroimaging studies, showing that longitudinal declines in functional coupling between MPFC and ventral striatum were associated with decreases in self-reported risk taking (Qu, Galvan, Fuligni, Lieberman, & Telzer, 2015). In addition, MPFC functional activation has consistently been found during high-risk decision-making, and with reward outcome processing following risky decisions during adolescence (Blankenstein et al., 2018; Van Leijenhorst et al., 2010). However, even though statistically significant, the effect was modest. It is currently unclear if this has predictive value and future studies should confirm if this relation exists in other samples. Furthermore, adding brain volume to the model after controlling for age, gender, perspective taking, and fun seeking intercepts and slopes, possibly accounted for little additional variance. In future studies it will be important to test these relations in new samples, but the current findings provide an important starting point for a possible role of the MPFC in these processes.

It was unexpected that relations were only observed for MPFC and not for NACC. Prior studies found relations between NACC volume and behavioral approach measures (Urosevic et al., 2012). Functional activation in the NACC is

also consistently observed as an important marker for reward reactivity in studies examining both risk taking behaviors as well as prosocial behaviors (Telzer, Fuligni, Lieberman, & Galvan, 2014). Future studies may also complement these findings with functional MRI measures specifically targeting prosocial and rebellious behaviors. For example, recent reviews show that especially for subcortical brain regions, functional activation is more state dependent (Herting, Gautam, Chen, Mezher, & Vetter, 2017), whereas studying volume changes over time does not capture these moment-to-moment fluctuations. Future research could examine more daily fluctuations in brain responses to fun seeking and perspective taking contexts, and test the relation with prosocial and rebellious outcomes.

Limitations and Future directions

This study has several strengths, including a longitudinal design with three waves spanning ages 8-29 years, relatively large sample sizes, and the inclusion of behavior and brain measures. The age coverage in this study is more extended than in previous adolescent research, which is important when focusing on developmental outcomes. However, the study also has several limitations and open questions that should be addressed in future research. First, not all measurements were available at each time point. Specifically, the empathy questionnaire was only available at the final wave and perspective taking was only available at the second and final wave for the majority of participants. The greater contribution of BAS fun seeking may therefore be related to more measurement waves (available at all waves). Second, the current study made use of self-report measures, because previous studies showed that these have more stability than experimental tasks (Peper et al., 2018). The selection of measures in this study all had sufficient reliability and ICC values, increasing the strength of the results. However, questionnaires do not capture the variations in behavior under different experimental contexts and may be sensitive to social desirability. Therefore, an important avenue for future research is to develop experiments with good test-retest reliability which assess prosocial and rebellious behaviors, and possibly test the specific role of fun seeking tendencies in these dynamic situations. Third, in our analyses we controlled for age and did not examine age-specific associations. Future research, preferable using larger sample sizes, may further unravel whether our findings are specific to or differentially pronounced in different phases of adolescence, and across males and females. Finally, there was no assessment of environmental influences on behavioral outcomes. This is an important next step for a test of developmental susceptibility, to examine if the same sensitivity can lead to multiple developmental outcomes, depending on how environmental influences interact with sensitivity measures.

Conclusions and broader implications

This study tested the association between prosocial and rebellious behavior, and developmental pathways leading to these behaviors, in adolescent development. The results confirmed that seemingly paradoxical prosocial and rebellious behavior are positively associated, and show an important contribution of fun seeking to these behavioral outcomes, where both current levels, as well as longitudinal changes, predicted these outcomes. These findings suggest that fun seeking may be a differential susceptibility marker for diverse adolescent outcomes (Do et al., 2017; Schriber & Guyer, 2015; Telzer, 2016). Furthermore, there was preliminary evidence that faster adolescent brain development (i.e., faster maturity), specifically of the MPFC, predicted less rebellious behavior, contributing to the current question how structural brain development relates to adolescent behaviors (Foulkes & Blakemore, 2018). These findings point towards a more differentiated perspective on adolescent development, where similar sensitivity markers may lead to multiple developmental outcomes.

Supplementary materials

Mixed model building procedure for longitudinal measures

To test which developmental trajectories best described the longitudinal measures (Perspective Taking, BAS, and brain structures), we used a mixed-models approach in R using the *nlme* package (R Core Team, 2014; Pinheiro, Bates, DebRoy, Sarkar, & R Core Team, 2013). For all measures, we tested for linear, quadratic, and cubic effects of age, reflecting an age-related increase or decrease, a non-linear adolescent-specific U- or inverted-U pattern, and a non-linear adolescent emerging or declining pattern, respectively. Age was a polynomial predictor, and because the data were nested within participants we included a random intercept for participants in our models (see also Schreuders et al., 2018). Finally, after determining which age pattern best described the data, we tested whether Gender (dummy-coded 0 (female) or 1 (male)) improved model fit. In the case of a main effect of Gender, we also tested for Age*Gender interaction effects. We used the Akaike Information Criterion (AIC; Akaike, 1974) to compare model fits and the log-likelihood ratio to assess significance of model improvement. We also report the Bayesion Information-Criterion values (BIC; Schwarz, 1978). Model fit summaries are depicted in Table S1.

Longitudinal developmental trajectories

Here we describe the longitudinal trajectories of the behavioral and neural predictors. The developmental trajectory of the BAS scales have previously been described in Schreuders et al. (2018). In brief, BAS Drive shows a cubic age effect for males and a linear increase in girls; BAS Fun Seeking shows a cubic effect of age (depicting an adolescent-emergent pattern of fun seeking across development), but no effect of Gender; and BAS Reward Responsiveness shows a cubic effect of age and a main effect of Gender (with higher levels in girls than in boys).

The longitudinal development of IRI Perspective Taking has not yet been reported. The best-fitting model included a cubic effect of age and a main effect of Gender, described best as an adolescent-emergent pattern of Perspective Taking increasing into adulthood, and higher levels of Perspective Taking in girls than in boys (see Figure 1A in the main manuscript and Table S1 and Table S2 below). No Age * Gender interaction effect was observed.

The developmental trajectory of nucleus accumbens volume is described in (Wierenga et al., 2018) and shows a linear decrease with age, and greater volumes in boys than in girls. The development of MPFC volume has not yet been reported. MPFC volume was best described by a declining cubic effect of age and a main effect of Gender (with boys having greater volumes than girls; Figure 1B in the main

manuscript; Table S1, Table S2). Developmental trajectories of the MPFC subregions (i.e., superior frontal, rostral anterior cingulate, and caudal anterior cingulate of the Desikan-Killiany-Tourville atlas) also show similar cubic effects of age and a main effect of Gender (Figure S1, Table S3). Finally, no Age * Gender interaction effects were observed in any of the brain structures.

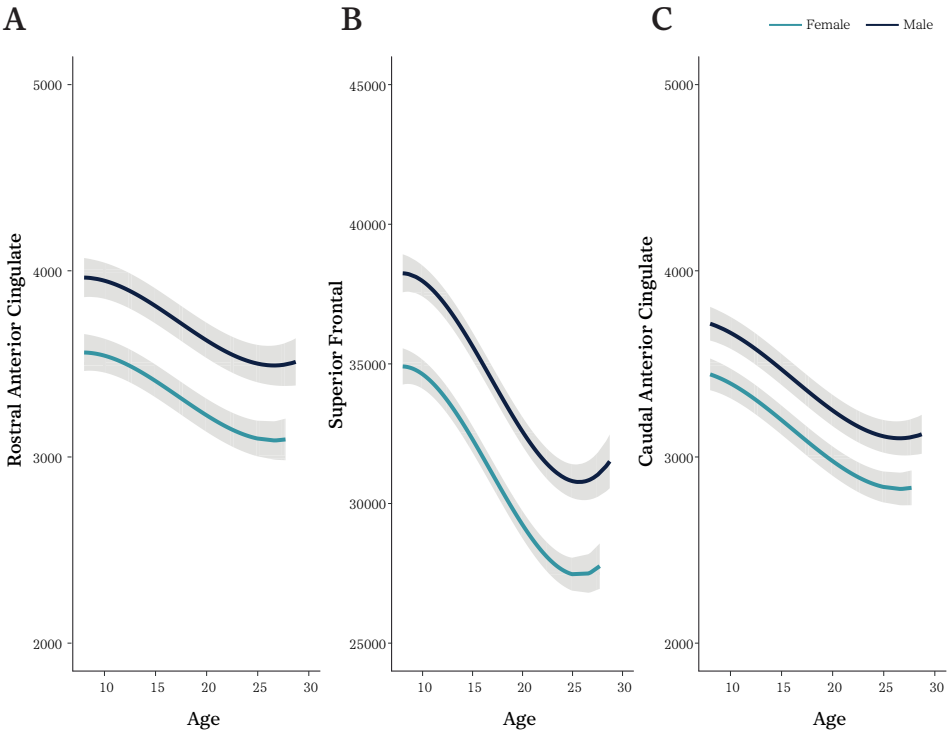


Figure S1. *Developmental trajectories of MPFC subregions (in cubic millimeters).* ***A.*** *Rostral anterior cingulate.* ***B.*** *Superior frontal.* ***C.*** *Caudal anterior cingulate. Light blue lines indicate females, dark blue lines indicate males, and grey areas mark the 95% confidence interval.*

Table S1. AIC and BIC values for Null, Linear, Quadratic, and Cubic models to describe the relation with age and each of the longitudinal measures.

	Null		Linear	
Dependent variable	AIC	BIC	AIC	BIC
Perspective Taking	3130.85	3143.93	3098.27	3115.71
MPFC total	12727.04	12740.6	12239.42	12257.52
Rostral anterior cingulate	9388.46	9402.04	9153.16	9171.27
Superior frontal	12525.85	12539.43	12042.69	12060.80
Caudal anterior cingulate	9326.06	9339.64	8851.66	8869.77

Bold values indicate best fit measures.

Table S2. Coefficient statistics for the longitudinal mixed-model results of Perspective Taking and the combined MPFC.

	Perspective Taking		MPFC	
Predictor	b	SE	b	SE
(Constant)	36.52 ***	9.09	35591.76 ***	1806.29
Age Linear	-3.08 *	1.55	1798.58 ***	321.63
Age Quadratic	.19 *	.09	-149.81 ***	18.72
Age Cubic	-.004 *	.001	2.97 ***	.35
Gender	-1.61 ***	.37	4010.11 ***	426.62

$^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

Quadratic		Cubic		Cubic + Gender	
AIC	BIC	AIC	BIC	AIC	BIC
3099.92	3121.73	3095.40	3121.57	**3079.16**	**3109.69**
12233.52	12256.15	12167.24	12194.40	**12092.21**	**12123.90**
9154.61	9177.24	9136.59	9163.75	**9103.10**	**9134.78**
12036.86	12059.50	11969.49	11996.65	**11891.87**	**11923.56**
8840.53	8863.16	8808.85	8836.00	**8789.78**	**8821.47**

Table S3. Coefficient statistics for the longitudinal mixed-model results of MPFC subregions.

	Rostral anterior cingulate		Superior frontal		Caudal anterior cingulate	
Predictor	b	SE	b	SE	b	SE
(Constant)	3241.76 ***	169.15	29081.75 ***	1612.86	3301.60 ***	126.95
Age Linear	90.09 **	29.42	1637.58 ***	287.85	62.72 **	21.74
Age Quadratic	-7.42 ***	1.71	-135.09 ***	16.75	-6.73 ***	1.27
Age Cubic	.14 ***	.03	2.68 ***	.31	.139 ***	.02
Gender	402.52 ***	65.61	3334.98 ***	348.14	272.07 ***	58.35

*$p < .05$, **$p < .01$, ***$p < .001$.

Chapter 7

Summary and General Discussion

Summary

The primary aim of this thesis was to unravel the behavioral and neural mechanisms underlying risky decision-making in adolescents. First, I decomposed risky choice behavior into their underlying components (risk and ambiguity attitudes), and investigated their neural mechanisms in adolescence. Second, I focused on how individual differences in real-life (risky) decision-making contribute to our understanding of adolescence as period of risks versus opportunities.

Risk and ambiguity attitudes in adolescence

In the first empirical chapter **(chapter 2)**, I applied a behavioral wheel of fortune paradigm in a developmental sample of adolescents and young adults (N = 157, age range 10-25 years). Here, participants were presented with pairs of wheels and were asked to choose which wheel they preferred to (hypothetically) spin. One wheel was a consistent sure gain (i.e., a 100% chance of gaining a small amount of money). The other wheel reflected a gamble, which could result in more money but could also result in nothing. This gambling wheel thus varied in the gain amount and in the probability of gaining that amount. In addition, to manipulate the level of ambiguity associated with the gain probability, we varied the size of various 'lids' that could cover more or less of the gambling wheel. Using a model-based approach, I tested 1) the developmental trajectories of risk and ambiguity attitudes across adolescent development and 2) the extent to which risk and ambiguity attitudes were related to risk taking in real life. Given that risk taking in real life more often takes place within an ambiguous, rather than risky, choice context (i.e., real life risks rarely present known probabilities), it was expected that ambiguity attitude would show more prominent development change compared with risk attitude, and that real-life risk taking would be more prominently related to ambiguity attitude than to

risk attitude. A linear increase in ambiguity attitude, but not in risk attitude, was observed, such that ambiguity aversion slightly increased across adolescence. Given that ambiguity aversion is not yet present in childhood (8-9 years old; Li, Brannon, & Huettel, 2014), this finding suggests that ambiguity aversion may emerge in early adolescence. Moreover, real-life risk-taking behavior was related to attenuated ambiguity aversion, but not to risk aversion, further suggesting that ambiguity may be better reflective of risk taking in real life.

Additionally, in this study I explored whether social context influenced risk and ambiguity attitude. Specifically, I studied the effects of peers' choices as a source of information for individuals' own risky choices .To this end I added a social condition to the wheel of fortune task in which participants were shown the decisions of a high risk-taking peer before making their own choice. Tentatively, it was observed that individuals' risk attitudes, but not ambiguity attitudes, became more aligned (i.e., more risk seeking) with that of the observed choices, which appeared most pronounced for the youngest participants (10-12 years old). This finding suggests that risk taking may vary under conditions of social advice, and sets the stage for future studies on peer information in conditions varying in uncertainty.

In sum, these findings suggest that early adolescence (10-12 years) may be a starting point for emerging ambiguity aversion as is typically observed in adulthood, and that behavior under ambiguity may be a better naturalistic reflection of adolescent risk taking in daily life. Furthermore, first steps were taken to study effects of observed information from peers in a risky and ambiguous context. Most importantly, this chapter illustrates the potential of using a model-based method of disentangling risk and ambiguity attitude in a developmental sample, and investigating individual differences in these attitudes.

Risk and ambiguity attitudes in the adult brain

In **chapter 3** I studied risk and ambiguity processing in 50 young adults (18-28 years), and charted their underlying neural mechanisms. The goal of this study was to examine to what extent these two types of risk are processed differentially within individuals. A way to examine the neural specificity of risk and ambiguity processing is to include individual differences in risk and ambiguity attitudes, which I estimated using the wheel of fortune task. Subsequently I related these risk and ambiguity attitudes to neural activation during a simplified fMRI version of the wheel of fortune task. This fMRI task resulted in a robust measure of neural activation of risky and ambiguous gambling in a general network typically associated with risky decision-making. Including risk and ambiguity attitudes revealed that relatively more risk-seeking attitudes were associated with greater activation in medial and

lateral orbital frontal cortex; while more ambiguity-seeking attitudes were reflected in greater medial temporal cortex activation. These findings suggest that different neural correlates underlie individual differences in risk and ambiguity attitude, and that risk and ambiguity impact overt risk-taking behavior in different ways.

Another question I addressed in this study was whether the neural coding of reward outcome processing differed following risky versus ambiguous gambling. The fMRI version of the wheel of fortune task therefore also included a reward outcome phase (i.e., gains and no gains, following risky and ambiguous gambles). Although ventral striatum activation reflected reward outcome processing irrespective of risk or ambiguity, greater dorsomedial prefrontal cortex activation was specifically observed during reward outcome processing following ambiguity. This activation pattern may function as a general signal of uncertainty coding, which may be particularly salient following ambiguous decision contexts. Together, this adult study set the stage for a developmental perspective on the neural coding of risk and ambiguity attitudes. In the next chapter I build on these findings and those described in chapter 2, in a study on the neural tracking of adolescents' subjective choice valuation under risk and ambiguity.

Subjective value tracking under risk and ambiguity in the adolescent brain

In **chapter 4**, I further tested how risk and ambiguity attitudes are coded in the brain, in a second adolescent sample spanning a broad age range (N = 188, 12-22 years). However, here I integrated participants' separately estimated risk and ambiguity attitudes, with the fMRI task during choice, on a trial-by-trial basis. That is, I inferred participants' *subjective value* of the choices presented in the fMRI task. As such, I studied which brain regions coded changes in subjective choice valuation under risk versus ambiguity, and possible overlap between these conditions. Parametric fMRI analyses showed that increasing subjective value under risk was coded by activation in ventral striatum and superior parietal cortex. In contrast, decreasing subjective value under ambiguity was coded by dorsolateral prefrontal cortex and superior temporal gyrus activation. Finally, dorsomedial prefrontal cortex activation reflected a general signal of decreasing subjective valuation, such that this region coded subjective value in both conditions. Interestingly, preliminary evidence suggested that these findings were less pronounced in a model testing for objective expected value (that is, the probability * amount, not weighted by individuals' risk and ambiguity attitudes). This suggests that making use of subjective - rather than objective - measures of valuation, is more meaningful when studying the neural underpinnings of adolescent choice valuation. Indeed, although limited age effects

were observed, there were pronounced individual differences in behavioral risk and ambiguity attitudes, which were reflected in participants' perceived riskiness of the risky and ambiguous wheels. Together, these findings indicate that distinct as well as similar patterns of brain activation underlie subjective value tracking under risk and ambiguity in adolescence, and illustrates the potential of combining model-based behavioral analyses with (parametric) fMRI in adolescents, which may ultimately explain who takes risks and why.

Individual differences in task-based and self-reported risk taking under risk and ambiguity in the adolescent brain

In **chapter 5**, I focused on the relation between neural risk and ambiguity processing and individual differences in risk-taking tendencies. Specifically, I focused on individual differences in task-related risk taking, as well as self-reported real-life risk taking, in relation to the neural correlates of risky and ambiguous choice and reward outcome processing (N = 198, 12-25 years, including the sample of chapter 4). Distinct neural correlates were observed when contrasting risky and ambiguous gambling, with risk more pronounced in parietal cortex and ambiguity more prominently with dorsolateral prefrontal cortex activation, as well as medial prefrontal cortex during reward outcome processing (as in chapter 2). When including individual differences in task-related risk taking (i.e., proportion gambling under risk and under ambiguity), a positive association was found in the ventral striatum activation in the choice phase, specifically for risk, and a negative association with insula and dorsomedial prefrontal cortex activation, specifically for ambiguity. Moreover, lateral prefrontal cortex activation during reward outcome processing seemed a prominent marker for individual differences in task-related risk taking under ambiguity, and indices of real-life risk taking (i.e., self-reported rebellious behavior and the drive to obtain rewards). Here, lower levels of risk taking were associated with greater dorsolateral prefrontal cortex activation. Together, these findings demonstrate the importance of including multiple risk-taking measures (lab-based and self-report measures), and multiple decision contexts (risk and ambiguity; choice and outcome), in understanding the neural mechanisms underlying adolescent risk taking. As such, this multidimensional perspective on risk taking contributes to our understanding of which individuals are most prone to display risk-taking behavior.

Predicting risk taking and prosociality from longitudinal behavioral and structural brain development

Finally, in **chapter 6,** I further studied adolescent susceptibility to risk taking. However, given that adolescence may also be an important phase for the development

of positive, other-oriented behavior, I also tested contributions to prosocial behavior, that is, behaviors intended to benefit someone else. To date, the relation between risk-taking behavior and prosocial behavior has been overlooked, while this is key to our understanding of how these two seemingly paradoxical behaviors develop in tandem in adolescence. This study addressed whether risk-taking behavior and prosocial behavior are related constructs in adolescence, and which processes predict these two disparate behaviors. To these ends I used longitudinal self-report and structural brain development data from the three-wave, biannual, Braintime study (N = 210 at the final wave, 8-29 years, including the sample of chapter 4 and 5). First, risk-taking behavior and prosocial behavior assessed at the final wave were positively correlated. Furthermore, it was found that higher levels of empathy, and perspective taking abilities (current levels and longitudinal change) uniquely predicted prosocial behavior, whereas higher levels of fun-seeking tendencies (current levels and longitudinal change) predicted *both* prosocial and risk-taking behaviors. Moreover, these changes were accompanied by reductions in nucleus accumbens and medial prefrontal cortex volume across development, regions previously implicated in both risk-taking and prosocial behavior. Preliminary evidence indicated that faster maturity of the medial prefrontal cortex was related to less rebellious behavior at the final wave, suggesting that structural brain maturity may be an informative predictor of behavior. This study points towards a 'differential susceptibility' marker (namely, fun seeking), as a predictor of diverse adolescent outcomes. Understanding the possible mechanisms that underlie these two seemingly disparate behaviors may help to identify pathways for reducing risks and promoting opportunities often inherent in adolescence, and point towards a more differentiated perspective on adolescent development.

General Discussion

The studies presented in this thesis converge to a number of main findings. First, I demonstrated that risk and ambiguity attitudes are distinguishable components of risky choice behavior in adolescence and (young) adulthood. That is, I showed that risk and ambiguity are reflected in distinct behavioral attitudes, processed by different underlying mechanisms, and separately inform – individual differences in – overt risk-taking behavior in adolescence. Second, the studies in this thesis suggest that adolescence may be a period of risks, but also of opportunities. For instance, by investigating risk-taking and prosocial behavior in relation to individual differences in their behavioral and neurobiological pathways, I provided evidence

that a single underlying trait may result in these diverse outcomes. In the following sections, I discuss this thesis' main findings in further detail within a neuroeconomic developmental framework, and provide recommendations for future research.

Risk and ambiguity: Distinguishable components underlying risk-taking behavior across adolescence

Across the first three empirical chapters, I showed that risk and ambiguity attitude can be behaviorally disentangled within individuals using a model-based approach. Across three separate samples (chapters 2, 3, and 4), risk and ambiguity attitude were not significantly correlated, suggesting they may reflect different aspects of risky choice behavior. In addition, I focused on the underlying neural mechanisms of risk and ambiguity (attitude) in an adult and adolescent sample (chapters 3; and chapters 4 and 5, respectively). Here I showed that risk and ambiguity are reflected in different brain systems, when considering individuals' risk and ambiguity attitudes. A number of key regions specifically tracked risk and ambiguity preferences. That is, in chapter 3 (adults) greater risk seeking attitudes positively scaled with activation in the medial and lateral orbital frontal cortex, regions part of the valuation network. Interestingly, in chapter 4 (adolescents) we observed that subjective value increases under risk (determined with individuals' risk attitudes), were coded by ventral striatum activation, a region also part of this network, and parietal cortex. Activation in this latter region was also heightened when contrasting risky versus ambiguous gambling in chapter 5. Furthermore, in chapter 3, greater ambiguity-seeking attitudes were related to greater temporal cortex activation, while in chapter 4 subjective value decreases under ambiguity were also coded in temporal cortex activation. Another ambiguity-specific region was the dorsolateral prefrontal cortex, which coded subjective value decreases under ambiguity (chapter 4), was heightened when contrasting ambiguous versus risky gambling (chapter 5), and showed greater reward activation for individuals who gambled less often under ambiguity (chapter 5). Finally, the (dorso)medial prefrontal cortex may reflect a common signal of uncertainty, since this region coded subjective value decreases under risk *and* ambiguity during choice (chapter 4). However, lower mean levels of gambling under ambiguity, but not risk, were related to greater activation in this region during choice (chapter 5). Moreover, during outcome this region particularly differentiated between gain and no gain outcomes following ambiguous gambles (chapters 2 and 5). This suggests the dorsomedial prefrontal cortex codes general uncertainty, but may be especially pronounced in ambiguous contexts. In sum, whereas valuation regions of the brain (e.g., ventral striatum, OFC, parietal cortex) primarily reflect explicit risk, conflict- and uncertainty-related regions (dorsolateral

PFC, temporal cortex, dorsomedial PFC) seem to primarily reflect ambiguous risk. The studies in this thesis thus point towards a neural distinction between risk and ambiguity in adolescence and (young) adulthood, which are particularly evidenced when including individual differences in behavior under risk and ambiguity.

Across studies, there were limited developmental effects, but prominent individual differences in behavior under risk and ambiguity. That is, although in chapter 2 we observed a linear increase in ambiguity aversion with age, we did not observe a similar effect in chapter 4 and 5. Similarly, risk attitude did not show consistent age effects across studies. The different age ranges across samples seem to suggest that a more narrow age range (starting at 12 years; chapters 4 and 5) results in less pronounced developmental differences than a broader age range (starting at 10 years; chapter 2). Furthermore, as described in chapters 4 and 5, there were no prominent age effects on neural activation under risk and ambiguity. Other studies did find more pronounced age differences in risk and ambiguity attitude, such as Tymula et al. (2012) who compared a group of adolescents (12-17 years) with a group of older adults (30-50 years). Here, adolescents were more tolerant towards ambiguity, and more averse to risk, than adults. Another, more recent, study on risk and ambiguity attitude in participants aged 8-22 years found pronounced age differences, but only in a loss frame (van den Bos & Hertwig, 2017). Specifically, a linear decrease in risk seeking with age was observed, and a quadratic peak in ambiguity tolerance in mid-adolescence (van den Bos & Hertwig, 2017). Together, these disparate findings across studies highlight the importance of 1) replication across different samples, 2) sample size, 3) the specific age ranges included, and 4) different choice contexts (i.e., gain versus loss), in determining the robustness of age effects.

Another explanation for the limited developmental differences across different studies is the relatively 'cold' nature of the wheel of fortune paradigm (e.g., see Defoe, Dubas, Figner, & van Aken, 2015; Rosenbaum, Venkatraman, Steinberg, & Chein, 2018). That is, a 'hot', affectively-laden task that includes reinforcing decision outcomes (such as the Balloon Analogue Risk-Taking task; e.g., Braams, van Duijvenvoorde, Peper, & Crone, 2015), or the presence of peers (such as the Stoplight driving game; e.g., Chein, Albert, O'Brien, Uckert, & Steinberg, 2011), is more likely to yield pronounced age differences than a 'cold', description-based task (e.g., the behavioral wheel of fortune paradigm in the current thesis) in which choice preferences are assessed in a relatively neutral context (Defoe et al., 2015). Future studies may test whether ambiguity, given its more naturalistic reflection of real life, heightens the affective nature of a relatively 'cold' task.

In addition to influencing affective processing, a recent review suggested that ambiguity (or less information) may lower the engagement of cognitive control and

therefore may result in less advantageous decision-making (Li, 2017). As such, the recruitment of cognitive control is flexible based on the available information.

Furthermore, this review suggests that this cognitive control recruitment interacts with age, such that children make poor decisions when information is lacking (such as in ambiguity), but also show the most improvement when information is present, also referred to as a 'flexing dual-systems' model (Li, 2017). The current thesis provides evidence that cognitive control regions like the lateral prefrontal cortex are involved in ambiguity processing (chapter 4, 5), but we did not observe pronounced age effects on neural risk and ambiguity processing. Although the current studies focused more on a neuroeconomic than imbalance perspective, an opportunity for future research is to integrate these two views, by including participants from childhood and early adolescence (8-10 years, an age range in which the most pronounced changes in ambiguity preferences may occur (chapter 2; Li et al., 2014).

Adolescence as a developmental phase of risks and opportunities

A second overarching goal of this thesis was to investigate how individual differences in risk-taking tendencies inform our understanding of adolescence as a period of risks and opportunities. In all studies, individual differences were examined across a variety of risk-taking domains, such as risk and ambiguity attitude (chapters 2, 3, and 4; discussed above), but also indices of real-life risk taking, trait-like reward sensitivity (chapters 2, 5, and 6), and social functioning (chapter 6). As shown across studies, these individual differences help us to better understand the underlying mechanisms of risk-taking behavior, yet also inform our understanding of adolescence as a period of risks and opportunities.

For instance, particularly in chapter 2 I showed that ambiguity attitude was related to real-life reckless behavior. On the neural level, it was showed that the lateral prefrontal cortex (a region particularly implicated in ambiguity processing, see above), was related to real-life risk taking, such that those participants who showed more real-life rebellious behavior and reward drive showed less activation in this region during reward outcome processing. Possibly, this concurs with the idea that those individuals who display higher levels of risk taking show lowered self-control in response to rewards. Finally, in chapter 6 I provided preliminary evidence that faster longitudinal maturity of the medial prefrontal cortex predicted less rebellious behavior. Together, these findings provide insights into the use of behavioral and neural measures in predicting which individuals will take excessive risks, and for whom adolescence is a developmental phase of risks.

However, as chapter 6 suggests, risk-taking behavior may not necessarily be maladaptive. That is, in chapter 6 it was demonstrated that prosocial and rebellious

behavior were positively correlated. This suggests that a subgroup of individuals display both high levels of prosocial, as well as high levels of risk-taking behavior, otherwise referred to as 'prosocial risk takers': individuals who may take risks in order to help others (Do, Guassi Moreira, & Telzer, 2017). As such, in some instances, high levels of risk-taking behavior such as rebellious behavior may be useful. Likewise, individual differences in fun-seeking tendencies predicted rebellious behavior, but also prosocial behavior. This underlying tendency of risk taking may function as a differential susceptibility marker, rather than solely predict potentially negative behaviors. Although future studies should confirm these findings in experimental studies in addition to self-report measures, these findings suggest that adolescence is a phase of opportunities, too, and that risk-taking behavior may give rise to these opportunities.

Outstanding questions

A number of future directions remain. For instance, this thesis had a strong focus on individual differences in adolescence, yet it was not explicitly tested whether adolescence is a time of heightened individual differences relative to adulthood. An opportunity for future research is to investigate whether adolescence is marked by *greater variability* between, and within, individuals, compared with adulthood, which may give rise to better predictions of positive versus negative life outcomes.

Another interesting question is whether risk taking fosters exploration and learning (Hartley & Somerville, 2015). Suggestively, a tolerance to ambiguity may be a factor that fosters these behaviors in adolescence (Tymula et al., 2012). A finding in support of testing this hypothesis is the heightened (dorso)medial prefrontal cortex activation that was observed during outcome processing specifically following ambiguity (chapter 2 and 5), potentially functioning as a saliency signal for future behavior. Future studies may formally address whether ambiguity tolerance is beneficial to learning, and the role of the (dorso)medial prefrontal cortex in this relation. Another adaptive purpose of ambiguity tolerance is prosocial behavior. For example, a recent study with adults showed that ambiguity tolerance predicted costly prosocial behaviors during cooperation and trust decisions (Vives & FeldmanHall, 2018). Future studies may test positive (e.g., learning, prosocial behavior) versus negative (e.g., health-detrimental risk taking) influences of ambiguity tolerance in adolescence.

Finally, an outstanding question for future studies is to what extent the current findings generalize to atypically developing individuals, such as those with extremely high levels of risk taking (such as those with externalizing disorders), or those with extremely low levels of risk taking (such as those with internalizing disorders). For

instance, a recent study showed that adults with antisocial personality disorder displayed blunted ambiguity aversion, but not risk aversion, compared to healthy controls (Buckholtz, Karmarkar, Ye, Brennan, & Baskin-Sommers, 2017). This blunted ambiguity aversion was evident for those characterized by impulsivity and aggression (but not for those characterized by psychopathy and rule-breaking), and predicted real-world arrest frequency (Buckholtz et al., 2017). In contrast, a study with adult patients suffering from obsessive-compulsive disorder (characterized by pathological indecisiveness and self-doubt) showed that they were considerably more ambiguity averse, but not more risk averse, than healthy controls (Pushkarskaya et al., 2015). Together, these studies suggest that ambiguity aversion is a prominent marker of aberrant decision-making. Whether similar or different findings can be established for adolescents diagnosed with such disorders remains an open question, and may provide insights for interventions within a decision-making domain. Relatedly, as the findings in chapter 5 illustrate, longitudinal studies are crucial if we want to track the development of precursors to positive (i.e., normative developmental) versus negative (i.e., atypical developmental) life outcomes. By using longitudinal studies, a central question that can be addressed is which developmental trajectories underlie such diverse adolescent outcomes (Crone & Dahl, 2012).

Conclusions

The title of this thesis (Risky business?) refers to two key questions. First, I addressed whether choices are perceived as 'risky business' *depending on the choice context*, specifically, when probabilities are known (explicit risk) or unknown (ambiguous risk), and *depending on the individual.* Using a model-based decomposition approach and by including neuroimaging, I demonstrated that these aspects of risks are differentially manifested in behavior and in their underlying neural mechanisms, and may differentially impact overt adolescent risk-taking behavior. In addition, I demonstrated that there are profound individual differences between adolescents in risk and ambiguity attitudes, self-report measures, and neural activation. These individual differences are very useful to better understand the underlying mechanisms of risk taking, but also strengthen the notion that not all adolescents are risk takers. Finally, a related question concerned whether adolescence can solely be conceived as a developmental period of 'risky business', or alternatively, of *risks and opportunities.* This thesis points towards the latter interpretation, since risk taking and its underlying components may fulfill adaptive purposes, and that underlying traits of risk taking may also be predictive of positive, other-oriented behavior.

The study of adolescent risk-taking behavior is complex and multifaceted. By adopting a multidisciplinary approach of behavioral economics, developmental psychology, and neuroscience, this thesis demonstrates that risk-taking behavior can be unraveled into separate constructs. This enables us to make predictions about who takes risks, what drives this behavior, and ultimately, which individuals are prone to positive versus negative life outcomes.

Addendum

Nederlandstalige samenvatting

Dit proefschrift

Tijdens het nemen van beslissingen worden we vaak geconfronteerd met onzekerheid. Als je bijvoorbeeld het ijs op gaat na de eerste vorst, weet je niet of je door het ijs zal zakken of onbezorgd kan genieten van het schaatsweer. Zelfs het opgooien van een muntje behelst onzekerheid: je weet niet of de uitkomst kop of munt zal zijn. De uitkomsten op deze keuzes komen dus voor met een zekere *kans*. Hoewel iemand meestal wel een idee heeft welke uitkomsten kunnen volgen op de keuze (door het ijs zakken of niet; kop of juist munt gooien), kan de *informatie* over de kans ontbreken. Bij het opgooien van een muntje is de kans op kop bekend (dit is 50%). Dit wordt in de gedragseconomie *expliciet risico* genoemd, ofwel *risico* (Tversky & Kahneman, 1992). In vele situaties zijn de kansen op de verschillende uitkomsten echter niet bekend. De kans dat je door het ijs zakt is bijvoorbeeld niet in te schatten. Dit wordt *risico onder ambiguïteit* genoemd, ofwel *ambiguïteit* (Tversky & Kahneman, 1992). Of iemand risicovolle keuzes maakt (zoals het ijs op stappen) wordt sterk beïnvloed door risico (bekende kansen) en ambiguïteit (onbekende kansen; Tversky & Kahneman, 1992; Tymula, Rosenberg Belmaker, Ruderman, Glimcher, & Levy, 2013).

Een ontwikkelingsfase die gekenmerkt wordt door verhoogd risicogedrag is de adolescentie, ofwel de overgangsfase tussen de kindertijd en volwassenheid (Somerville, Jones, & Casey, 2010; Steinberg, 2008). Vergeleken met kinderen en volwassenen laten adolescenten meer risicogedrag zien zoals excessief middelengebruik en roekeloos gedrag in het verkeer (Eaton et al., 2008; Steinberg, 2008). Eerdere studies hebben leeftijdsveranderingen in risicogedrag onderzocht in experimenten waarin de kans op verschillende uitkomsten bekend is (risico). Het echte leven daarentegen bevat vooral onbekende kansen (ambiguïteit). Het is zelden onderzocht hoe adolescenten omgaan met risico en ambiguïteit, en hoe zich dit verhoudt tot risicogedrag in het echte leven. In dit proefschrift heb ik risicogedrag in de

adolescentie onderzocht als gedrag dat wordt gedreven door risico en ambiguïteit. Dit heb ik zowel gedragsmatig als neurowetenschappelijk onderzocht, wat een mechanistische verklaring biedt voor hoe risico en ambiguïteit verwerkt worden in verschillende leeftijden. Daarnaast heb ik me gericht op individuele verschillen in risicogedrag in de adolescentie. Hoewel de adolescentie namelijk gemiddeld gezien een periode is van verhoogd risicogedrag, nemen niet alle adolescenten (even veel) risico's. Deze individuele verschillen worden vaak over het hoofd gezien (Bjork & Pardini, 2015). Tot slot hoeft risicogedrag niet per se slecht te zijn, maar kan dit ook nuttig zijn. Voorbeelden zijn het nemen van risico's om de omgeving te ontdekken, of om anderen te helpen (Hartley & Somerville, 2015; Do, Guassi-Moreira, & Telzer, 2017). Gegeven de positieve èn negatieve aspecten van risicogedrag, heb ik daarom onderzocht hoe individuele verschillen in risicogedrag ons begrip van de adolescentie kunnen informeren als een fase van kwetsbaarheden, maar óók van kansen (Crone & Dahl, 2012).

Achtergrondinformatie

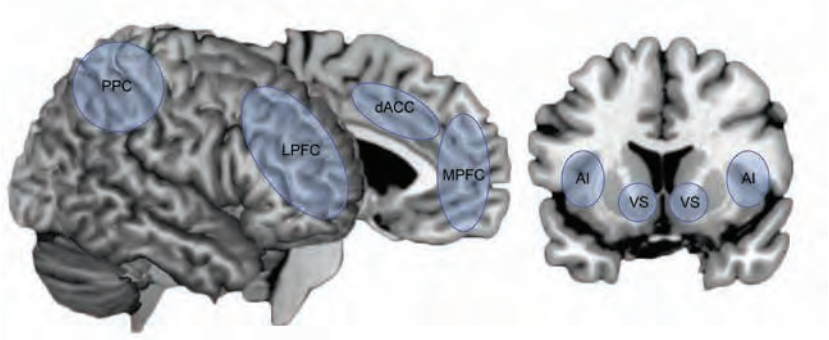
Beslissingen maken onder onzekerheid: risico en ambiguïteit

Klassiek gedragseconomisch onderzoek heeft aangetoond dat mensen in het algemeen een aversie hebben tegen risico en ambiguïteit, maar dat deze aversie sterker is tegen ambiguïteit dan tegen risico (Camerer & Weber, 1992; Ellsberg, 1961; Von Gaudecker, Van Soest, & Wengström, 2011). Hoe men risico en ambiguïteit benadert is echter zwak gecorreleerd. Dit suggereert dat risicogedrag verschillend wordt gedreven door risico en ambiguïteit (Tversky & Kahneman, 1992). Daarnaast verschillen mensen sterk in hun risico- en ambiguïteitsaversie: niet iedereen is even aversief, en iemand die risicoaversief is, is niet per se ambiguïteitsaversief (Levy, Snell, Nelson, Rustichini, & Glimcher, 2010). Een manier om te meten hoe mensen omgaan met risico en ambiguïteit is om keuzegedrag van proefpersonen te analyseren aan de hand van een economische keuzetaak. Hierin worden de kans op winst, het bedrag dat gewonnen kan worden, en het niveau van ambiguïteit gevarieerd (e.g., Tymula et al., 2013). Door een modelmatige benadering toe te passen op gedrag in een dergelijke taak kunnen hieruit iemands *risicoattitude* en *ambiguïteitsattitude* geschat worden. Deze maten reflecteren iemands gedragsmatige neiging om risico en ambiguïteit te mijden of juist op te zoeken. Om echter te begrijpen of risico en ambiguïteit verschillend verwerkt worden binnen, maar ook tussen individuen, is een fundamenteel begrip van de onderliggende mechanismen nodig.

Een neuroeconomisch perspectief

Met de opkomst van cognitieve neurowetenschappelijke studies (Poldrack, 2008) zijn onderzoekers steeds meer in staat gekomen om de onderliggende mechanismen van risicovol keuzegedrag te ontleden. Ten eerste kan men met structurele *magnetic resonance imaging* (MRI), de relatie tussen hersenvolume en keuzepreferenties onderzoeken (e.g., Levy, 2016). Ten tweede kan men met *functionele* MRI de functie van de hersenen, bijvoorbeeld tijdens een keuzetaak, relateren aan keuzepreferenties. Eerdere studies met volwassenen hebben in kaart gebracht welke breingebieden actief zijn tijdens het maken van risicovolle keuzes (zie Figuur 1; voor overzichtsartikelen zie Knutson & Huettel, 2015; Mohr, Biele, & Heekeren, 2010; Platt & Huettel, 2008). Het ventrale striatum (VS) en de (ventro)mediale prefrontale cortex (PFC) zijn bijvoorbeeld actief tijdens het verwerken van beloningen (Bartra, McGuire, & Kable, 2013; Delgado, 2007; Sescousse, Caldú, Segura, & Dreher, 2013) en tijdens het leren van beloningen (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). Daarnaast zijn de anterieure insula, de dorsale anterieure cingulate cortex (dACC/dorsomediale PFC) en de ventrolaterale PFC actief bij toenemende onzekerheid binnen keuzeopties (Levy, 2016; Mohr et al., 2010). Tot slot zijn de dorsolaterale PFC en de posterieure pariëtale cortex (PPC) actief tijdens het beoordelen van kans en waarde.

Deze hersengebieden zijn echter een *algemene* reflectie van risicovol keuzegedrag, en zijn dus niet per se specifiek voor risico en ambiguïteit. De zeldzame studies naar de neurale correlaten van risico en/of ambiguïteit hebben tegenstrijdige bevindingen



Figuur 1. *Gebieden die geassocieerd zijn met verschillende aspecten van risicovol keuzegedrag. PPC = posterieure pariëtale cortex; LPFC = laterale prefrontale cortex; dACC = dorsale anterieure cingulate cortex; MPFC = mediale prefrontale cortex; AI = anterieure insula; VS = ventrale striatum. Figuur gebaseerd op de overzichtsartikelen van Knutson & Huettel, 2015; Mohr et al, 2010; Platt & Huettel, 2008.*

opgeleverd, en zijn uitgevoerd in relatief kleine steekproeven van volwassen proefpersonen (e.g., Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005; Huettel, Stowe, Gordon, Warner, & Platt, 2006; Levy et al., 2010). Het is dus nodig om deze neurale mechanismen verder te onderzoeken in grotere steekproeven en, belangijker nog, in de adolescentie. Dit is niet alleen een ontwikkelingsfase die gekenmerkt wordt door veranderingen in het brein, maar ook door een verhoogde mate van risicogedrag.

Modellen van de ontwikkeling van risicogedrag in de adolescentie

De adolescentie wordt gekenmerkt door sterke veranderingen in de hersenen (Giedd, 2004; Giedd et al., 1999). Diepgelegen, subcorticale gebieden (belangrijk voor affectieve processen) ontwikkelen zich relatief snel, terwijl corticale gebieden (belangrijk voor cognitieve controle) zich relatief langzamer ontwikkelen, zeker tot het 25e levensjaar. Invloedrijke theorieën hebben voorgesteld dat deze 'disbalans' in hersenontwikkeling ten grondslag ligt aan het verhoogde risicogedrag wat geobserveerd wordt in de adolescentie: de affectieve gebieden zijn 'hyperactief' ten opzichte van de cognitieve controlegebieden (Casey, Jones, & Hare, 2008; Casey, 2015; Somerville & Casey, 2010; Steinberg, 2008). Daarnaast suggereert experimenteel onderzoek dat deze disbalans versterkt is in contexten die een meer realistische weergave van risicogedrag zijn, zoals ambiguïteit (Defoe, Dubas, Figner, & van Aken, 2015). Deze zogenaamde *imbalance,* of *dual-systems,* modellen zijn dus beschrijvend voor veranderingen in risicogedrag in de adolescentie in verschillende contexten, en zijn nuttig om algemene uitspraken te doen over adolescenten op groepsniveau.

Een mogelijk nadeel van deze modellen is echter dat ze sterke verschillen tussen adolescenten over het hoofd zien. De recente wetenschappelijke literatuur stipt het belang aan van het onderzoeken van individuele verschillen, waarbij benadrukt wordt dat de adolescentie niet hetzelfde is voor iedereen (e.g., Foulkes & Blakemore, 2018). Eerder neurowetenschappelijk onderzoek met adolescenten heeft aangetoond dat individuele verschillen in risicogedrag gerelateerd zijn aan activiteit in het VS, de (ventro)mediale PFC, dorsomediale PFC, insula, en de laterale PFC (voor een overzicht, zie Sherman, Steinberg, & Chein, 2018). Hoewel deze gebieden overeenkomen met volwassenenstudies (zie Figuur 1), zijn ook deze studies in relatief kleine steekproeven gedaan, en is dit nog niet onderzocht binnen condities van risico versus ambiguïteit. Bovendien is de relatie met risicogedrag in het echte leven relatief onderbelicht.

Tot slot stellen gerelateerde modellen dat de adolescentie niet alleen een ontwikkelingsfase van kwetsbaarheden is. Risicogedrag kan adaptief zijn, zoals met het nemen van risico's om de omgeving te ontdekken (Hartley & Somerville, 2015; Romer, Reyna, & Satterthwaite, 2017), of om anderen te helpen (i.e., prosociaal

risicogedrag; Do, Guassi Moreira, & Telzer, 2017). Bovendien is de adolescentie ook een fase waarin positief gedrag zich ontwikkeld, zoals prosociaal gedrag (iets goeds doen voor een ander) en sociaal perspectief nemen (Blakemore & Mills, 2014; Dumontheil, Apperly, & Blakemore, 2010; Güroğlu, van den Bos, & Crone, 2014). Naar dit beeld van de adolescentie (d.w.z., van positieve versus negatieve ontwikkelingstrajecten) is echter relatief weinig onderzoek gedaan.

Doelen

Het overkoepelende doel van dit proefschrift was om de gedragsmatige en neurale mechanismen ten grondslag aan risicovol keuzegedrag in de adolescente te onderzoeken. Ten eerste heb ik risicovol keuzegedrag ontleed in twee onderliggende componenten –risico- en ambiguïteitsaversie– en hun neurale mechanismen onderzocht. Ten tweede heb ik onderzocht hoe individuele verschillen in (risicovol) keuzegedrag ons informeert van de adolescentie als een fase van kwetsbaarheden en kansen. Deze overkoepelende onderzoeksvragen zijn behandeld in vijf empirische hoofdstukken, die hieronder zijn samengevat.

Samenvatting van de resultaten

Risico- en ambiguïteitsattitudes in de adolescentie

In het eerste empirische hoofdstuk (**hoofdstuk 2**) heb ik een 'rad van fortuin' taak afgenomen in een steekproef van adolescenten en jongvolwassenen (N = 157, leeftijden 10-15 jaar). Proefpersonen werden gepresenteerd met twee raden en gevraagd om te kiezen welk rad ze liever zouden draaien. Eén rad gaf een constante, zekere winst (een 100% kans op het winnen van een klein geldbedrag). Het andere rad was een gok: dit rad kon méér opleveren, maar kon ook niets opleveren. Dit rad varieerde in het geldbedrag en de kans op dat geldbedrag. Daarnaast varieerden we ook het niveau van ambiguïteit, door het rad deels te bedekken met een grijs vlak. Hierdoor kon niet gezien worden wat er (deels) onder dit vlak lag, waardoor de kans op winst in mindere mate/niet bekend was: dit rad was dus in meer of mindere mate ambigu. Met een modelmatige benadering heb ik **1)** de ontwikkelingstrajecten van risico- en ambiguïteitsattitude getoetst, en **2)** de mate onderzocht waarin risico- en ambiguïteitsattitude gerelateerd waren aan risicogedrag in het echte leven. We vonden dat ambiguïteitsaversie, maar niet risicoaversie, lineair toenam met leeftijd. Gegeven dat ambiguïteitsaversie nog niet aanwezig is in de kindertijd (8-9 jaar oud; Li, Brannon, & Huettel, 2014), suggereert deze bevinding dat ambiguïteitsaversie voor het eerst optreedt in de vroege adolescentie. Daarnaast was méér risicogedrag in het echte

leven gerelateerd aan minder ambiguïteitsaversie, maar niet aan risicoaversie. Dit suggereert dat ambiguïteit een betere reflectie van risicogedrag in het echte leven is. Daarnaast heb ik in deze studie ook geëxploreerd of de sociale context risico- en ambiguïteitsattitude beïnvloedt. Hiervoor heb ik onderzocht of adolescenten de keuzes van een leeftijdsgenoot in acht nemen bij het maken van hun eigen keuzes. Proefpersonen zagen de keuzes van een risicovolle leeftijdsgenoot voordat zij hun eigen keuzes maakten. Hier vonden we dat risicoattitudes, maar niet ambiguïteitsattitudes, meer overeenkwamen met de keuzes van de leeftijdsgenoot, vooral voor de jongste leeftijdsgroep (10-12 jaar oud). Dit suggereert dat risicogedrag kan variëren onder verschillende condities van sociaal advies, en biedt aanknopingspunten voor toekomstig onderzoek naar het effect van leeftijdsgenoten op condities die variëren in onzekerheid.

Samengevat suggereren deze bevindingen dat de vroege adolescentie (10-12 jaar) een startpunt is voor ambiguïteitsaversie en dat gedrag onder ambiguïteit een realistischere weergave van adolescent risicogedrag in het echte leven is. Tot slot illustreert dit hoofdstuk het potentieel van een modelmatige methode om risico- en ambiguïteitsattitudes te ontleden binnen adolescenten, en om individuele verschillen in deze attitudes te onderzoeken.

Risico- en ambiguïteitsattitudes in het volwassen brein

In **hoofdstuk 2** heb ik de neurale mechanismen ten grondslag aan risico en ambiguïteit in 50 jongvolwassenen (18-28 jaar) onderzocht. Het doel van deze studie was om te onderzoeken of risico en ambiguïteit verschillend worden verwerkt binnen individuen. Hiervoor maakte ik weer gebruik van de rad-van-fortuintaak om risico- en ambiguïteitsattitudes te schatten. Vervolgens relateerde ik deze attitudes aan hersenactiviteit tijdens een fMRI-versie van deze taak. De resultaten lieten zien dat meer risicozoekende attitudes geassocieerd waren met hogere activiteit in de mediale en laterale orbitofrontale cortex, en dat meer ambiguïteitszoekende attitudes geassocieerd waren met hogere activiteit in de mediale temporale cortex. Dit suggereert dat verschillende neurale mechanismen ten grondslag liggen aan individuele verschillen in risico-en ambiguïteitsattitudes.

Een tweede onderzoeksvraag in deze studie was of hersenactiviteit tijdens keuzeuitkomsten verschilde afhankelijk van of deze volgde op risico of ambiguïteit. In de fMRI-versie van de rad-van-fortuintaak kregen deelnemers daarom ook de uitkomsten van hun keuzes te zien (i.e., winst of geen winst na gokken onder risico of ambiguïteit). Het ventrale striatum was actief tijdens het verwerken van de uitkomst winst (vergeleken met de uitkomst geen winst), ongeacht of de keuze onder risico of onder ambiguïteit gemaakt was. Maar het gebied wat vooral dissocieerde tussen risico en

ambiguïteit was de mediale PFC. Dit gebied was vooral actief tijdens uitkomsten die volgden op ambiguïteit, en reflecteert een onzekerheidssignaal wat waarschijnlijk verhoogd is in ambigue situaties. Deze studie, en de studie beschreven in hoofdstuk 2, vormden de basis voor het volgende hoofdstuk, waarin ik de neurale mechanismen van risico- en ambiguïteitsattitudes heb onderzocht in een steekproef van adolescente proefpersonen.

Subjectieve waarde onder risico en ambiguïteit in het ontwikkelende brein

In **hoofdstuk 4** heb ik verder onderzocht hoe risico- en ambiguteïtsattitudes gecodeerd worden in het brein, in een tweede steekproef van adolescenten (*N* = 188, 12-22 jaar). Hier integreerde ik de risico- en ambiguïteitsattitudes van proefpersonen met de keuzes tijdens de fMRI-taak op trialniveau, en leidde ik per proefpersoon de *subjectieve waarde* van iedere keuze tijdens de fMRI-taak af. Op deze manier kon ik onderzoeken welke hersengebieden veranderingen in subjectieve waarde detecteren onder risico en onder ambiguïteit, en of hier mogelijk overlap in zit. Parametrische fMRI-analyses lieten zien dat toenames in subjectieve waarde onder risico gecodeerd werden door activiteit in het ventrale striatum en de superieure pariëtale cortex. Daarnaast werden afnames in subjectieve waarde onder ambiguïteit gecodeerd door activiteit in de dorsolaterale PFC en de superieure temporale gyrus. Tot slot werd subjectieve waarde onder zowel risico als ambiguïteit gecodeerd door de dorsomediale PFC. Dit zou een algemeen signaal van onzekerheid kunnen weergeven. Een interessante bevinding was dat deze resultaten minder uitgesproken waren wanneer géén rekening werd gehouden met de risico- en ambiguïteitsattitudes van proefpersonen. Dit suggereert dat het gebruik van subjectieve maten, in plaats van objectieve maten, betekenisvoller is in dit type onderzoek naar adolescent keuzegedrag. Samengevat laat deze studie verschillende, en overlappende, patronen van hersenactiviteit zien voor subjectieve waarde onder risico en ambiguïteit. De combinatie van modelmatige gedragsanalyses met (parametrische) fMRI-analyses is waardevol en kan meer inzichten bieden in welke adolescenten meer of minder risico nemen en waarom.

Individuele verschillen in risicogedrag in het ontwikkelende brein

In **hoofdstuk 5** onderzocht ik de relatie tussen hersenactiviteit tijdens de fMRI-taak en individuele verschillen in risicogedrag. Ik keek hierbij naar risicogedrag tijdens de taak (het aantal keer gokken) en naar risicogedrag in het echte leven (gemeten met vragenlijsten), in deels dezelfde steekproef als hoofdstuk 4 (*N* = 198, 12-25 jaar). Ten eerste vond ik dat proefpersonen die *méér* gokten in de taak, specifiek onder risico,

meer activiteit lieten zien in het ventrale striatum. Daarnaast lieten proefpersonen die *minder* gokten tijdens de taak, specifiek onder ambiguïteit, meer activiteit zien in de insula en de dorsomediale PFC. Tot slot was activiteit in de laterale PFC tijdens het verwerken van keuzeuitkomsten gerelateerd aan gokken onder ambiguïteit, èn voor zelfgerapporteerd risicogedrag. Hier bleek dat proefpersonen die *minder* risicogedrag lieten zien meer activiteit lieten zien in dit gebied. Samengevat laten deze bevindingen zien dat het belangrijk is om meerdere maten van risicogedrag mee te nemen (taakgedrag en zelfrapportage), en meerdere keuzecontexten te onderzoeken (risico en ambiguïteit; keuze en keuzeuitkomsten), om de neurale mechanismen ten grondslag aan adolescent risicogedrag beter te begrijpen. Een dergelijk multidimensionaal perspectief draagt bij aan betere voorspellingen over welke individuen het meeste risicogedrag laten zien.

Een longitudinale studie naar risicogedrag en prosociaal gedrag: Invloeden van gedrag en hersenstructuur

In het laatste hoofdstuk, **hoofdstuk 6**, keek ik wederom naar invloeden op risicogedrag in de adolescentie. Maar gegeven dat de adolescentie ook een belangrijke fase is voor de ontwikkeling van positief gedrag, keek ik ook naar invloeden op prosociaal gedrag, ofwel gedrag dat anderen ten goede komt. De relatie tussen risicogedrag en prosociaal gedrag is tot nog toe over het hoofd gezien. Deze relatie is echter belangrijk om te onderzoeken omdat deze schijnbare tegenstrijdige gedragingen zich gelijktijdig ontwikkelen in de adolescentie. In deze studie heb ik onderzocht of risicogedrag en prosociaal gedrag gerelateerde constructen zijn, en welke ontwikkelingsprocessen bijdragen aan deze gedragingen. Hiervoor gebruikte ik longitudinale data van vragenlijsten en hersenstructuur van drie meetmomenten (N = 210 op het derde meetmoment, 8-29 jaar). Risicogedrag en prosociaal gedrag, gemeten op het derde meetmoment, waren positief gecorreleerd. Met andere woorden, meer risicogedrag (zoals alcohol drinken) hing samen met meer prosociaal gedrag (zoals anderen helpen). Niet onverwacht voorspelden hogere niveaus van empathie, en een sterkere toename over tijd in sociaal perspectief nemen, meer prosociaal gedrag. Een interessante bevinding was dat hogere niveaus en sterkere veranderingen in de neiging om leuke en spannende dingen op te zoeken (*fun seeking)* voorspellend waren voor zowel prosociaal gedrag als risicogedrag. Naast veranderingen in gedrag keek ik ook naar de ontwikkeling van de nucleus accumbens (onderdeel van het striatum) en de mediale PFC. Dit zijn gebieden die in eerder onderzoek samenhingen met risicogedrag èn prosociaal gedrag. We vonden dat een snellere volwassenwording van de mediale PFC voorspellend was voor *minder* rebels gedrag. Dit laat zien dat de structurele ontwikkeling van hersengebieden een

informatieve voorspeller van gedrag kan zijn.

Deze studie suggereert dat *fun seeking* diverse uitkomsten (risicogedrag en prosociaal gedrag) in de adolescentie kan voorspellen. Het begrijpen van de mechanismen die ten grondslag liggen aan deze schijnbaar tegenstrijdige gedragingen, kan helpen om ontwikkelingstrajecten te identificeren die nodig zijn om kwetsbaarheden in de adolescenten te verminderen, en kansen te bevorderen.

Algemene Discussie

De studies in dit proefschrift laten een aantal hoofdbevindingen zien. Ten eerste heb ik gedemonstreerd dat risico- en ambiguïteitsattitudes te onderscheiden componenten zijn van risicovol keuzegedrag in de adolescentie en (jong)volwassenheid. Ik heb aangetoond dat risico en ambiguïteit gereflecteerd worden in verschillende attitudes, verwerkt worden in verschillende onderliggende neurale mechanismen, en verschillend samenhangen met geobserveerd risicogedrag in de adolescentie. Ten tweede suggereerden de studies in dit proefschrift dat de adolescentie niet alleen een periode van kwetsbaarheden is, maar ook van kansen. Door te onderzoeken hoe risicogedrag en prosociaal gedrag samenhangen en hun gedragsmatige en neurobiologische ontwikkelingstrajecten te bekijken, heb ik aangetoond dat één onderliggende trek voorspellend is voor deze verschillende uitkomstvariabelen. In de volgende paragrafen bespreek ik de hoofdbevindingen van dit proefschrift in verder detail vanuit een neuroeconomisch ontwikkelingsperspectief, en geef ik aanbevelingen voor toekomstig onderzoek.

Risico en ambiguïteit: Aparte componenten van risicogedrag in de adolescentie

In de eerste drie empirische hoofdstukken heb ik aangetoond dat risico- en ambiguïteitsattitudes onderscheiden kunnen woorden middels een modelmatige benadering. In drie aparte steekproeven (hoofdstuk 2, 3, en 4) vond ik dat risico- en ambiguïteitsattitude niet significant gecorreleerd waren, wat suggereert dat ze verschillende aspecten van risicogedrag reflecteren. Daarnaast heb ik gekeken naar de onderliggende neurale mechanismen van risico en ambiguïteit in steekproeven van (jong) volwassen (hoofdstuk 3) en adolescenten (hoofdstuk 4 en 5). Hier heb ik aangetoond dat risico en ambiguïteit worden verwerkt in verschillende hersensystemen, en dat een aantal hersengebieden specifiek samenhangen met risico- of ambiguïteitsattitudes. Waar gebieden die onderdeel zijn van het *valuation* (of 'waarde') netwerk (zoals het ventraal striatum, orbitofrontale cortex, pariëtale cortex) voornamelijk

risico coderen, coderen gebieden gerelateerd aan conflict en onzekerheid (zoals de dorsolaterale PFC, temporele cortex, en dorsomediale PFC) voornamelijk ambiguïteit. De bevindingen in dit proefschrift suggereren dat er een neurale distinctie is tussen risico en ambiguïteit in de adolescentie en (jong)volwassenheid, vooral wanneer we kijken naar individuele verschillen in gedrag.

Over de verschillende studies waren er weinig leeftijdseffecten. Hoewel ik in hoofdstuk 2 een lineaire toename in ambiguïteitsaversie vond met leeftijd, vond ik dit niet in hoofdstuk 4 en 5. Risico-aversie liet ook geen consistente leeftijdseffecten zien over studies. Een nauwere leeftijds*range* (beginnend met 12 jaar; hoofdstuk 4 en 5) resulteerde in minder uitgesproken leeftijdseffecten dan een bredere leeftijdsrange (beginnend bij 10 jaar, hoofdstuk 2). Er waren ook geen prominente leeftijdseffecten op hersenactiviteit (hoofdstuk 4 en 5). Andere studies vonden wel uitgesproken leeftijdsverschillen in risico- en ambiguïteitsattitudes (Tymula et al., 2012; van den Bos & Hertwig, 2017), afhankelijk van de geïncludeerde leeftijden en of keuzes over winst of over verlies gemaakt moesten worden. Deze uiteenlopende bevindingen in verschillende studies tonen het belang aan van 1) replicatie over verschillende steekproeven, 2) steekproefgroottes, 3) de specifieke leeftijdsranges, en 4) verschillende keuzecontexten (bijvoorbeeld winst versus verlies) om robuuste conclusies over leeftijdseffecten te kunnen trekken.

Een andere verklaring voor de uiteenlopende leeftijdsbevindingen kan te maken hebben met de aard van de rad-van-fortuintaak, die relatief *cold* was (zie bijvoorbeeld Defoe, Dubas, Figner, & van Aken, 2015; Rosenbaum, Venkatraman, Steinberg, & Chein, 2018). Een *cold* beschrijvende context (zoals de rad-van-fortuintaak waarin keuzepreferenties in een relatief neutrale context gemeten worden) laat vaak minder sterke leeftijdseffecten zien dan een *hot context,* ofwel een affectief geladen context (zoals in aanwezigheid van leeftijdsgenoten). Toekomstige studies kunnen onderzoeken of ambiguïteit, gegeven de sterkere relatie met risicogedrag in het echte leven, de affectieve aard van een relatieve *cold* taak verhoogt.

Naast de invloed op affectieve processen, suggereert een recent artikel dat ambiguïteit de betrokkenheid van cognitieve controle kan verlagen. De verlaagde cognitieve controle door ambiguïteit zou leiden tot minder optimale keuzes (Li, 2017). Daarnaast zouden vooral jongere kinderen minder optimale keuzes maken wanneer informatie ontbreekt (zoals tijdens ambiguïteit), maar ook de grootste vooruitgang in keuzegedrag vertonen wanneer informatie wel beschikbaar is (kinderen zijn hierin dus flexibeler). Dit wordt ook wel het *flexing dual-systems* model genoemd (Li, 2017). In het huidige proefschrift is bewijs gevonden dat gebieden die belangrijk zijn voor cognitieve controle inderdaad actief zijn tijdens ambiguïteit (zoals de laterale PFC, hoofdstuk 4 en 5), maar we vonden hierin geen leeftijdsverschillen. Hoewel het

huidige proefschrift meer gericht was op een neuroeconomisch perspectief dan een *imbalance/dual systems* perspectief, zou toekomstig onderzoek deze twee perspectieven kunnen integreren door 8-10 jarigen te includeren, een leeftijdsrange waarin de grootste veranderingen zouden kunnen optreden (hoofdstuk 2, Li et al., 2014).

De adolescentie als ontwikkelingsfase van kwetsbaarheden en kansen

Een tweede overkoepelend doel van dit proefschrift was om te onderzoeken hoe individuele verschillen in risicogedrag ons begrip van de adolescentie informeren als een periode van kwetsbaarheden en kansen. In de studies werden individuele verschillen onderzocht in meerdere gedragsmaten: risico- en ambiguïteitsattitude (hoofdstuk 2, 3, en 4), maten van risicogedrag in het echte leven (hoofdstuk 2, 5, en 6), en maten van sociaal functioneren (hoofdstuk 6). Zoals aangetoond helpen deze individuele verschillen om de onderliggende mechanismen van risicogedrag beter te begrijpen, maar informeren ze ons ook over de adolescentie als fase van kwetsbaarheden en kansen. In hoofdstuk 2 liet ik bijvoorbeeld zien dat ambiguïteitsattitude samenhing met roekeloos gedrag in het echte leven. Op neuraal niveau liet ik zien dat de laterale PFC (belangrijk voor ambiguïteit) ook samenhing met risicogedrag in het echte leven: proefpersonen die meer roekeloos gedrag vertoonden in het echte leven hadden minder activiteit in dit gebied tijdens het verwerken van keuzeuitkomsten. Dit past bij het idee dat individuen, die meer risicogedrag laten zien, minder zelfcontrole hebben wanneer ze geconfronteerd worden met keuzeuitkomsten. Tot slot liet ik in hoofdstuk 6 zien dat een snellere volwassenwording van de mediale PFC voorspellend was voor minder rebels gedrag. Deze bevindingen bieden ons inzichten in het gebruik van gedragsmaten en neurobiologische maten in het voorspellen van welke individuen excessieve risico's nemen, en voor wie de adolescentie een fase van kwetsbaarheden is.

Wat hoofdstuk 6 echter suggereert, is dat risicogedrag niet per se slecht is. In hoofdstuk 6 werd aangetoond dat prosociaal gedrag en rebels gedrag positief samenhangen. Dit suggereert dat een subgroep van individuen zowel veel prosociaal gedrag als veel risicogedrag vertonen. Dit worden ook wel '*prosocial risk takers*' genoemd, personen die risico's nemen om anderen te helpen (Do et al., 2017). In sommige gevallen kunnen hoge niveaus van risicogedrag, zoals rebels gedrag, dus gunstig zijn. Daarnaast vonden we dat *fun seeking* zowel rebels gedrag als prosociaal gedrag voorspelde. Deze trek hangt dus niet louter samen met potentieel negatief gedrag. Hoewel toekomstig onderzoek de huidige bevindingen moet repliceren in experimenten in aanvulling op resultaten uit vragenlijsten, suggereren deze bevindingen dat de adolescentie ook een fase is van kansen, en dat risicogedrag aanleiding kan geven tot deze kansen.

Openstaande vragen

Dit proefschrift had een sterke focus op individuele verschillen in de adolescentie, maar er was niet expliciet getoetst of de adolescentie een fase is van verhoogde individuele verschillen ten opzichte van andere leeftijdsgroepen. Toekomstig onderzoek zou expliciet kunnen toetsen of de adolescentie gekenmerkt wordt door verhoogde variabiliteit, tussen, maar ook binnen, personen wat betreft risicogedrag. Dit zou kunnen bijdragen aan betere voorspellingen van positieve versus negatieve levensuitkomsten.

Een andere interessante vraag is of risicogedrag gunstig is voor exploratie en leren (Hartley & Somerville, 2015). Er is gesuggereerd dat een tolerantie voor ambiguïteit dit soort gedrag in de adolescentie zou kunnen bevorderen (Tymula et al., 2012). In dit proefschrift vond ik dat activiteit in de dorsomediale PFC specifiek na ambigue keuzes een onzekerheidssignaal zou kunnen zijn wat toekomstige keuzes zou kunnen beïnvloeden (hoofdstuk 2 en 5). Toekomstige studies kunnen onderzoeken of een tolerantie voor ambiguïteit leren zou kunnen bevorderen, en welke rol de dorsomediale PFC hierin speelt. Een andere adaptieve rol van ambiguïteitstolerantie is prosociaal gedrag. Uit onderzoek met volwassenen is bijvoorbeeld gebleken dat ambiguïteitstolerantie voorspellend was voor prosociaal gedrag in beslissingen over coöperatie en vertrouwen (Vives & FeldmanHall, 2018). Toekomstige studies zouden zowel positieve invloeden (bijvoorbeeld leren en prosociaal gedrag) als negatieve invloeden (bijvoorbeeld risicogedrag) van ambiguïteitstolerantie in de adolescentie kunnen onderzoeken.

Tot slot is een openstaande vraag in welke mate de huidige bevindingen gegeneraliseerd kunnen worden naar adolescenten die een atypische ontwikkeling doormaken, zoals adolescenten gekenmerkt door extreem veel risicogedrag (zoalsin het geval van externaliserende stoornissen) of adolescenten gekenmerkt door extreem weinig risicogedrag (zoals in het geval van internaliserende stoornissen). Een recente studie heeft laten zien dat volwassenen met een antisociale persoonlijkheidsstoornis minder ambiguïteitsaversief zijn, maar niet minder risicoaversief, vergeleken met gezonde controles (Buckholtz, Karmarkar, Ye, Brennan, & Baskin-Sommers, 2017). Deze 'afgestompte' ambiguïteitsaversie was vooral aanwezig voor individuen gekenmerkt door impulsiviteit en agressie, en voorspelde bovendien hoe vaak deze mensen waren gearresteerd. Uit een ander onderzoek bleek dat volwassenen met een obsessief-compulsieve stoornis (gekenmerkt door een pathologisch onvermogen om beslissingen te maken, en zelftwijfel), juist veel meer ambiguïteitsaversief waren dan gezonde controles (Pushkarskaya et al., 2015). Deze studies suggereren dat ambiguïteitsaversie een kenmerk is van afwijkend keuzegedrag. Of dezelfde resultaten gevonden zullen worden in adolescenten gediagnosticeerd met

dergelijke stoornissen is een nog onbeantwoorde vraag, maar zou inzichten kunnen bieden voor interventies binnen het beslissingsdomein. Zoals de resultaten uit hoofdstuk 6 illustreren, zijn longitudinale studies cruciaal om de voorlopers van positieve (typische ontwikkeling) en negatieve (atypische ontwikkeling) ontwikkelingstrajecten te kunnen volgen. Met longitudinale studies kan onderzocht worden welke ontwikkelingstrajecten onderliggend zijn aan zulke diverse uitkomsten in de adolescentie (Crone & Dahl, 2012).

Conclusies

De titel van dit proefschrift (*Risky business?)* verwijst naar twee vragen. Ten eerste heb ik geadresseerd of keuzes waargenomen worden als '*risky business*', *afhankelijk van de keuzecontext* - wanneer kansen bekend zijn (risico) en onbekend zijn (ambiguïteit) - en *afhankelijk van het individu.* Door een modelmatige decompositiebenadering toe te passen in combinatie met neuroimaging, heb ik gedemonstreerd dat deze twee aspecten van risico verschillend gemanifesteerd zijn in gedrag en in de onderliggende neurale mechanismen, en risicogedrag op een verschillende manier beïnvloeden. Daarnaast heb ik aangetoond dat er zeer grote individuele verschillen zijn tussen adolescenten in risico- en ambiguïteitsattitude, zelfrapportage, en hersenactiviteit. Deze individuele verschillen zijn erg nuttig om de onderliggende mechanismen van risicogedrag beter in kaart te brengen, maar versterken ook het punt dat niet alle adolescenten risico nemen. Tot slot stelde ik de vraag of de adolescentie kan worden beschouwd als een ontwikkelingsfase van '*risky business',* of van kwetsbaarheden èn kansen. Dit proefschrift wijst op de tweede interpretatie, omdat risicogedrag en diens onderliggende componenten adaptieve functies kan vervullen, en ook voorspellend kunnen zijn voor positief sociaal gedrag.

De studie naar risicogedrag in de adolescentie is complex en veelzijdig. Door een multidisciplinaire benadering toe te passen van de gedragseconomie, ontwikkelingspsychologie, en neurowetenschappen, laat dit proefschrift zien dat risicogedrag ontrafeld kan worden in afzonderlijke constructen. Dit stelt ons in staat om betere voorspellingen te maken over wie risico neemt, wat dit gedrag drijft, en uiteindelijk welke adolescenten vatbaar zijn voor positieve of negatieve ontwikkelingstrajecten

Addendum

References

Achterberg, M., Peper, J. S., van Duijvenvoorde, A. C. K., Mandl, R. C., & Crone, E. A. (2016). Frontostriatal white matter integrity predicts development of delay of gratification: A longitudinal study. *Journal of Neuroscience, 36*(6), 1954–1961.

Arnett, J. (1992). Reckless behavior in adolescence: A developmental perspective. *Developmental Review, 12*(4), 339–373.

Barkley–Levenson, E., & Galván, A. (2014). Neural representation of expected value in the adolescent brain. *Proceedings of the National Academy of Sciences, 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.

Bechara, A., Damasio, H., & Damasio, A. R. (2000). Emotion, decision making and the orbitofrontal cortex. *Cerebral Cortex, 10*(3), 295–307.

Becht, A. I., Bos, M. G., Nelemans, S. A., Peters, S., Vollebergh, W. A., Branje, S. J., . . . Crone, E. A. (2018). Goal-directed correlates and neurobiological underpinnings of adolescent identity: A multimethod multisample longitudinal approach. *Child Development*, *89*(3), 823–836.

Birnbaum, M., & Navarrete, J. (1998). Testing descriptive utility theories: Violations of stochastic dominance and cumulative independence. *Journal of Risk and Uncertainty, 17*(1), 49–79.

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.

Blais, A.–R., & Weber, E. U. (2006). A domain–specific risk–taking (DOSPERT) scale for adult populations. *Judgment and Decision Making, 1*(1), 33–47.

Blakemore, S. J., & Mills, K. L. (2014). Is adolescence a sensitive period for sociocultural processing? *Annual Review of Psychology, 65,* 187–207.

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, 29*(11), 1–15.

Blankenstein, N. E., Schreuders, E., Peper, J. S., Crone, E. A., & van Duijvenvoorde, A. C. K. (2018). Individual differences in risk–taking tendencies modulate the neural processing of risky and ambiguous decision–making in adolescence. *NeuroImage, 172,* 663–673.

Bos, M. G., Peters, S., van de Kamp, F. C., Crone, E. A., & Tamnes, C. K. (2018). Emerging depression in adolescence coincides with accelerated frontal cortical thinning. *Journal of Child Psychology and Psychiatry 59*(9), 994–1002.

Bossaerts, P., Ghirardato, P., Guarnaschelli, S., & Zame, W. (2010). Ambiguity in asset Markets: Theory and experiment. *The Review of Financial Studies, 23*(4), 1325–1359.

Braams, B. R., & Crone, E. A. (2017). Peers and parents: A comparison between neural activation when winning for friends and mothers in adolescence. *Social Cognitive and Affective Neuroscience, 12*(3), 417–426.

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

Braams, B. R., Peters, S., Peper, J. S., Güroğlu, B., & Crone, E. A. (2014). Gambling for self, friends, and antagonists: Differential contributions of affective and social brain regions on adolescent reward processing. *NeuroImage, 100,* 281–289.

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. *Journal of Neuroscience, 35*(18), 7226–7238.

Brett, M., Anton, J., Valabregue, R., & Poline, J. (2002). Region of interest analysis using an SMP toolbox, paper presented at: 8th International Conference on Functional mapping of the Human Brian.

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.

Byrnes, J. P., Miller, D. C., & Schafer, W. D. (1999). Gender differences in risk taking: A meta–analysis. *Psychological Bulletin, 125*(3), 367.

Camerer, C., & Mobbs, D. (2016). Differences in behavior and brain activity during hypothetical and real choices. *Trends in Cognitive Sciences, 21*(1), 46–56.

Camerer, C., & Weber, M. (1992). Recent developments in modeling preferences: Uncertainty and ambiguity. *Journal of Risk and Uncertainty, 5*(4), 325–370.

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. (2015). Beyond simple models of self–control to circuit–based accounts of adolescent behavior. *Annu Rev Psychol, 66*(1), 295–319.

Casey, B., Jones, R. M., & Hare, T. A. (2008). The adolescent brain. *Annals of the New York Academy of Sciences, 1124*(1), 111–126.

Chassin, L., Hussong, A., & Beltran, I. (2004). *Adolescent substance use*. In R. Lerner & L. Steinberg (Eds.), Handbook of adolescent psychology (2nd ed., pp. 665–696). New York, NY: Wiley.

Chein, J., Albert, D., O'Brien, L., Uckert, K., & Steinberg, L. (2011). Peers increase adolescent risk taking by enhancing activity in the brain's reward circuitry. *Developmental Science, 14*(2), F1–F10.

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

Chung, D., Christopoulos, G. I., King–Casas, B., Ball, S. B., & Chiu, P. H. (2015). Social signals of safety and risk confer utility and have asymmetric effects on observers' choices. *Nature Neuroscience, 18*(6), 18(6), 912–916.

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.

Crone, E. A., & Elzinga, B. M. (2015). Changing brains: How longitudinal functional magnetic resonance imaging studies can inform us about cognitive and social–affective growth trajectories. *Wiley Interdiscip Rev Cogn Sci, 6*(1), 53–63.

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

Crone, E. A., van Duijvenvoorde, A. C. K., & Peper, J. S. (2016). Annual Research Review: Neural contributions to risk-taking in adolescence–Developmental changes and individual differences. *Journal of Child Psychology and Psychiatry, 57*(3), 353–368.

Dahl, R. E. (2004). Adolescent brain development: A period of vulnerabilities and opportunities. Keynote address. *Ann N Y Acad Sci, 1021*, 1–22.

Dale, A. M. (1999). Optimal experimental design for event–related fMRI. *Human Brain Mapping, 8*(2–3), 109–114.

Davis, M. H. (1983). Measuring individual differences in empathy: Evidence for a multidimensional approach. *Journal of Personality and Social Psychology, 44*(1), 113.

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

Delgado, M. R. (2007). Reward-related responses in the human striatum. *Ann N Y Acad Sci, 1104*(1), 70–88.

Delgado, M. R., Nystrom, L. E., Fissell, C., Noll, D., & Fiez, J. A. (2000). Tracking the hemodynamic responses to reward and punishment in the striatum. *Journal of Neurophysiology, 84*(6), 3072–3077.

Dixon, M. L. (2015). Cognitive control, emotional value, and the lateral prefrontal cortex. *Frontiers in Psychology, 6,* 758.

Do, K. T., Guassi Moreira, J. F., & Telzer, E. H. (2017). But is helping you worth the risk? Defining Prosocial Risk Taking in adolescence. *Developmental Cognitive Neuroscience, 25,* 260–271.

Dumontheil, I., Apperly, I. A., & Blakemore, S. J. (2010). Online usage of theory of mind continues to develop in late adolescence. *Developmental Science, 13*(2), 331–338.

Eaton, D. K., Kann, L., Kinchen, S., Shanklin, S., Ross, J., Hawkins, J., . . . Wechsler, H. (2008). Youth risk behavior surveillance–United States, 2007. Morbidity and mortality weekly report. Surveillance summaries (Washington, DC: 2002), 57(4), 1–131.

Eisenberg, N. (2000). Emotion, regulation, and moral development. *Annu Rev Psychol, 51*, 665–697.

Eisenberg, N., Fabes, R. A., Murphy, B., Karbon, M., Maszk, P., Smith, M., . . . Suh, K. (1994). The relations of emotionality and regulation to dispositional and situational empathy–related responding. *Journal of Personality and Social Psychology, 66*(4), 776–797.

Ellsberg, D. (1961). Risk, ambiguity, and the Savage axioms. *The Quarterly Journal of Economics, 74*, 643–669.

Engelmann, J. B., & Tamir, D. (2009). Individual differences in risk preference predict neural responses during financial decision–making. *Brain Research, 1290*, 28–51.

Engelmann, J. B., Moore, S., Monica Capra, C., & Berns, G. S. (2012). Differential neurobiological effects of expert advice on risky choice in adolescents and adults. *Social Cognitive and Affective Neuroscience, 7*(5), 557–567.

Eppinger, B., Hämmerer, D., & Li, S. C. (2011). Neuromodulation of reward-based learning and decision making in human aging. *Annals of the New York Academy of Sciences, 1235*(1), 1–17.

Ernst, M., Nelson, E. E., McClure, E. B., Monk, C. S., Munson, S., Eshel, N., . . . Pine, D. S. (2004). Choice selection and reward anticipation: An fMRI study. *Neuropsychologia, 42*(12), 1585–1597.

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

Fecteau, S., Pascual–Leone, A., Zald, D. H., Liguori, P., Theoret, H., Boggio, P. S., & Fregni, F. (2007). Activation of prefrontal cortex by transcranial direct current stimulation reduces appetite for risk during ambiguous decision making. *Journal of Neuroscience, 27*(23), 6212–6218.

Figner, B., & Weber, E. U. (2011). Who takes risks when and why? Determinants of risk taking. *Current Directions in Psychological Science, 20*(4), 211–216.

Figner, B., Mackinlay, R. J., Wilkening, F., & Weber, E. U. (2009). Affective and deliberative processes in risky choice: Age differences in risk taking in the Columbia Card Task. *Journal of Experimental Psychology: Learning, Memory,and Cognition, 35*(3), 709–730.

Forbes, E. E., & Dahl, R. E. (2010). Pubertal development and behavior: Hormonal activation of social and motivational tendencies. *Brain and Cognition, 72*(1), 66–72.

Foulkes, L., & Blakemore, S.–J. (2018). Studying individual differences in human adolescent brain development. *Nature Neuroscience, 21*(3), 315–323.

Frey, R., Pedroni, A., Mata, R., Rieskamp, J., Hertwig. R. (2017). Risk preference shares the psychometric structure of major psychological traits. *Science Advances, 3*(10), e1701381.

Gabrieli, J. D., Ghosh, S. S., & Whitfield–Gabrieli, S. (2015). Prediction as a humanitarian and pragmatic contribution from human cognitive neuroscience. *Neuron, 85*(1), 11–26.

Galvan, A., Hare, T., Voss, H., Glover, G., & Casey, B. (2007). Risk-taking and the adolescent brain: Who is at risk? *Developmental Science, 10*(2), 8–14.

Gardner, M., & Steinberg, L. (2005). Peer influence on risk taking, risk preference, and risky decision making in adolescence and adulthood: An experimental study. *Developmental Psychology, 41*(4), 625–635.

Gianotti, L. R. R., Knoch, D., Faber, P. L., Lehmann, D., Pascual–Marqui, R. D., Diezi, C., . . . Fehr, E. (2009). Tonic activity level in the right

prefrontal cortex predicts individuals' risk raking. *Psychological Science, 20*(1), 33–38.

Giedd, J. N. (2004). Structural magnetic resonance imaging of the adolescent brain. *Ann N Y Acad Sci, 1021*(1), 77–85.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., . . . Rapoport, J. L. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. *Nature Neuroscience, 2*(10), 861.

Gilaie–Dotan, S., Tymula, A., Cooper, N., Kable, J. W., Glimcher, P. W., & Levy, I. (2014). Neuroanatomy predicts individual risk attitudes. *Journal of Neuroscience, 34*(37), 12394–12401.

Gilboa, I., & Schmeidler, D. (1989). Maxmin expected utility with non–unique prior. *Journal of Mathematical Economics, 18*(2), 141–153.

Glimcher, P. W., & Rustichini, A. (2004). Neuroeconomics: The consilience of brain and decision. *Science, 306*(5695), 447–452.

Gullone, E., Moore, S., Moss, S., & Boyd, C. (2000). The Adolescent Risk–Taking Questionnaire: Development and psychometric evaluation. *Journal of Adolescent Research, 15*(2), 231–250.

Gunther Moor, B., Crone, E. A., & van der Molen, M. W. (2010). The heartbrake of social rejection: Heart rate deceleration in response to unexpected peer rejection. *Psychological Science, 21*(9), 1326–1333.

Guroglu, B., van den Bos, W., & Crone, E. A. (2014). Sharing and giving across adolescence: An experimental study examining the development of prosocial behavior. *Frontiers in Psychology, 5*, 291.

Hall, G. S. (1904). *Adolescence: Its psychology and its relation to physiology, anthropology, sociology, sex, crime, religion, and education*. NJ: Prentice–Hall.: Englewoord Cliffs.

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.

Hartley, C. A., & Somerville, L. H. (2015). The neuroscience of adolescent decision–making. *Current Opinion in Behavioral Sciences, 5*, 108–115.

Hawk, S. T., Keijsers, L., Branje, S. J., Graaff, J. V., Wied, M., & Meeus, W. (2013). Examining the Interpersonal Reactivity Index (IRI) among early and late adolescents and their mothers. *Journal of Personality Assessment, 95*(1), 96–106.

Herting, M. M., Gautam, P., Chen, Z., Mezher, A., & Vetter, N. C. (2017). Test–retest reliability of longitudinal task–based fMRI: Implications for developmental studies. *Developmental Cognitive Neuroscience, 33,* 17–26.

Herting, M. M., Johnson, C., Mills, K. L., Vijayakumar, N., Dennison, M., Liu, C., . . . Tamnes, C. K. (2018). Development of subcortical volumes across adolescence in males and females: A multisample study of longitudinal changes. *NeuroImage, 172*, 194–205.

Hsu, M., Bhatt, M., Adolphs, R., Tranel, D., & Camerer, C. F. (2005). Neural systems responding to degrees of uncertainty in human decision–making. *Science, 310*(5754), 1680–1683.

Huettel, S. A., Song, A. W., & McCarthy, G. (2005). Decisions under uncertainty: Probabilistic context influences activation of prefrontal and parietal cortices. *Journal of Neuroscience, 25*(13), 3304–3311.

Huettel, S. A., Stowe, C. J., Gordon, E. M., Warner, B. T., & Platt, M. L. (2006). Neural signatures of economic preferences for risk and ambiguity. *Neuron, 49*(5), 765–775.

Humphrey, G., & Dumontheil, I. (2016). Development of risk–taking, perspective–taking, and inhibitory control during adolescence. *Developmental Neuropsychology, 41*(1–2), 59–76.

Kahneman, D., & Tversky, A. (1979). Prospect theory: An analysis of decision under risk. *Econometrica: Journal of the Econometric Society, 47,* 263–291.

Klein, A., & Tourville, J. (2012). 101 labeled brain images and a consistent human cortical labeling protocol. *Frontiers in Neuroscience, 6*, 171.

Klucharev, V., Hytönen, K., Rijpkema, M., Smidts, A., & Fernández, G. (2009). Reinforcement learning signal predicts social conformity. *Neuron, 61*(1), 140–151.

Knight, F. H. (1921). *Risk, uncertainty, and profit*. New York, NY: Houghton Mifflin.

Knoch, D., Gianotti, L. R. R., Pascual–Leone, A., Treyer, V., Regard, M., Hohmann, M., & Brugger, P. (2006). Disruption of right prefrontal cortex by low–frequency repetitive Transcranial Magnetic Stimulation induces risk–taking behavior. *Journal of Neuroscience, 26*(24), 6469–6472.

Knoll, L. J., Magis–Weinberg, L., Speekenbrink, M., & Blakemore, S. J. (2015). Social influence on risk perception during adolescence. *Psychological Science, 26*(5), 583–592.

Knutson, B., & Huettel, S. A. (2015). The risk matrix. *Current Opinion in Behavioral Sciences, 5*, 141–146.

Knutson, B., Taylor, J., Kaufman, M., Peterson, R., & Glover, G. (2005). Distributed neural representation of expected value. *Journal of Neuroscience, 25*(19), 4806–4812.

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

Lejuez, C., 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.

Lenroot, R. K., & Giedd, J. N. (2006). Brain development in children and adolescents: Insights from anatomical magnetic resonance imaging. *Neuroscience & Biobehavioral Reviews, 30*(6), 718–729.

Levy, D. J., & Glimcher, P. W. (2012). The root of all value: A neural common currency for choice. *Current Opinion in Neurobiology, 22*(6), 1027–1038.

Levy, I. (2016). Neuroanatomical substrates for risk behavior. *The Neuroscientist, 23*(3), 275–286.

Levy, I., Snell, J., Nelson, A. J., Rustichini, A., & Glimcher, P. W. (2010). Neural representation of subjective value under risk and ambiguity. *Journal of Neurophysiology, 103*(2), 1036–1047.

Li, R. (2017). Flexing dual–systems models: How variable cognitive control in children informs our understanding of risk–taking across development. *Developmental Cognitive Neuroscience, 27*, 91–98.

Li, R., Brannon, E. M., & Huettel, S. A. (2014). Children do not exhibit ambiguity aversion despite intact familiarity bias. *Frontiers in Psychology, 5*, 1519.

Mamerow, L., Frey, R., & Mata, R. (2016). Risk taking across the life span: A comparison of self–report and behavioral measures of risk taking. *Psychology and Aging, 31*(7), 711–723.

McCormick, E. M., & Telzer, E. H. (2017a). Failure to retreat: Blunted sensitivity to negative feedback supports risky behavior in adolescents. *Neuroimage, 147*, 381–389.

Mills, K. L., Goddings, A.–L., Clasen, L. S., Giedd, J. N., & Blakemore, S.–J. (2014). The developmental mismatch in structural brain maturation during adolescence. *Developmental Neuroscience, 36*(3–4), 147–160.

Mills, K. L., Goddings, A.–L., Herting, M. M., Meuwese, R., Blakemore, S.–J., Crone, E. A., . . . Sowell, E. R. (2016). Structural brain development between childhood and adulthood: Convergence across four longitudinal samples. *Neuroimage, 141*, 273–281.

Mills, K. L., Lalonde, F., Clasen, L. S., Giedd, J. N., & Blakemore, S. J. (2014). Developmental changes in the structure of the social brain in late childhood and adolescence. *Social Cognitive and Affective Neuroscience, 9*(1), 123–131.

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

Nichols, T., Brett, M., Andersson, J., Wager, T., & Poline, J.–B. (2005). Valid conjunction inference with the minimum statistic. *Neuroimage, 25*(3), 653–660.

O'Doherty, J. P. (2004). Reward representations and reward–related learning in the human brain: Insights from neuroimaging. *Current Opinion in Neurobiology, 14*(6), 769–776.

O'Doherty, J., Kringelbach, M. L., Rolls, E. T., Hornak, J., & Andrews, C. (2001). Abstract reward and punishment representations in the human orbitofrontal cortex. *Nature Neuroscience, 4*(1), 95–102.

Overgaauw, S., Guroglu, B., Rieffe, C., & Crone, E. A. (2014). Behavior and neural correlates of empathy in adolescents. *Developmental Neuroscience, 36*(3–4), 210–219.

Overgaauw, S., Rieffe, C., Broekhof, E., Crone, E. A., & Guroglu, B. (2017). Assessing empathy across childhood and adolescence: Validation of the Empathy Questionnaire for Children and Adolescents (EmQue–CA). *Frontiers in Psychology, 8*, 870.

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.

Peper, J. S., Braams, B. R., Blankenstein, N. E., Bos, M. G., & Crone, E. A. (2018). Development of multifaceted risk taking and the relations to sex steroid hormones: A longitudinal study. *Child Development, 89*(5), 1887–1907.

Peters, S., & Crone, E. (2017). Increased striatal activity in adolescence benefits learning. *Nature Communications, 8*(1), 1983.

Peters, S., Van Duijvenvoorde, A. C., Koolschijn, P. C. M., & Crone, E. A. (2016). Longitudinal development of frontoparietal activity during feedback learning: Contributions of age, performance, working memory and cortical thickness. *Developmental Cognitive Neuroscience, 19*, 211–222.

Pfeifer, J. H., & Peake, S. J. (2012). Self–development: Integrating cognitive, socioemotional, and neuroimaging perspectives. *Developmental Cognitive Neuroscience, 2*(1), 55–69.

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

Poldrack, R. A. (2008). The role of fMRI in Cognitive Neuroscience: Where do we stand? Current Opinion in Neurobiology, 18(2), 223–227.

Pushkarskaya, H., Smithson, M., Joseph, J. E., Corbly, C., & Levy, I. (2015). Neural correlates of decision–making under ambiguity and conflict. *Frontiers in Behavioral Neuroscience, 9,* 325.

Qu, Y., Galvan, A., Fuligni, A. J., Lieberman, M. D., & Telzer, E. H. (2015). Longitudinal changes in prefrontal cortex activation underlie declines in adolescent risk taking. *Journal of Neuroscience, 35*(32), 11308–11314.

RCore Team. (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Retrieved from http://www.R–project.org/.

Rangel, A., & Clithero, J. A. (2014). *The computation of stimulus values in simple choice.* In Neuroeconomics (Second Edition) (pp. 125–148): Elsevier.

Rao, H., Korczykowski, M., Pluta, J., Hoang, A., & Detre, J. A. (2008). Neural correlates of voluntary and involuntary risk taking in the human brain: An fMRI Study of the Balloon Analog Risk Task (BART). *Neuroimage, 42*(2), 902–910.

Raven, J., Raven, J. C., & Court, J. H. (1998). Manual for Raven's Progressive Matrices and Vocabulary Scales. *Section 3,The Standard Progressive Matrices*. Oxford, England: Oxford Psychologists Press/San Antonio, TX: The Psychological Corporation.

Romer, D., Reyna, V. F., & Satterthwaite, T. D. (2017). Beyond stereotypes of adolescent risk taking: Placing the adolescent brain in developmental context. *Developmental Cognitive Neuroscience 27,* 19–34.

Schienle, A., Köchel, A., Ebner, F., Reishofer, G., & Schäfer, A. (2010). Neural correlates ofintolerance of uncertainty. *Neuroscience Letters, 479*(3), 272–276.

*S*chreuders, E., Braams, B. R., Blankenstein, N. E., Peper, J. S., Güroğlu, B., & Crone, E. A. (2018). Contributions of reward sensitivity to ventral striatum activity across adolescence and early adulthood. *Child Development, 89*(3), 797–810.

Schriber, R. A., & Guyer, A. E. (2015). Adolescent neurobiological susceptibility to social context. *Developmental Cognitive Neuroscience, 19*, 1–18.

Sescousse, G., Caldú, X., Segura, B., & Dreher, J.–C. (2013). Processing of primary and secondary rewards: A quantitative meta–analysis and review of human functional neuroimaging studies. *Neuroscience & Biobehavioral Reviews, 37*(4), 681–696.

Shenhav, A., Botvinick, M. M., & Cohen, J. D. (2013). The expected value of control: an integrative theory of anterior cingulate cortex function. *Neuron, 79*(2), 217–240.

Sherman, L., Steinberg, L., & Chein, J. (2018). Connecting brain responsivity and real–world risk taking: Strengths and limitations of current methodological approaches. *Developmental Cognitive Neuroscience, 33,* 27–41.

Shiffman, S., Stone, A. A., & Hufford, M. R. (2008). Ecological momentary assessment. *Annual Review of Clinical Psychology, 4*, 1–32.

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.

Simons–Morton, B., Lerner, N., & Singer, J. (2005). The observed effects of teenage passengers on the risky driving behavior of teenage drivers. *Accident Analysis & Prevention, 37*(6), 973–982.

Smith, A. R., Chein, J., & Steinberg, L. (2014). Peers increase adolescent risk taking even when

the probabilities of negative outcomes are known. *Developmental Psychology, 50*(5), 1564.

Smith, A. R., Steinberg, L., & Chein, J. (2014). The role of the anterior insula in adolescent decision making. *Developmental Neuroscience, 36*(3–4), 196–209.

Somerville, L. H., & Casey, B. J. (2010). Developmental neurobiology of cognitive control and motivational systems. *Current Opinion in Neurobiology, 20*(2), 236–241.

Somerville, L. H., Hare, T. A., Casey, B. J. (2011). Frontostriatal maturiation predicts cognitive control failure to appetitive cues in adolescents. *Journal of Cognitive Neuroscience, 23*(9). 2123–2134.

Somerville, L. H., Jones, R. M., & Casey, B. J. (2010). A time of change: Behavioral and neural correlates of adolescent sensitivity to appetitive and aversive environmental cues. *Brain and Cognition, 72*(1), 124–133.

Steinberg, L. (2004). Risk taking in adolescence: What changes, and why? *Annals of the New York Academy of Sciences, 1021*(1), 51–58.

Steinberg, L. (2007). Risk taking in adolescence new perspectives from brain and behavioral science. *Current Directions in Psychological Science, 16*(2), 55–59.

Steinberg, L. (2008). A social neuroscience perspective on adolescent risk–taking. *Developmental Review, 28*(1), 78–106.

Studer B., Apergis–Schoute A. M., Robbins, T. W., & Clark, L. (2012). What are the odds? The neural correlates of active choice during gambling. *Frontiers in Neuroscience, 6*(46), 1–16.

Tamnes, C. K., Herting, M. M., Goddings, A. L., Meuwese, R., Blakemore, S. J., Dahl, R. E., . . . Mills, K. L. (2017). Development of the cerebral cortex across adolescence: A multisample study of inter–related longitudinal changes in cortical volume, Surface area, and thickness. *Journal of Neuroscience, 37*(12), 3402–3412.

Tamnes, C. K., Overbye, K., Ferschmann, L., Fjell, A. M., Walhovd, K. B., Blakemore, S.–J., & Dumontheil, I. (2018). Social perspective taking is associated with self–reported prosocial behavior and regional cortical thickness across adolescence. [Advance online publication]

Telzer, E. H. (2016). Dopaminergic reward sensitivity can promote adolescent health: A new perspective on the mechanism of ventral striatum activation. *Developmental Cognitive Neuroscience, 17*, 57–67.

Telzer, E. H., Fuligni, A. J., Lieberman, M. D., & Galván, A. (2013). Meaningful family relationships: Neurocognitive buffers of adolescent risk taking. *Journal of Cognitive Neuroscience, 25*(3), 374–387.

Telzer, E. H., Fuligni, A. J., Lieberman, M. D., & Galvan, A. (2013). Ventral striatum activation to prosocial rewards predicts longitudinal declines in adolescent risk taking. *Developmental Cognitive Neuroscience, 3,* 45–52.

Telzer, E. H., Fuligni, A. J., Lieberman, M. D., & Galvan, A. (2014). Neural sensitivity to eudaimonic and hedonic rewards differentially predict adolescent depressive symptoms over time. *Proceedings of the National Academy of Sciences*, *USA*, *111*(18), 6600–6605.

Telzer, E. H., Masten, C. L., Berkman, E. T., Lieberman, M. D., & Fuligni, A. J. (2010). Gaining while giving: an fMRI study of the rewards of family assistance among white and Latino youth. *Social Neuroscience, 5*(5–6), 508–518.

Thijssen, S., Wildeboer, A., Muetzel, R. L., Bakermans–Kranenburg, M. J., El Marroun, H.,

Hofman, A., . . . White, T. (2015). Cortical thickness and prosocial behavior in school–age children: A population–based MRI study. *Social Neuroscience, 10*(6), 571–582.

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.

Tricomi, E. M., Delgado, M. R., & Fiez, J. A. (2004). Modulation of caudate activity by action contingency. *Neuron, 41*(2), 281–292.

Turner, L., Mermelstein, R., & Flay, B. (2004). Individual and contextual influences on adolescent smoking. *Ann N Y Acad Sci, 1021*(1), 175–197.

Tversky, A., & Kahneman, D. (1992). Advances in prospect theory: Cumulative representation of uncertainty. *Journal of Risk and Uncertainty, 5*(4), 297–323.

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*, *109*(42), 17135–17140.

Tymula, A., Rosenberg Belmaker, L. A., Ruderman, L., Glimcher, P. W., & Levy, I. (2013). Like cognitive function, decision making across the life span shows profound age–related changes. *Proceedings of the National Academy of Sciences, 110*(42), 17143–17148.

Urosevic, S., Collins, P., Muetzel, R., Lim, K., & Luciana, M. (2012). Longitudinal changes in behavioral approach system sensitivity and brain structures involved in reward processing during adolescence. *Developmental Psychology, 48*(5), 1488–1500.

Van den Bos, W., & Hertwig, R. (2017). Adolescents display distinctive tolerance to ambiguity and to uncertainty during risky decision making. *Scientific Reports, 7*, 40962.

Van den Bos, W., Bruckner, R., Nassar, M. R., Mata, R., & Eppinger, B. (2017). Computational neuroscience across the lifespan: Promises and pitfalls. *Developmental Cognitive Neuroscience, 33,* 42–53.

Van den Bos, W., Rodriguez, C. A., Schweitzer, J. B., & McClure, S. M. (2014). Connectivity strength of dissociable striatal tracts predict individual differences in temporal discounting. *Journal of Neuroscience, 34*(31), 10298–10310.

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 Duijvenvoorde, A. C. K., Figner, B., Weeda, W. D., Van der Molen, M. W., Jansen, B. R., & Huizenga, H. M. (2016). Neural mechanisms underlying compensatory and noncompensatory strategies in risky choice. *Journal of Cognitive Neuroscience, 28*(9), 1358–1373

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. *Journal of Neuroscience, 35*(4), 1549–1560.

Van Duijvenvoorde, A. C. K., Jansen, B. R. J., Bredman, J. C., & Huizenga, H. M. (2012). Age–related changes in decision making: Comparing informed and noninformed situations. *Developmental Psychology, 48*(1), 192–203.

Van Duijvenvoorde, A. C. K., Jansen, B. R. J., Griffioen, E. S., Van der Molen, M. W., & Huizenga, H. M. (2013). Decomposing developmental

differences in probabilistic feedback learning: A combined performance and heart–rate analysis. *Biological Psychology, 93*(1), 175–183.

Van Duijvenvoorde, A. C. K., Op de Macks, Z. A., Overgaauw, S., Gunther Moor, B., Dahl, R. E., & Crone, E. A. (2014). A cross–sectional and longitudinal analysis of reward–related brain activation: Effects of age, pubertal stage, and reward sensitivity. *Brain and Cognition, 89*, 3–14.

Van Duijvenvoorde, A. C. K., Peters, S., Braams, B. R., & Crone, E. A. (2016). What motivates adolescents? Neural responses to rewards and their influence on adolescents' risk taking, learning, and cognitive control. *Neuroscience & Biobehavioral Reviews, 70*, 135–147.

Van Duijvenvoorde, A. C. K., Jansen, B. R., Visser, I., & Huizenga, H. M. (2010). Affective and cognitive decision–making in adolescents. *Developmental Neuropsychology, 35*(5), 539–554.

Van Duijvenvoorde, A. C. K., Peters, S., Braams, B. R., & Crone, E. A. (2016). What motivates adolescents? Neural responses to rewards and their influence on adolescents' risk taking, learning, and cognitive control. *Neuroscience and Biobehavioral Reviews, 70*, 135–147.

Van Hoorn, J., Van Dijk, E., Güroğlu, B., & Crone, E. A. (2016). Neural correlates of prosocial peer influence on public goods game donations during adolescence. *Social Cognitive and Affective Neuroscience, 11*(6), 923–933.

Van Leijenhorst, L., Gunther Moor, B., Op de Macks, Z. A., Rombouts, S. A., 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.

Van Noordt, S. J. R., & Segalowitz, S. J. (2012). Performance monitoring and the medial prefrontal cortex: A review of individual differences and context effects as a window on self–regulation. *Frontiers in Human Neuroscience, 6*, 197.

Varnum, M. E., Shi, Z., Chen, A., Qiu, J., & Han, S. (2014). When "Your" reward is the same as "My" reward: Self–construal priming shifts neural responses to own vs. friends' rewards. *NeuroImage, 87*, 164–169.

Venkatraman, V., Payne, J. W., Bettman, J. R., Luce, M. F., & Huettel, S. A. (2009). Separate neural mechanisms underlie choices and strategic preferences in risky decision making. *Neuron, 62*(4), 593–602.

Volz, K. G., Schubotz, R. I., & von Cramon, D. Y. (2003). Predicting events of varying probability: Uncertainty investigated by fMRI. *Neuroimage, 19*(2), 271–280.

Volz, K. G., Schubotz, R. I., & von Cramon, D. Y. (2004). Why am I unsure? Internal and external attributions of uncertainty dissociated by fMRI. *Neuroimage, 21*(3), 848–857.

Von Gaudecker, H.–M., Van Soest, A., & Wengström, E. (2011). Heterogeneity in risky choice behavior in a broad population. *The American Economic Review, 101*(2), 664–694.

Wierenga, L. M., Bos, M. G. N., Schreuders, E., Vd Kamp, F., Peper, J. S., Tamnes, C. K., & Crone, E. A. (2018). Unraveling age, puberty and testosterone effects on subcortical brain development across adolescence. *Psychoneuroendocrinology, 91,* 105–114.

Wildeboer, A., Thijssen, S., Muetzel, R. L., Bakermans–Kranenburg, M. J., Tiemeier, H., White, T., & van, I. M. H. (2017). Neuroanatomical correlates of donating behavior in middle childhood. *Social Neuroscience*, *13*(5), 541–552.

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

Wolf, L. K., Wright, N. D., Kilford, E. J., Dolan, R. J., & Blakemore, S.–J. (2013). Developmental changes in effects of risk and valence on adolescent decision–making. *Cognitive Development, 28*(3), 290–299.

Woo, C.–W., Krishnan, A., & Wager, T. D. (2014). Cluster–extent based thresholding in fMRI analyses: pitfalls and recommendations. *Neuroimage, 91*, 412–419.

Xue, G., Lu, Z., Levin, I. P., Weller, J. A., Li, X., & Bechara, A. (2009). Functional dissociations of risk and reward processing in the medial prefrontal cortex. *Cerebral Cortex, 19*(5), 1019–1027.

Yarkoni, T. (2009). Big correlations in little studies: Inflated fMRI correlations reflect low statistical power—Commentary on Vul et al.(2009). *Perspectives on Psychological Science, 4*(3), 294–298.

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large–scale automated synthesis of human functional neuroimaging data. *Nature Methods, 8*(8), 665–670.

Yarkoni, T., Poldrack, R. A., Van Essen, D. C., & Wager, T. D. (2010). Cognitive neuroscience 2.0: Building a cumulative science of human brain function. *Trends in Cognitive Sciences, 14*(11), 489–496.

Addendum

List of Publications

Blankenstein, N. E., Telzer, E. H., Do, K. T., Van Duijvenvoorde, A. C. K., & Crone E. A. (revision under review, 2018). Behavioral and neural pathways supporting the development of prosocial and risk-taking behavior across adolescence.

Blankenstein, N. E. & Van Duijvenvoorde, A. C. K. (in revision, 2018). Neural tracking of subjective value under risk and ambiguity in adolescence.

Blankenstein N. E., Peper, J. S., & Crone, E. A. (under review, 2018). Cognitive control and decision-making across child and adolescent development. To appear in O. Houdé & G. Borst (Eds.),The Cambridge Handbook of Cognitive Development. Cambridge: Cambridge University Press.

Blankenstein, N. E., Schreuders, E., Peper, J. S.,Crone, E. A., & Van Duijvenvoorde, A. C. K. (2018). Individual differences in risk-taking tendencies modulate the neural processing of risky and ambiguous decision-making in adolescence. *NeuroImage, 172,* 663-673.

Bos, M. G., Wierenga, L. M., **Blankenstein, N. E.,** Schreuders, E., Tamnes, C. K., & Crone, E. A. (2018). Longitudinal structural brain development and externalizing behavior in adolescence. *Journal of Child Psychology and Psychiatry, 59*(10), 1061-1072.

Peper, J. S., Braams, B. R., **Blankenstein, N. E.**, Bos, M. G. N., & Crone, E. A. (2018). Development of multiple-faceted risk-taking and the relations to testosterone: A longitudinal study. *Child Development, 89*(5), 1887-1907.

Schreuders, E., Braams, B. R., **Blankenstein, N. E.,** Peper, J. S., Güroğlu, B., & Crone, E. A. (2018). Contributions of reward sensitivity to ventral striatum activity across adolescence and early adulthood. *Child Development, 89*(3), 797-810.

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, 29*(11), 1-15.

Van Duijvenvoorde, A. C. K., **Blankenstein, N. E.,** Crone, E. A., & Figner, B. (2017). Towards a better understanding of adolescent risk taking: Contextual moderators and model-based analysis. In M. E. Toplak & J. Weller (Eds.), *Individual differences in judgment and decision making: A developmental perspective* (8-27). New York: Psychology Press.

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, 1*(1-2), 77-92.

Addendum

Curriculum Vitae

Nelia (Neeltje) Eliza Blankenstein was born on February 2nd 1991 in Leiden, the Netherlands. After graduating secondary school (Stedelijk Gymnasium Leiden) in 2009, Neeltje obtained her Bachelor's degree in Psychology in 2012 from Utrecht University and her Research Master's degree in Cognitive Neuroscience (cum laude) in 2014 from Leiden University. During her studies she completed her research internship at the Brain and Development Research Center at Leiden University, where she gained experience with functional MRI. In 2014Neeltje started her PhD project at the Brain and Development Research Center under supervision of dr. Anna van Duijvenvoorde and prof. dr. Eveline Crone. Neeltje investigated the behavioral and neural mechanisms underlying risky decision-making in adolescents from a developmental neuroeconomic perspective. In 2018 Neeltje started working as a post-doctoral researcher at Leiden University (Clinical Neurodevelopmental Sciences at the Institute of Education and Child Studies) and the VU Medical Center (Child and Adolescent Psychiatry), to investigate the contribution of behavioral and neurobiological factors to the development of antisocial behavior in adolescence.

It is our choices,
that show what we truly are,
far more than our abilities.

J. K. Rowling

Propositions

Accompanying the public defense of Neeltje Blankenstein's dissertation:
'Risky business? Behavioral and neural mechanisms underlying
risky decision-making in adolescents' on February 14, 2019.

1. Attitudes towards explicit risk and ambiguous risk are two separate tendencies that drive (adolescent) risk-taking behavior differently, and are reflected in different neural mechanisms *(this thesis).*

2. Behavior under ambiguity, rather than under risk, is a more naturalistic reflection of adolescent risk-taking behavior in real life *(this thesis).*

3. Individual differences in task-based and real-life risk taking are reflected in brain activation. These individual differences are equally important as general age differences *(this thesis).*

4. Fun seeking behavior is a potential differential susceptibility marker that predicts both risk taking and prosocial tendencies *(this thesis).*

5. Adolescent risk-taking behavior is a multifaceted construct and studying it therefore warrants a multidisciplinary, multi-methodological approach.

6. Models on adolescent risk taking should give more weight to effects of individual differences and context. Not all adolescents are risk takers, and adolescents do not always take risks.

7. Adolescent risk taking is not necessarily maladaptive, since it may serve positive outcomes such as helping others and learning.

8. Studying longitudinal change in brain and behavior is essential to predict positive or negative life outcomes.

9. The significance of research should not be measured by the presence of significant results, but by the hypotheses and the methods used.

10. The scientific process is too ambiguous: open and collaborative science is the way forward.