IMPULSIVITY IN ADOLESCENTS: COGNITIVE, NEURAL, HORMONAL AND SOCIAL FACTORS

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Propositions

1) Contrary to popular belief, not all adolescents are impulsive. However, adolescents who are highly impulsive differ from their less impulsive peers in their decision-making, decision-related brain activity, and peer status (this thesis).

2) Developmental psychology could benefit strongly from research that combines cognitive, neural and social methods, since such a multidisciplinary approach provides both excellent experimental control and high ecological validity, and may provide unique insights into the underlying mechanisms of adolescent behavior (this thesis).

3) The importance of studying the fundamental mechanisms of behavior cannot be overstated. While intervention studies are highly valuable, such studies cannot be designed properly without the vital insights gained by fundamental, well-controlled experimental research (this thesis).

4) Neurobiological models of adolescent impulsivity can only be adequately tested using longitudinal designs that include neural and behavioral measures (this thesis).

5) Gender differences should only be explored if there is consistent prior research suggesting potential gender differences, and these differences should only be explained by scientific theories and not by stereotypes about gender.

6) Paying for open access of scientific publications is not necessary and not sufficient to truly share one’s research with the general public.

7) Early career researchers should have the freedom to conduct research that is creative, risky, and only yields results in the long run, and they should be evaluated on the quality of their research, not the quantity.

8) The many advantages of being a scientist should be emphasized more in the media, instead of only reporting on the disadvantages of working in a competitive, publish-or-perish industry.

9) People who have trouble getting up early in the morning are not lazy. They may need more time to get started, but once they do, they are unstoppable!

10) While Italian food, Mexican food and all-you-can-eat sushi are close contenders, the number one food in the world definitely comes from Peru.
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Cognitive, Neural, Hormonal and Social Factors

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CHAPTER 1

INTRODUCTION
Adolescence is the developmental transition period between childhood and adulthood. Adolescence starts with the onset of physiological changes associated with the beginning of puberty, between the ages of 9 and 12 years (Crone & Dahl, 2012). The end of adolescence differs by culture and occurs when adolescents assume adult social roles and responsibilities, between 20-25 years in most western cultures (Crone & Dahl, 2012).

Adolescence is a developmental period characterized by heightened impulsivity (Steinberg, 2008). Impulsivity is a multidimensional construct that includes poor inhibition of motor responses, a relatively strong preference for immediate rewards over long-term rewards, increased engagement in risky behaviors, and aggression (Dalley, Everitt, & Robbins, 2011). Compared to children and adults, adolescents engage in higher levels of impulsive behaviors in daily life, such as excessive alcohol use, smoking cigarettes, having unprotected sex and violent and criminal behaviors (Steinberg, 2008). Not all adolescents are highly impulsive and most adolescents reach adulthood without major problems (Dahl, 2004). But those who are highly impulsive have an increased risk of developing behavioral problems later in life, such as substance abuse and dependence, and their reckless behaviors might also pose a threat to the well-being of others (Steinberg, 2004). Therefore, it is important to better understand the different factors that contribute to high levels of impulsive behaviors in adolescents. A wide array of factors contribute to impulsivity in adolescents, most notably cognitive, neural, hormonal and social factors.

**Cognitive Factors: Risky Decision-making and Temporal Discounting**

Adolescents’ decision-making abilities are still developing, which has been hypothesized to contribute to their daily life impulsivity (Boyer, 2006). A growing number of researchers have examined age-related differences in decision-making from childhood to adulthood. Two types of decisions in particular have been frequently studied: decisions involving risk, and intertemporal decisions between small, immediate rewards and larger, delayed rewards. Both risk and time are important factors in impulsivity (Dalley et al., 2011): impulsive behaviors that adolescents may engage in such as texting while driving may be a reflection of a relatively strong tendency to take risks, and also of a relatively strong tendency to place a high value on the present over the future.

Decisions involving risk are typically studied with gambling tasks in which individuals choose between a low-risk and a high-risk option. The low-risk option typically has a high probability of winning a small monetary reward (e.g., 67% probability of winning €2), and a low probability of not winning a reward. The high-risk option typically has a low probability of winning a larger reward (e.g., 33% probability of winning €8), and a high probability of not winning a reward.

Intertemporal decisions are often studied with Temporal Discounting (TD) tasks (see Scheres, de Water, & Mies, 2013, for a review), in which participants choose between small, immediate rewards (e.g., €2 today) and larger, delayed rewards (e.g., €10 in 14 days). In TD
tasks, both the amount of the immediate reward and the delay preceding the larger reward are varied, in order to determine an individual’s subjective value of the delayed reward at a specific delay. The subjective value is equal to the \textit{indifference point}: the immediate reward value at which an individual has no clear preference for either the delayed reward or the immediate reward. TD refers to the decrease in subjective value of a reward as the delay preceding its delivery increases. A relatively strong preference for immediate rewards is interpreted as a sign of impulsivity and is usually labelled as steep or increased TD (Scheres et al., 2006).

There are several important reasons to study age-related differences in risky decision-making and TD. First, age-related differences in risky decisions and TD might underlie age-related differences in impulsive behaviors in daily life. Specifically, adolescents may show more risky decision-making and/or a stronger preference for immediate rewards than adults, which might explain why they also engage in more impulsive behaviors (e.g., substance use) than adults. Second, in order to develop adequate interventions aimed at reducing highly impulsive behaviors in adolescents, it is important to understand which decision-making processes should be targeted. Several cognitive interventions have been shown to successfully reduce risky decision-making (Reyna, Weldon, & McCormick, 2015) and the preference for immediate rewards in adolescents (Daniel, Said, Stanton, & Epstein, 2015). It is important to tease apart age-related differences in risky decision-making and TD, as they are distinct components of impulsivity (Dalley et al., 2011), and may require different interventions.

Prior studies of age-related differences in risky decision-making have provided inconsistent results (see Defoe, Dubas, Figner, & van Aken, 2015, for a review). Several studies have reported a linear decrease with age in risky decision-making, with adults showing less risky decision-making than adolescents (Crone, Somsen, van Beek, & van der Molen, 2004; Mitchell, Schoel, & Stevens, 2008; Steinberg et al., 2008; van Duijvenvoorde, Jansen, Bredman, & Huizenga, 2012), and adolescents less than children (Crone & van der Molen, 2007; Hooper, Luciana, Conklin, & Yarger, 2004). However, other studies have reported no differences in risky decision-making between adolescents and adults (Cauffman et al., 2010; Overman et al., 2004). Other studies have reported non-linear age-related differences, with adolescents demonstrating more risky decision-making than either children or adults (Burnett, Bault, Coricelli, & Blakemore, 2010; Smith, Xiao, & Bechara, 2012). Differences in task characteristics across studies may have contributed to these inconsistent findings, as some studies suggest that adolescents show more risky decision-making than adults only under emotionally arousing conditions (Figner, Mackinlay, Wilkening, & Weber, 2009; van Duijvenvoorde, Jansen, Visser, & Huizenga, 2010).

While the evidence for age-related differences in risky decision-making is mixed, studies of \textit{individual differences} have consistently shown that adolescents who make the riskiest decisions in gambling tasks, also report the highest levels of risk-taking in daily life, such as high levels of sensation-seeking (van Leijenhorst, Westerberg, & Crone, 2008),
alcohol use (Xiao et al., 2009), and smoking (Lejuez, Aklin, Bornovalova, & Moolchan, 2005b; Xiao et al., 2008). Thus, while it is still unclear how risky decision-making develops from childhood to adulthood, it has been consistently shown to correlate with real-life risk behaviors in adolescents.

Similar to risky decision-making, inconsistent findings have been reported for age-related differences in TD from childhood to adulthood. Several studies have reported that children show steeper discounting of delayed rewards than adolescents (Prencipe et al., 2011; Scheres et al., 2006), and that adolescents show steeper discounting than adults (Olson, Hooper, Collins, & Luciana, 2007; Steinberg et al., 2009), suggesting a linear association between age and TD. In contrast, one study reported no differences in discounting of delayed rewards between adolescents and adults (Audrain-McGovern et al., 2009). Further, another study has reported non-linear age-related differences in TD, with adolescents showing less discounting of delayed rewards than both children and adults (Scheres, Tontsch, Thoery, & Sumiya, 2014). In addition to age differences, there are large individual differences among adolescents in TD, that are associated with daily life impulsive behaviors and impulse control problems (MacKillop et al., 2011; Patros et al., 2016). Specifically, adolescents who show relatively steep discounting of delayed rewards report increased alcohol use (Field, Christiansen, Cole, & Goudie, 2007) and smoking (Audrain-McGovern et al., 2009; Reynolds & Fields, 2012; Reynolds et al., 2007). Adolescents with impulse control problems, such as ADHD (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2012; Patros et al., 2016; Scheres, Tontsch, Thoery, & Kazakurkin, 2010) and conduct disorder (White et al., 2014), also have shown steeper discounting of delayed rewards than typically developing adolescents.

Given inconsistent earlier findings, more research on the development of risky decision-making and TD clearly is needed. Several important gaps in prior research need to be adressed, including: 1) focusing on individuals across a wide age range; 2) examining age-related differences in risky decision-making and TD and their correlation in the same participants; 3) investigating the potentially confounding effect of age-related differences in monetary reward valuation. First, most previous studies focused on individuals within a relatively narrow age range, in that they compared children and early adolescents, or late adolescents and young adults. Ideally, studies should examine decision-making in early, middle, and late adolescents, and in adults, in order to compare developmental groups with relatively low levels of daily-life impulsivity (i.e., early adolescents and adults) with developmental groups in which daily-life impulsivity peaks (i.e., middle and late adolescents). Second, few studies have examined age-related differences in both risky decision-making and TD and their correlation in the same participants. Risky decision-making and TD are hypothesized to be distinct components of impulsivity (Dalley et al., 2011), but it is not yet clear whether they show similar age-related differences and whether they are correlated across adolescence and young adulthood. Third, risky decision-making and TD usually have been studied with tasks that include monetary rewards. Yet, a 12-year-old might value a €2 reward more than a 20-year-old. It is not yet clear whether age differences in the valuation...
of such rewards contribute to the observed age differences in decision-making. Therefore, the first goal of this thesis was to examine age-related differences in risky decision-making and TD, their correlation, and the role of monetary reward valuation, in adolescents and young adults across a wide age range (12-27 years).

**Neural Factors: Development of Reward and Control Brain Areas**

The development of functional magnetic resonance imaging (fMRI) has allowed researchers to study brain development in a non-invasive way. Broadly, fMRI is a technique that can be used to measure the amount of oxygenated blood that is present in specific brain areas (Harris, Reynell, & Attwell, 2011) - a proxy for the activity of these areas - during the performance of a cognitive task, or at rest. Decision-making tasks can be administered to adolescents while they are scanned with fMRI, in order to probe brain activity during their different decisions.

There are multiple advantages of studying neural factors contributing to impulsivity in adolescence. First, these studies enable one to gain more insight into the detailed underlying mechanisms of impulsive behaviors and decisions in adolescents, and could thus improve neurobiological models of adolescent development. Second, studying brain development and its correlation with impulsivity in typically developing adolescents may inspire hypotheses about aberrant functioning of specific brain areas in adolescents with impulse-control disorders, such as ADHD and substance abuse. Further, studies that establish the neural correlates of heightened impulsivity in adolescents could inform researchers who are developing neurofeedback interventions (e.g., real-time fMRI neurofeedback) that are designed to change activity of specific brain areas (Cohen Kadosh et al., 2016; Sulzer et al., 2013), in order to reduce certain behaviors (e.g., impulsivity).

In recent years, a growing number of researchers have studied brain development from childhood through adulthood, which has inspired neurobiological models of adolescent development. These neurobiological models propose that adolescents are more impulsive than adults and children because of an imbalance between relatively mature brain areas involved in reward processing (i.e., the ventral striatum; VS) and relatively immature brain areas involved in cognitive control (i.e., the prefrontal cortex; PFC) (Casey, Getz, & Galvan, 2008; Shulman et al., 2016; Somerville & Casey, 2010; Steinberg, 2008). Indeed, fMRI studies have demonstrated differential functioning of the VS and PFC in adolescents compared to children and adults. Specifically, adolescents show increased VS activity during reward processing (compared to children and adults), and either increased or decreased PFC activity during cognitive control tasks (compared to adults) (Crone & Dahl, 2012). Few studies have examined neural mechanisms underlying individual differences in daily-life impulsivity and risky decision-making and TD in adolescents. The handful of studies that did investigate individual differences suggest that the imbalance between the VS and PFC is enhanced in adolescents who are the most impulsive. Specifically, adolescents who reported more
alcohol use and other daily-life risk-taking behaviors than their peers showed increased VS activation during reward processing (Braams, Peper, van der Heide, Peters, & Crone, 2016; Galvan, Hare, Voss, Glover, & Casey, 2007). Further, adolescents who discounted delayed rewards more steeply than peers, engaged the VS more but the PFC less during TD choices (Stanger et al., 2013).

While previous studies have provided important insights into the neural factors contributing to impulsivity in adolescents, there are still several gaps in this research area. First, most previous fMRI studies of adolescent impulsivity have been cross-sectional. These studies certainly have been highly valuable, but longitudinal studies are more sensitive to developmental changes (Crone & Elzinga, 2015), and can address additional research questions, such as how stable impulsive behavior and brain activation are, and whether changes in brain activity are associated with changes in behavior. This last research question in particular has been overlooked in prior research, since most studies either compared neural activity between age groups without investigating whether neural differences also were associated with age differences in impulsivity, or focused on cross-sectional correlations between impulsivity and brain activity. In order to test neurobiological models of adolescent impulsivity, it is vitally important to test whether longitudinal changes in brain activity are correlated with changes in impulsivity. Therefore, the second goal of this thesis was to examine the neural mechanisms underlying individual differences between adolescents in TD, a key component of impulsivity, using a longitudinal design.

**Puberty and Hormonal Development**

At the onset of puberty (around 9-12 years of age), sex steroid hormones such as testosterone and estradiol surge, driving the physical changes associated with puberty (Crone & Dahl, 2012). In girls, estradiol is produced by the ovaries, and stimulates breast development and the onset of menarche. Testosterone is produced by the adrenal glands in girls and stimulates the growth of pubic and axillary hair (Grumbach & Styne, 2003). In boys, testosterone is produced by the testes, and promotes the deepening of the voice and the growth of body and facial hair. Testosterone is converted into estradiol by the enzyme aromatase in boys and girls (Grumbach & Styne, 2003). In addition to stimulating physical changes, recent research has suggested that testosterone and estradiol might also influence brain activation and impulsive behavior in adolescents (Peper & Dahl, 2013).

Exploring the potential effects of puberty-related hormones on impulsivity and its neural correlates in adolescents is highly relevant for several reasons. First, puberty marks the transition from childhood to adolescence. Throughout adolescence, testosterone and estradiol levels increase dramatically: testosterone levels are 45 times higher in late adolescent boys than in pre-pubescent boys (Biro, Lucky, Huster, & Morrison, 1995). Estradiol levels are 4-9 times higher in late adolescent girls than in pre-pubescent girls (Ikegami et al., 2001). Moreover, testosterone and estradiol are known to activate certain brain areas in
adolescents; their receptors are particularly abundant in subcortical brain areas that play a key role in adolescent impulsivity, such as the VS (McEwen, 2001; Stevens, 2002). Given the links to these brain areas, it has been proposed that puberty-related hormones play a role in promoting impulsive behavior (Crone & Dahl, 2012; Nelson, Leibenluft, McClure, & Pine, 2005).

Indeed, adolescent boys and girls with more advanced pubertal maturation and higher testosterone and estradiol levels than their peers report greater alcohol use, when controlling for age (Costello, Sung, Worthman, & Angold, 2007; de Water, Braams, Crone, & Peper, 2013; Eriksson, Kaprio, Pulkkinen, & Rose, 2005; Martin, Mainous, Curry, & Martin, 1999). Higher testosterone levels are also associated with increased VS responses to rewards in adolescents, even when controlling for age (Braams, van Duijvenvoorde, Peper, & Crone, 2015; Op de Macks et al., 2011). Additionally, a recent study suggests that sex steroid hormones are also correlated with risky decision-making; Peper and colleagues (2013) found that higher testosterone levels were associated with increased risky decision-making in adolescents, when controlling for age.

Despite these promising findings on the association between puberty-related hormones and impulsivity and its underlying cognitive and neural mechanisms, much remains to be explored. For instance, little is known about how pubertal maturation and puberty-related hormones are associated with TD and its neural mechanisms in adolescents. Nevertheless, the subcortical regions that contribute to steep TD (i.e., the VS) are rich in testosterone and estradiol receptors, and steep TD is positively associated with alcohol use (Field et al., 2007), which has been linked to advanced pubertal maturation and relatively high levels of testosterone and estradiol in prior research (Costello et al., 2007; de Water et al., 2013; Eriksson et al., 2005; Martin et al., 1999). Thus, it can be hypothesized that one mechanism through which puberty-related hormones stimulate impulsive behaviors in adolescents, such as alcohol use, is through influencing their intertemporal decisions and the brain areas subserving these decisions. Further, TD is an excellent paradigm to test neurobiological models of puberty-related influences on brain activation, as it has been argued that puberty-related hormones affect the activity of affective subcortical brain areas but not of cognitive prefrontal areas (Nelson et al., 2005). Decision-making in TD tasks reliably recruits both affective (e.g., the VS) and cognitive brain areas (e.g., the lateral PFC) (Scheres et al., 2013). Thus, the third goal of this thesis was to examine whether pubertal development and sex steroid hormones (testosterone and estradiol) are associated with TD and its neural correlates in adolescents.

Social Factors: Peer Status and Peer Influence

During adolescence, a social reorientation occurs, in that adolescents spend an increasing amount of time with peers instead of parents (Steinberg & Morris, 2001). Peers influence adolescents’ behaviors both positively and negatively. Peers are particularly
influential when it comes to impulsive behaviors. One of the best predictors of drinking, smoking, and marijuana use in adolescence is having a best friend with high levels of substance use (Burk, van der Vorst, Kerr, & Stattin, 2012; de Vries, Engels, Kremers, Wetzels, & Mudde, 2003; Knecht, Burk, Weesie, & Steglich, 2011; Laursen, Hafen, Kerr, & Stattin, 2012; Mercken, Steglich, Knibbe, & de Vries, 2012; Tucker, de la Haye, Kennedy, Green, & Pollard, 2014). Further, the presence of peers is associated with increased risky decision-making (Gardner & Steinberg, 2005) and steeper discounting of delayed rewards (O’Brien, Albert, Chein, & Steinberg, 2011; Weigard, Chein, Albert, Smith, & Steinberg, 2014). But not all peers are equally influential: popular peers have more influence on adolescent risk-taking than less popular peers (Cohen & Prinstein, 2006; Prinstein, Brechwald, & Cohen, 2011; Teunissen et al., 2012).

Given that peers, in particular popular peers, exert such strong influence on the adolescents’ impulsive behaviors, it is critically important to study the mechanisms through which this influence occurs. As indicated above, previous studies have suggested that the presence of peers increases risky decision-making and steep TD (Gardner & Steinberg, 2005; O’Brien et al., 2011; Weigard et al., 2014). It further has been shown that peer presence is associated with increased activation of affective brain areas (i.e., the VS) during decision-making (Chein, Albert, O’Brien, Uckert, & Steinberg, 2011). The effect of popular peers on decision-making and neural processing has not yet been investigated, despite the fact that popular peers are considered most influential in the peer group (Cohen & Prinstein, 2006; Prinstein et al., 2011; Teunissen et al., 2012). More insight into the cognitive (decision-making) and neural mechanisms that explain the impact of popular adolescents on the impulsive behaviors of less popular adolescents could inform interventions aimed at reducing impulsive behaviors for which peer influence is a contributing factor.

It is not surprising that popular adolescents are highly influential, since adolescents prioritize being popular with their peers over other goals (LaFontana & Cillessen, 2010), and many adolescents want to be affiliated with their popular peers to increase their own group status (Dijkstra, Cillessen, Lindenberg, & Veenstra, 2010). In adolescence, two moderately correlated types of high peer status are distinguished: popularity and acceptance (Parkhurst & Hopmeyer, 1998). Popular adolescents are dominant and visible in the peer group, and show high levels of both prosocial as well as antisocial behaviors, such as enhanced substance use and relational aggression (e.g., ignoring and excluding their peers) (Allen, Porter, McFarland, Marsh, & McElhaney, 2005; Mayeux, Sandstrom, & Cillessen, 2008; Rose, Swenson, & Waller, 2004; Sandstrom & Cillessen, 2006; Tucker et al., 2013). Engaging in substance use and relational aggression helps adolescents achieve and maintain popularity (Cillessen & Mayeux, 2004; Mayeux et al., 2008). The mixed profile of positive and negative behaviors of popular adolescents is also reflected in their peers’ responses to them: while popular adolescents are positively evaluated on an explicit level (by self-report), adolescents’ implicit evaluations (as measured by an approach-avoidance task) indicate a more negative, avoidant response to popular peers (Lansu, Cillessen, & Karremans, 2012).
contrast, accepted adolescents are well-liked by their peers, since they show high levels of prosocial behaviors, without the enhanced antisocial behaviors that are observed in popular adolescents. In childhood, popularity and acceptance are highly correlated, indicating that children who are well-liked are also considered popular (Cillessen & Mayeux, 2004). However, in adolescence, the correlation between popularity and acceptance becomes moderate or even negative, reflecting the fact that popular adolescents use both prosocial and antisocial strategies to attain their desired goals (Cillessen & Mayeux, 2004).

While the associations between peer status and impulsive daily life behaviors have been well-established, several important research questions have not yet been examined. Notably, it is not exactly known why popular adolescents engage in heightened impulsive behaviors; the mechanisms that underlie the positive association between adolescent popularity and impulsive behaviors have been relatively unexplored. Given that popular adolescents engage in impulsive behaviors that may cause harm to themselves or others (i.e., substance use, aggression), it is vital to understand the underlying mechanisms of these behaviors. Potential mechanisms may be adolescents’ risky decision-making and steep TD and their neural mechanisms, which have been linked consistently to the impulsive behaviors that popular adolescents frequently engage in (Field et al., 2007; Lejuez, Aklin, Bornovalova, & Moolchhan, 2005a; Lejuez, Aklin, Zvolensky, & Pedulla, 2003; Reynolds, 2006; Stanger et al., 2013; Xiao et al., 2008; Xiao et al., 2009). In addition, given popular adolescents’ strong involvement in the social exclusion of peers (Cillessen & Mayeux, 2004), one of the most frequently used forms of aggression by adolescents, the underlying (neural) mechanisms of being excluded by popular peers deserve to be explored. Thus, the fourth and final goal of this thesis was to examine the role of peer group status in adolescents’ risky decision-making and TD, and the effects of peer status on neural responses to social exclusion.

Summary of Research Aims

This dissertation had four main aims. The first aim was to examine age-related differences in risky decision-making and TD, their correlation, and the role of monetary reward valuation, in adolescents and young adults. The second aim was to examine the neural mechanisms associated with individual differences among adolescents in a key component of impulsivity, TD, using a longitudinal design. The third aim was to examine whether pubertal development and sex steroid hormones (testosterone and estradiol) are associated with TD and its neural correlates in adolescents. The fourth aim was to examine the role of peer status (popularity and acceptance) and dyadic peer relationships (best friendships) in adolescents’ impulsivity. I examined the role of peer status and friendships in substance use, TD, and risky decision-making. In addition, I investigated the effects of peer status on neural responses to social exclusion, one of the most frequently used forms of relational aggression.
Thesis Outline

In Chapter 2, I examined age-related differences in risky decision-making and TD, and their correlation, in adolescents and young adults (12-27 years). I further explored the effects of monetary reward valuation and pubertal maturation on risky decision-making and TD.

In Chapter 3, I examined the neural mechanisms underlying individual differences in TD of money and primary rewards in 12-16 year-old adolescents. I used a mixed-effects model approach to decompose TD choices into distinct components: 1) average impatience, reflecting both the contribution of the immediate reward amount and the delay preceding the larger reward to TD choice; 2) amount sensitivity, or the unique contribution of the immediate reward amount to choice; 3) delay sensitivity, or the unique contribution of the delay preceding the larger reward to TD choice. In addition, I compared TD of money and primary rewards at the behavioral and neural level, and explored the effects of testosterone and estradiol levels on TD and its neural correlates.

In Chapter 4, I report on the longitudinal follow-up of the adolescents who participated in the study of Chapter 3. Approximately one year later, I administered the same TD task to these participants. This allowed me to examine: 1) the stability of TD choices and neural activity during these choices; 2) longitudinal changes in brain activity during TD choices; 3) whether longitudinal changes in brain activity and structure were associated with changes in TD.

In Chapter 5, I examined whether adolescent best friends (12-18 years) were similar in their substance use and risky and impulsive (TD) decision-making, whether adolescents’ decision-making was associated with their own and their best friends’ substance use, and whether the relative popularity within a best friendship dyad influenced the associations between decision-making and substance use.

In Chapter 6, I investigated the effects of peer status on neural responses to social exclusion and inclusion in 12-16 year-old adolescents. I examined the effects of the popularity of the excluders and of adolescents’ own popularity and peer acceptance.
CHAPTER 2

Distinct Age-Related Differences in Temporal Discounting and Risk-taking in Adolescents and Young Adults

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Abstract

Age-related differences in temporal discounting (TD) and risk-taking, and their association, were examined in adolescents and young adults ($n = 337$) aged 12-27 years. Since monetary rewards are typically used in TD and risk-taking tasks, the association between monetary reward valuation and age and decision-making in these tasks was explored as well. TD declined linearly with age, with a particularly sharp decline from 15 to 16 years. In contrast, risk-taking was not correlated with age and TD. Reward valuation was not associated with TD and risk-taking, and age-related differences in TD remained significant after controlling for reward valuation. Together, these findings suggest that risk-taking and TD are two separate constructs with distinct age-related differences in adolescence and young adulthood.
Adolescents frequently engage in impulsive and risky behaviors, such as substance use, unprotected sex, and reckless driving (Hibell et al., 2012). Impulsivity is a multifaceted construct, and has been defined as including both a preference for smaller, immediate rewards over larger, delayed rewards, as well as engaging in risky behaviors (Dalley, Everitt, & Robbins, 2011). Given this definition of impulsivity and the fact that many risky behaviors could also be characterized as impulsive, one might assume that impulsivity and risk-taking are positively related constructs in adolescence and young adulthood. However, several studies have suggested otherwise, by showing that impulsive and risky decision-making are not correlated in children, adolescents and young adults (Olson, Hooper, Collins, & Luciana, 2007; Prencipe et al., 2011; Scheres et al., 2006).

At present, little is known about whether age-related differences in both constructs are similar or distinct in adolescence and young adulthood. Age-related differences in impulsive and risky decision-making are often assessed with tasks in which the delay to a monetary reward or the probability of receiving that reward is systematically varied, respectively. Temporal discounting (TD) tasks, which measure one aspect of impulsivity (i.e., preference for immediate rewards), involve choices between smaller, immediate rewards (e.g., €5 today), and larger rewards that are delivered after a delay (e.g., €10 in 2 weeks). Risk-taking on the other hand, is frequently measured by gambling tasks, in which participants must choose between receiving a small reward with a high probability, or a larger reward with a low probability.

**Age-related differences in Temporal Discounting**

TD refers to the decrease in subjective value of a reward when the delay to that reward increases. TD tasks measure the preference for immediate rewards (Green & Myerson, 2004), which is a component of impulsivity that is distinct from the failure to inhibit inappropriate behaviors (Solanto et al., 2001). Impulsive individuals typically display an increased preference for smaller, immediate rewards (i.e., increased discounting). Indeed, it has been found that adolescents with ADHD, and adolescent smokers, show relatively steep discounting of delayed rewards (i.e., strong preference for immediate rewards) in TD tasks (Audrain-McGovern et al. 2009; Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2012a; Reynolds & Fields, 2012; Scheres, Tontsch, Thoeny, & Kaczkurkin, 2010b).

Although discounting of delayed rewards decreases across the lifespan (Green, Fry, & Myerson, 1994), findings on age-related differences in TD during childhood, adolescence and adulthood are limited to a small number of studies, and inconsistent. Some studies have shown a linear decrease in TD from childhood (6-11 years) to adolescence (12-17 years) (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2012b; Prencipe et al., 2011; Scheres et al., 2006), and from adolescence to young adulthood (18-30 years) (Olson et al., 2007; Steinberg et al., 2009). In contrast, others have reported non-linear age-related differences in TD, with decreased discounting in adolescents compared to children and young adults (Scheres, Tontsch, Thoeny, & Sumiya, 2013). Finally, in a longitudinal study, Audrain-McGovern et al.
(2009) showed that discounting was stable between the ages of 15 and 20 years.

One explanation for the inconsistent findings on age-related differences in TD might be the use of different TD tasks. Linear decreases in TD with age have mostly been reported by researchers using TD tasks with relatively large monetary rewards (e.g., $10-100) and long delays (e.g., up to 1 year) (Olson et al., 2007; Steinberg et al., 2009; but see Scheres et al., 2006 for an exception). The increased preference for delayed rewards with increasing age observed in these studies could be due to improvements in cognitive control functions during adolescence, such as working memory and response inhibition (Huizinga, Dolan, & van der Molen, 2006; Luciana, Conklin, Hooper, & Yarger, 2005).

Non-linear age-related differences were reported when all rewards and delays were actually experienced (Scheres et al., 2013). It may be hypothesized that in TD tasks with real rewards, affective processes, such as reward sensitivity, influence one’s preferences more strongly than cognitive processes. As such, differential discounting behavior on real TD tasks by adolescents relative to adults or children could reflect adolescents’ heightened reward sensitivity (Casey, Getz, & Galvan, 2008; Crone & Dahl, 2012).

In sum, studies on age-related differences in TD have produced mixed results, and further research is clearly warranted. There is a particular need for studies testing both linear and non-linear age-related differences in TD. The majority of previous studies were not able to directly compare linear and non-linear changes, due to including participants from a relatively narrow age range, such as only children and adolescents, or only adolescents (Demurie et al., 2012b; Prencipe et al., 2011; Scheres et al., 2006). Other studies did include individuals with a wide age range, but they did not test or report non-linear age-related differences (Olson et al., 2007). In the present study, we therefore included a large sample from a broad age range (12-27 years), in order to test both linear and non-linear age-related differences in TD during adolescence and young adulthood.

**Age-related differences in Risky Decision-Making**

Similar to the aforementioned TD studies, findings regarding age-related differences in risky decision-making have been mixed. Several studies have reported a linear decrease in risky decisions from childhood to adolescence (Crone & van der Molen, 2007; Hooper, Luciana, Conklin, & Yarger, 2004), and from adolescence to adulthood (Crone & van der Molen, 2004; Mitchell, Schoel, & Stevens, 2008; Steinberg et al., 2008; van Duijvenvoorde, Jansen, Bredman, & Huizenga, 2012). Further, with increasing age, adolescents and young adults are able to use more sophisticated decision rules in risk-taking tasks (Huizenga, Crone, & Jansen, 2007; Jansen, van Duijvenvoorde, & Huizenga, 2012). However, in other studies, no differences in risky decisions were found between adolescents (from age 14 onwards) and young adults (Cauffman et al., 2010; Overman et al., 2004). In addition, non-linear age-related differences in risky decision-making has been reported as well, with a peak in risky decisions in (mid) adolescence relative to childhood and adulthood (Burnett, Bault, Coricelli, & Blakemore, 2010; Smith, Xiao, & Bechara, 2012).
Differences in task characteristics might contribute to these inconsistent findings, since it has been found that adolescents made riskier choices than adults in an emotionally arousing version of a risk-taking task, but no age differences were found in a more deliberative version of the same task (Figner, Mackinlay, Wilkening, & Weber, 2009; see also van Duijvenvoorde, Jansen, Visser, & Huizenga, 2010). In addition, many previous studies used (modified versions of) the Iowa Gambling Task (IGT), in which participants must learn to make more advantageous decisions based on feedback during the experiment. While the IGT closely resembles real-life decision making, it also draws heavily upon working memory (van Duijvenvoorde et al., 2012) and other complex executive functions which are still developing during adolescence.

To address this issue, recent studies have employed gambling tasks in which all the information that is required to make a decision is presented visually during each trial. For instance, in the Cake Gambling Task (van Leijenhorst et al., 2010; van Leijenhorst, Westenberg, & Crone, 2008), a cake is used to visually display the probability of obtaining a monetary reward associated with two choice options. The cake consists of six wedges that are either brown or pink, with a 4:2 ratio. Selection of the color that is most prevalent in the cake, results in a high probability of obtaining a small monetary reward. Thus the more prevalent colored wedge is considered to be the low-risk option. Choosing the least prevalent color is associated with a low probability of obtaining a larger reward, and is considered the high-risk option. In the Cake Gambling Task, the reward magnitudes associated with each option are depicted as a stack of coins. Using this task, van Leijenhorst and colleagues (2008) originally did not find a difference in the percentage of high-risk decisions between adolescents and adults. However, the expected value (EV; probability x reward magnitude) of the high-risk option was always higher than the EV of the low-risk option in this study.

In a later study, van Leijenhorst et al. (2010) did find that adolescents (12-14 years) made more high-risk decisions than young adults, but only in trials in which the EV of the high-risk and low-risk option were equal. They interpreted this result as indicating that adolescents take more risks than adults when choices are relatively ambiguous. Thus, these findings point to the importance of matching the EV of the high-risk and low-risk options. In the van Leijenhorst et al. (2010) study, both the probabilities associated with each option and the magnitude of the low-risk reward (€1) were held constant, while the high-risk reward (€2-8) was varied in magnitude, such that only the lowest high-risk reward (€2) was matched on EV with the low-risk reward. To control for the potentially confounding effects of EV differences between options, all high- and low-risk options were matched on EV in the current study, by systematically varying the reward magnitudes associated with both options.

**Relation between TD and Risky Decision-Making**

In prior research, age-related differences in TD and risky decision-making were mostly studied in isolation. Therefore, little is known about their relation across ages. One
might assume that TD and risk-taking are positively related, since impulsive actions (e.g., smoking) can frequently be characterized as risky and vice versa. A negative correlation between TD and risk-taking might also be expected, since choosing for a delayed reward entails the risk of not receiving that reward as something might prevent its reward delivery (Green & Myerson, 2004). Recent findings suggest that this is not necessarily the case, though. During childhood and adolescence, TD is not correlated with probability discounting (a measure of risky decision-making) (Scheres et al., 2006) and IGT performance (Prencipe et al., 2011). To our knowledge, only one study examined the relation between TD and risky decision-making during adolescence and adulthood (Olson et al., 2007). In this study, TD was not correlated with probability discounting, but more delayed reward choices were associated with less risky decisions in the IGT. Whether TD is related to risky decisions in a gambling task in which reward magnitudes are systematically varied, and whether this relation differs as a function of the reward magnitude of the risky options, remains an open question.

Reward valuation

In studies on age-related differences in TD and risky decision-making, it is of crucial importance to take age differences in (monetary) reward valuation into account (e.g., Demurie et al., 2012b), since participants of all ages make decisions involving the same monetary rewards. However, a 12-year-old might value a reward of €5 more than a 25-year-old would. Both the delayed reward in TD tasks and the risky option in gambling tasks are usually larger than the immediate reward and less risky option, respectively. Therefore, age differences in decision-making might actually reflect differences in reward valuation. To the best of our knowledge, no study to date has systematically evaluated whether reward valuation is associated with age and decision-making in TD tasks and gambling tasks, and whether age differences in these tasks remain after controlling for differences in reward valuation.

Pubertal Development

In addition to age-related differences in TD and risk-taking, other inter-individual differences are important to consider as well. Individual differences in adolescents might be related to their degree of pubertal development. Puberty, and particularly the associated surge of pubertal hormones, is proposed to be associated with enhanced activation in brain regions involved in reward processing (Op de Macks et al., 2011), thereby promoting impulsive and sensation-seeking behaviors (Crone & Dahl, 2012; Peper & Dahl, 2013a). Indeed, adolescents who report more advanced pubertal maturation relative to their peers also report higher levels of daily-life impulsive behaviors, such as alcohol use (de Water, Braams, Crone, & Peper, 2013). A couple of studies have suggested that pubertal development also contributes to decision-making in experimental tasks. Steinberg and colleagues (2008) found that adolescents who reported more advanced pubertal development, showed more sensation-seeking behavior in a computerized driving task. Similarly, Peper, Koolschijn, and
Crone (2013b) demonstrated that adolescents who reported greater pubertal maturation, particularly girls, engaged in higher levels of sensation-seeking behavior in the Balloon Analogue Risk Task (BART). Whether pubertal development is also associated with TD is unclear, since this has not yet been explored.

The Present Study

To summarize, the aims of the present study were: (1) to examine age-related differences in (a) TD and (b) risky decision-making during adolescence and young adulthood, (2) to investigate whether TD and risky decision-making are correlated across ages, (3) to study whether age differences in TD and risky decision-making remain after controlling for individual differences in reward valuation, and (4) to test whether pubertal development is associated with TD and risky decision-making. To this end, a TD task and the Cake Gambling Task were administered to 337 participants aged 12-27 years. Additionally, all participants were asked to rate four monetary rewards that were used in these tasks, and adolescent participants completed a pubertal development scale.

In relation to the four aims of this study, the following hypotheses were specified: (1a) regarding age-related differences in TD, several opposing hypotheses could be proposed due to inconsistent findings of prior research. Discounting might be hypothesized to decrease linearly with age during adolescence and young adulthood (Olson et al., 2007; Scheres et al., 2006; Steinberg et al., 2009). In contrast, non-linear age-related differences in TD, with decreased discounting (Scheres et al., 2013) in mid adolescence could also be predicted. Alternatively, discounting could be expected to remain stable during late adolescence and young adulthood (Audrain-McGovern et al., 2009). In order to address these competing hypotheses, we tested both linear and non-linear (i.e., quadratic and cubic) age effects in this study.

(1b) Based on previous research (van Leijenhorst et al., 2010), we anticipated that adolescents would make more high-risk decisions than young adults in our version of the Cake Gambling task in which the EV of the high- and low-risk options was matched. (2) Due to conflicting findings of prior studies, two competing hypotheses could be formulated regarding the correlation between TD and risky decision-making. It might be predicted that TD and risky-decision making are uncorrelated (Prencipe et al., 2011; Scheres et al., 2006), but a positive correlation (Olson et al., 2007) or a negative correlation (Green & Myerson, 2004) between discounting behavior and high-risk decisions in the Cake Gambling task could also be expected.

(3) Given the lack of prior research on the influence of reward valuation on age-related differences in TD and risky decision-making, we explored whether age differences in TD and risky decision-making remained after controlling for reward valuation without specifying an a priori hypothesis. (4) We hypothesized that advanced degree of pubertal development would be related to increased discounting and greater high-risk decisions in the Cake Gambling task (de Water et al., 2013; Peper et al., 2013b).
Method

Participants
A total of 337 individuals participated in the present study (see Table 2.1 for descriptive statistics). The sample consisted of 195 adolescents (96 girls) aged 12-17 years (M = 15.15 years, SD = 1.37 years), and 142 young adults (107 women) aged 18-27 years (M = 20.71 years, SD = 1.94). Adolescent participants were recruited by contacting local high schools, while adult participants were recruited from the Radboud University population using flyers and an online participant database (Sona systems). The gender distribution differed significantly between the adolescent and adult groups, \( \chi^2(2) = 30.65, p<.001 \). Specifically, females were overrepresented in the adult group, reflecting the uneven gender distribution of the student body of the Faculty of Social and Behavioral Sciences from which the adult group was mainly recruited. To address this potential issue, two sets of results are reported. First, we report findings based on the total sample of 337 participants, including all 142 adults. In addition, we repeated our analyses with the full sample of adolescents, and a subsample of 70 adults. The adult subsample consisted of all 35 male participants, and a random sample of 35 female adult participants (drawn from the total sample of female adults to match the even gender distribution of the adolescent group).

Informed consent was obtained from all adult participants, and adolescent participants gave informed assent. Parents of the adolescents gave passive consent. All procedures were approved by the institutional review board at the Faculty of Social Sciences, Radboud University Nijmegen, The Netherlands.

Table 2.1. Descriptive statistics of the sample

<table>
<thead>
<tr>
<th></th>
<th>Adolescents ( n = 195 )</th>
<th>Adults ( n = 142 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in Years ( M (SD) )</td>
<td>15.15 (1.37)</td>
<td>20.71 (1.94)</td>
</tr>
<tr>
<td>Range</td>
<td>12.49 - 17.97</td>
<td>18.02 - 27.50</td>
</tr>
<tr>
<td>Raven Score(^a)</td>
<td>33.06 (5.36)</td>
<td>36.60 (4.86)</td>
</tr>
<tr>
<td>Range</td>
<td>10 - 46</td>
<td>8 - 47</td>
</tr>
<tr>
<td>Reward Valuation Slope(^b)</td>
<td>0.25 (0.20)</td>
<td>0.31 (0.21)</td>
</tr>
<tr>
<td>Range</td>
<td>-0.48 - 0.80</td>
<td>-0.20 - 0.80</td>
</tr>
<tr>
<td>% High-risk Decisions in €2 Trials of CG task</td>
<td>42.63 (24.33)</td>
<td>35.80 (27.35)</td>
</tr>
<tr>
<td>% High-risk Decisions in €4 Trials of CG task</td>
<td>42.55 (25.52)</td>
<td>35.90 (24.52)</td>
</tr>
<tr>
<td>% High-risk Decisions in €6 Trials of CG task</td>
<td>43.95 (26.57)</td>
<td>37.25 (25.76)</td>
</tr>
<tr>
<td>% High-risk Decisions in €8 Trials of CG task</td>
<td>49.64 (27.54)</td>
<td>42.03 (27.94)</td>
</tr>
<tr>
<td>Area Under the Curve in TD task</td>
<td>.34 (.28)</td>
<td>.49 (.29)</td>
</tr>
<tr>
<td>Range</td>
<td>.01 -.99</td>
<td>.01 -.99</td>
</tr>
</tbody>
</table>

Note. \( M = \) Mean; \( SD = \) standard deviation; \( CG = \) Cake Gambling; \( TD = \) temporal discounting.

\(^a\) the number of correct answers on sets B-E (48 items) of the Raven’s SPM.

\(^b\) The unstandardized coefficient of the regression analysis with reward magnitude (€2.50, €5, €7.50, €10) as predictor and reward rating (7-point scale) as dependent variable.
Figure 2.1. (A) Trial procedure of the TD task. (B) Trial procedure of the Cake Gambling task

Note. The time indicated underneath the decision phase of both tasks is the maximum amount of time allowed to make a decision. When participants indicated their preference within this time period, the trial continued immediately after they pressed the button corresponding to their preference.

Measures

**TD Task.** In order to assess preferences for immediate rewards, a TD task was administered. In each trial of this task (see Figure 2.1A), participants chose between a relatively small immediate monetary reward (IR) they could receive today, or a reward of €10 they would receive after a delay (DR). By varying the amount of the IR and the delay preceding the larger reward (€10), participants’ subjective value of €10 could be estimated for each delay. Five delays were used: 2, 14, 30, 180, and 365 days. For each delay, participants were presented with a series of 6 choices. If they completed these choices, they began a new series of 6 choices at the next delay. The delays were presented in a random order for each participant. The IR was always €5 on the first choice at each delay. The amount of the
IR on later choices was adjusted based on participants’ preferences (Du, Green, & Myerson, 2002). If participants chose the IR, the amount of the IR was decreased by half on the next choice, whereas this amount was increased by half if they chose the DR. For example, a first choice would be between €5 today or €10 in 2 days. If a participant preferred the €5 today, the next choice would be between €2.50 today or €10 in 2 days.

The amount of the IR that would have been presented on the seventh trial of the series at each delay was used as the estimate of the participants’ subjective value (SV) of the DR. These SV’s were used to calculate the dependent variable: area under the curve (AUC). AUC was calculated using the procedure described by Myerson, Green, and Warusawitharana (2001). AUC ranges between 0 and 1, where smaller values indicate an increased preference for immediate rewards.

One of the rewards was presented on the right side of the screen and the other reward was presented on the left side of the screen. The position of the rewards was counterbalanced across trials. Participants had to indicate their preference by pressing the corresponding computer key. The preference of the participant was highlighted by a yellow line surrounding the option, followed by the presentation of a fixation cross. The TD task consisted of 6 practice choices at a delay that was not used in the actual task (1 day), and 30 experimental trials, with a duration of 5 minutes.

TD tasks demonstrate high validity, in that individuals with psychiatric disorders characterized by impaired impulse control (e.g., ADHD, substance abuse), show a strong preference for immediate rewards in these tasks (Demurie et al., 2012a; Scheres et al., 2010b). In addition, TD has been reported to show trait-like stability in young adults, with a test-retest reliability of up to .91 (Odum, 2011).

Cake Gambling Task. Risk-taking behavior was assessed using a modified version of the Cake Gambling (CG) task (van Leijenhorst et al., 2010; van Leijenhorst et al., 2008). In this task, participants made repeated choices between a high-risk option with a 33.3% probability of obtaining a large monetary reward, and a low-risk option with a 66.7% probability of obtaining a smaller monetary reward. The probabilities associated with the two options were kept constant but the reward associated with both options was varied. The reward associated with the high-risk option (4 magnitudes: €2, €4, €6 or €8) was always twice as large as the low-risk reward, such that the expected value (probability x reward magnitude) of both options was always equal. The high-risk option is considered more risky, because the probability of obtaining a reward is smaller, while the variance in potential outcomes is larger. The trial procedure of the CG task is illustrated in Figure 2.1B. First, participants viewed a cake composed of six wedges. These wedges were either pink (“strawberry- flavored”) or brown (“chocolate- flavored”) in a 4:2 ratio (the majority color was counterbalanced across trials). Underneath the cake, a pink and a brown square were presented on the left and right side of the screen (counterbalanced across trials), each containing a stack of 50 cent coins to indicate the reward associated with each flavor. During the time period in which the cake was presented on the screen, participants had to
choose which of the two flavors they wanted to gamble with, by pressing the corresponding computer key. After participants indicated their choice, it was highlighted by a yellow line surrounding the square. Participants subsequently viewed a fixation cross, during which the computer randomly selected one of the six wedges of the cake. If the flavor of the selected wedge matched the flavor chosen by participants, they gained the amount of coins associated with that flavor. If not, they did not gain any coins. Gain feedback was presented by showing the stack of coins participants had gambled with, while no-gain feedback was depicted by this stack of coins with a cross through them. The CG task consisted of 8 practice trials and 72 experimental trials (18 repetitions of each of the 4 reward magnitudes), with a duration of approximately 8 minutes.

High-risk decisions on the CG task have been shown to be positively associated with self-reported sensation-seeking behavior in daily life (van Leijenhorst et al., 2008).

**Reward Valuation.** All participants were asked to rate on a 7-point scale how much they enjoyed receiving each of four rewards that were within the range of rewards used in the CG and TD tasks (€2.50, €5, €7.50, €10). A regression analysis with reward magnitude (€2.50, €5, €7.50, €10) as predictor and reward rating (the 7-point scale rating of each reward) as dependent variable was performed for each participant separately. The slope (unstandardized regression coefficient) of this regression analysis was used as a measure of reward valuation in subsequent analyses. A positive and larger slope indicates that larger rewards are rated more positively than lower rewards. The mean of the four different reward ratings (α = .83 for the total sample) was highly correlated with the reward valuation slope (\( \rho = -.70, p<.001 \)), and findings were similar when analyses were conducted with this measure of reward valuation. Therefore, only the results in which the reward valuation slope was included as measure of reward valuation, are reported.

**Raven’s SPM.** Sets B-E (48 items) of the Raven’s Standard Progressive Matrices (SPM; Raven, Raven, & Court, 1998) were administered, with a 10-minute time limit, to screen for general intelligence. Set A was not administered, since prior research has shown that contrary to the items in sets B-E, the items in set A primarily measure visuospatial abilities instead of analogical reasoning abilities (van der Ven & Ellis, 2000). Performance on a speeded (e.g., including a time limit) Raven is highly correlated with performance on the same test when no time limit is imposed (Hamel & Schmittmann, 2006). The total number of correct responses on Raven’s SPM was used in the analyses, and will be referred to as Raven score from now on.

**Pubertal Development.** The Pubertal Development Scale (PDS) was administered to the adolescents to quantify pubertal development (Petersen, Crockett, Richards, & Boxer, 1988). Adolescents indicated their physical development on a 4-point scale (ranging from 1 = no development or change to 4 = complete development). Boys were asked to indicate their body growth, body hair (pubic and axillary hair), facial hair, skin changes and voice changes, whereas girls indicated their body growth, body hair, breast development, skin changes and whether they had reached menarche. The mean PDS score (mean of all items)
was used in subsequent analyses. Consistent with a recent study on pubertal development and sensation-seeking in an experimental task (Peper et al., 2013b), we also computed Puberty Category Scores (Crocket, 1988; see http://www.sleepforscience.org/contentmgr/showdetails.php?id/91). Mean PDS scores were highly correlated with Puberty Category Scores ($\rho = .66$ for girls; $\rho = .87$ for boys) and the findings were similar with either measure of pubertal development. Thus, only the findings with mean PDS score as measure of pubertal development are reported.

**Procedure**

Adolescents were tested in their school classroom, with a teacher present. One class (18-29 students) was tested at a time, using notebooks. Partitions were placed on both sides of each notebook to ensure adolescents’ privacy. Further, a team of research assistants was present during testing to explain the tasks and to answer participants’ questions. In order to mimic the test setting of the adolescents as closely as possible, adults were tested in groups (8-16 participants) in a room at their university, using the same type of notebooks and partitions that were used to administer the tasks to the adolescents.

The computer tasks and questionnaires were administered in a fixed order across all participants. First, sets B-E of Raven’s SPM were administered with a 10-minute time limit. Subsequently, adolescent participants completed a demographic questionnaire and the PDS on their notebooks, while adults filled out paper-and-pencil-versions of a demographic questionnaire. Finally, participants performed the CG task on their notebook, followed by the TD task and the reward valuation questions. To increase participant motivation and ecological validity, participants were told that at the end of the experimental session, one of their outcomes of the CG task and one choice of the TD task would be randomly selected by the computer, and that they would receive both outcomes. However, to keep differences between participants small and our expenses manageable, payment was actually determined at random from a narrow range of values (€6-€9).

**Statistical Analyses**

Data were analyzed using SPSS version 19. Extreme outliers (> 3SD + the mean of one’s age group on at least one of the dependent variables) were excluded from analyses (3 adolescents, and 2 adults). Analyses were first performed across all participants. Since the gender distribution was strongly skewed in the adult group, we subsequently repeated the analyses with all adolescent participants and a subsample of 70 adult participants (all 35 males, and a random sample of 35 females).

*Checks of experimental tasks.* To investigate whether the subjective value of the delayed reward decreased with increasing delay in the TD task, a repeated measures (RM) ANOVA was conducted, with delay as a within-subject variable, and subjective value of the
delayed reward as dependent variable. A RM ANOVA with high-risk reward magnitude as within-subject variable and % high-risk decisions in the CG task as dependent variable was performed, to test whether risk-taking increased with increasing magnitude of the high-risk reward. Similarly, we tested whether reward valuation increased with increasing reward magnitude by performing a RM ANOVA with reward magnitude as within-subject variable, and reward valuation as dependent variable. In case of a significant multivariate test of these RM ANOVA’s, follow-up pairwise comparisons were conducted, with a Bonferroni correction to adjust for multiple comparisons. The checks of the experimental tasks were performed for adolescent and adult participants separately.

**Age-related analyses.** To examine age-related differences in risk-taking and TD during adolescence and adulthood, a series of hierarchical multiple regression analyses were conducted across all participants with the percentage of high-risk decisions in the CG task and AUC on the TD task as dependent variables. To control for potential confounders, Raven score (which was positively related to age; \( \rho = .38, p < .001 \)) and reward valuation were first entered as predictors, and age was added to the model in the second step of the analysis. Both linear and non-linear (i.e., quadratic and cubic) age trends were tested. In case of a significant age effect, follow-up analyses were conducted to determine which specific ages differed from each other. Specifically, in order to test whether successive ages differed from each other (e.g. 12-year-olds from 13-year-olds, 13-year-olds from 14-year-olds, etc.), an ANCOVA was performed with age as independent variable and age as contrast factor (contrast type = repeated), Raven score and reward valuation as covariates, and AUC on the TD task or the percentage of high-risk decisions in the CG task as dependent variables.

To test whether risk-taking and TD are related across ages, multiple linear regression analyses were performed. The dependent variable in these analyses was AUC, with the percentage of high-risk decisions in the CG task as main predictor. Age, Raven score, and reward valuation were added as additional predictors to control for the potentially confounding effects of these variables. Further, in order to test whether the association between AUC and risk-taking was different for participants of different ages, the high-risk decisions x age interaction was added to these multiple regression analyses as predictor. The correlation between age and reward valuation slope was computed using Spearman’s \( \rho \).

To explore whether pubertal development was associated with risk-taking and TD in the group of adolescents, the mean PDS score was entered as a predictor in multiple regression analyses with the percentage of high-risk decision and AUC as dependent variables. In order to control for confounding effects of age in these analyses, age was entered as a predictor as well. These analyses were conducted separately for boys and girls.

**Reward valuation and decision-making.** The correlation between reward valuation and risk-taking and TD was examined by performing a multiple regression analysis
with reward valuation as dependent variable, and AUC and the percentage of high-risk decisions as predictors. Age and Raven score were entered as additional predictors to this regression to control for their potentially confounding effects.

**Gender differences.** Gender differences in the percentage of high-risk decisions and AUC were explored using independent samples t-tests, for adolescents and adults separately.

**Correction for multiple testing.** Given the large number of statistical tests that were performed, a False Discovery Rate (FDR) correction was applied to control for multiple testing. An FDR correction is a Bonferroni-type correction, which has greater power to detect an effect than the traditional Bonferroni correction (Benjamini & Hochberg, 1995). Based on an uncorrected p-value of .05 and the number of statistical tests performed in the current study, all p’s < .013 were considered significant after FDR correction for multiple testing (see Benjamini & Hochberg, 1995 for the procedure of determining the FDR-corrected p-value). Therefore, only p-values < .013 are reported as significant. Note, however, that this only applies to the regression analyses. The checks of the experimental tasks were done by performing RM Anova’s, which included Bonferroni-corrected pairwise comparisons. For these analyses, p-values <.05 are reported as significant.

**Results**

**Age-related differences in TD**

The subjective value of the delayed reward differed significantly as a function of delay duration in adolescents (F(4,191) = 91.40, p < .001, \( \eta^2_p = .66 \)) and adults (F(4,137) = 87.81, p < .001, \( \eta^2_p = .72 \)). Specifically, the subjective value of the delayed reward decreased significantly with each successive delay (i.e., 2, 14, 30, 180 and 365 days) in adolescents (all p’s < .026) and adults (all p’s < .013). In other words, both adolescents and adults showed TD (see Figure 2.2).

In line with our hypotheses, age was positively related to AUC after controlling for reward valuation and Raven score (\( \beta = 0.36, t = 3.49, p = .001 \)). This indicates that the ability to wait for a delayed reward increases with age. Only the linear age trend was significant, and not the quadratic (\( p = .52 \)) nor cubic age trends (\( p = .78 \)). Figure 2.3A illustrates this positive linear relation between age and AUC, and further shows that there seem to be increases in AUC at specific ages: from 12 to 13 years, from 15 to 16 years, and from 20 to 22 years. A follow-up ANCOVA (controlling for Raven score and reward valuation) in which all successive ages were tested against each other, indicated that only the 16-year-olds indeed have a significantly larger AUC than 15-year-olds (p = .009).

Adolescent boys and girls did not differ in AUC (p = .32). In contrast, male adult participants showed a significantly larger AUC than female adult participants (t (139) = 2.64, p = .009).
Figure 2.2. Temporal discounting curves of adolescents and young adults.

Figure 2.3. (A) Development of delayed reward preferences in the Temporal Discounting task. (B) Percentage of high-risk decisions in the Cake Gambling task as a function of age. (C) Number of participants per age group.

Note. AUC = area under the curve. Larger AUC values indicate a stronger preference for delayed rewards. 23-27-year-olds are shown as one age group due to the relatively small number of participants in the separate age groups (e.g., 23-year-olds, 24-year-olds, etc.)
**Age-related differences in Risk-taking Behavior**

High-risk decisions increased as a function of reward magnitude in adolescents ($F(3,192) = 13.78, p < .001, \eta_p^2 = .18$) and adults ($F(3,139) = 5.21, p = .002, \eta_p^2 = .10$). Specifically, the percentage of high-risk decisions was greater when the reward associated with the high-risk option was €8 compared to when this reward was €2, €4 or €6 (all p’s <.05 in adults; all p’s <.001 in adolescents). Risk-taking in the three lowest reward conditions (high-risk reward of €2, €4 and €6) did not differ significantly in adolescents and adults (all p’s = 1; see Figure 2.4). Therefore, we used two measures of risk-taking in subsequent analyses: the mean percentage of high-risk decisions in the three lowest reward conditions combined (Cronbach’s α = .90 for the total sample), and the percentage of high-risk decisions in the €8 condition.

Inconsistent with our predictions, age was not significantly correlated with high-risk decisions in the lower reward (€2-€6) condition and the €8 condition ($p$’s >.013; see Figure 2.3B). There were no significant gender differences in risk-taking in the group of adolescents (all $p$’s >.07) and adults (all $p$’s >.12).

![Figure 2.4. Mean percentage of high-risk decisions in the Cake Gambling task as a function of reward magnitude of the high-risk option.](image)

**Relation between TD and Risk-taking Behavior**

Risky decisions in the three lowest reward conditions and in the €8 condition were not significantly associated with AUC when controlling for Raven score, reward valuation, age and risky decisions in the other reward condition (which were controlled for to be able to examine the unique relation between TD and risk-taking when potential rewards are low vs. high) (all $p$’s>.013). The age x high-risk decisions interactions did not significantly predict AUC (all $p$’s > .33), indicating that risk-taking and TD were not correlated across ages.
Reward valuation

Ratings of the rewards significantly differed as a function of reward magnitude in adolescents \(F(3,191) = 100.45, p < .001, \eta^2_p = .61\) and adults \(F(3,136) = 97.01, p < .001, \eta^2_p = .68\). Reward ratings increased significantly (all \(p’s < .001\) in adolescents and adults) with each successive reward magnitude (€2.50, €5, €7.50, €10).

The enhanced reward valuation with increasing reward magnitude interacted with age (see Figure 2.5), as indicated by a significant positive correlation between reward valuation slope and age \((r = .15, p = .007)\). This finding indicates that younger participants value smaller monetary rewards more than older participants.

When controlling for age and Raven score, reward valuation was not significantly associated with AUC and high-risk decisions in the CG task in all participants (all \(p’s > .03\)). Further, as mentioned above, all significant age effects remained after controlling for individual differences in reward valuation. Together, these findings suggest that even though adolescents show subtle differences in monetary reward valuation relative to young adults, these differences cannot explain age differences in decision-making tasks in which monetary rewards are used.

![Figure 2.5. Mean reward valuation ratings (range = 1-7) for each of the four reward magnitudes.](image)

Pubertal development

Contrary to our expectations, when controlling for age, pubertal development was not significantly associated with risk-taking or TD in boys (all \(p’s > .09\)) and girls (all \(p’s > .41\)).
Controlling for unequal gender distribution: random sample of female adults

As mentioned above, the gender distribution was strongly skewed across the age groups in the present study, in that the adult group contained significantly more females than males compared to the group of adolescents. In order to address this potential issue, we randomly selected 35 female adult participants to match the number of male adult participants in our sample, and repeated our age-related differences analyses with this random sample of females ($n=35$), all male adult participants ($n=35$), and all adolescent participants ($n=195$). The random sample of women did not differ from the women who were not included in the random sample in terms of age, Raven score, risk-taking, AUC, and reward valuation (all $p$'s > .16).

Consistent with the analyses in the total sample, age was significantly positively related to AUC (when controlling for Raven score and reward valuation) ($\beta = 0.36$, $t = 2.98$, $p = .003$). Mirroring the findings in the total sample, only the linear age trend, and not the cubic or quadratic trends were significant (all $p$'s > .58). In keeping with the findings in the total sample, age was not significantly related to risk-taking in the lower reward conditions and the €8 reward condition ($p = .193$ and $p = .906$, respectively).

In sum, these findings suggest that the observed increase in AUC with age cannot be attributed to a greater proportion of females in the adult group.

Discussion

The goals of the present study were to examine: (1) age-related differences in TD and risk-taking in adolescents and young adults, (2) the association between TD and risk-taking across ages, (3) whether individual differences in monetary reward valuation could explain individual and age differences in TD and risky decision-making, and (4) the relation between pubertal development and TD and risk-taking in adolescents. Unlike many prior studies, we were able to directly compare linear and non-linear (i.e., quadratic and cubic) age-related differences in TD and risk-taking, due to our large sample of participants with a wide age range.

Age-related differences in TD

As predicted, we found that age was positively related to the ability to wait for a delayed reward (i.e., decreased TD). These age-related differences were described best by a linear, and not by a non-linear, trend. These findings are consistent with several other studies in which a linear decrease in TD with age has been reported in adolescents and young adults (Olson et al., 2007; Scheres et al., 2006; Steinberg et al., 2009). Interestingly, TD decreased particularly strongly from 15 to 16 years (even when controlling for Raven score and reward valuation) in the current study, which is similar to the findings of a prior study (Steinberg et al., 2009). Decreased discounting with increasing age might be accounted for by the maturation of several cognitive functions, and the brain regions subserving these functions.
Cognitive control processes, including working memory and response inhibition, improve during adolescence (Huizinga et al., 2006; Luciana et al., 2005), and might be associated with a greater ability to wait for a delayed reward.

At the neural level, choices between immediate and delayed rewards are associated with activation in both reward-related brain regions, such as the ventral striatum (VS) and ventromedial prefrontal cortex (vmPFC), and brain regions involved in self-control, including the dorsolateral prefrontal cortex (DLPFC) and parietal cortex (see Scheres, de Water, & Mies, 2013, for a review). Activation of self-control regions is thought to promote delayed reward choices, while activity in reward-related regions contributes to immediate reward choices. Indeed, disruption of the DLPFC results in increased discounting of delayed rewards (Figner et al., 2010). Additionally, increased discounting is correlated with poor integrity of white matter tracts that connect the prefrontal cortex with the VS (Peper et al., 2013c). Similarly, the handful of studies that have been conducted on the neurocognitive development of TD, have suggested that reductions in TD with increasing age are accompanied by increased activation of the DLPFC and parietal cortex, decreased activation of the VS, and enhanced functional connectivity between the vmPFC and VS in adolescents and young adults (Christakou, Brammer, & Rubia, 2011; Ripke et al., 2012). Whether the specific decrease in TD from 15 to 16 years that was observed in the present study, is driven by maturation of the DLPFC and parietal cortex remains an intriguing question for future study.

In contrast to the linear age-related differences in TD that were noted in this study, other studies (Scheres et al., 2013) have documented non-linear age-related differences in discounting, with decreased discounting in adolescence (13-17 years). These discrepant findings might be explained by the different delays and reward magnitudes that were used in the TD tasks across studies. Linear age effects are generally found in studies, including the current study, in which relatively large monetary rewards (e.g., $10-100) and long delays (e.g., up to 1 year) are used (Olson et al., 2007; Steinberg et al., 2009; but see Scheres et al., 2006 for an exception). Non-linear age effects have been observed when shorter delays and smaller reward magnitudes are used. For instance, Scheres et al. (2013) used a real (or experiential) TD task, in which all rewards and delays were actually experienced. Therefore, delays were in the range of seconds and the delayed reward was 10 cents in this study.

Both TD tasks with small rewards and short delays and TD tasks with larger rewards and longer delays are sensitive to individual differences in daily life impulsivity. In other words, the validity of both types of tasks is equally high. For instance, adolescents with ADHD and adolescents who report high levels of smoking show relatively steep discounting in both types of TD tasks (Demurie et al., 2012a; Reynolds & Fields, 2012; Scheres et al., 2010b). Nonetheless, discounting of delayed rewards in real TD tasks (which include small rewards and short delays), and in hypothetical TD tasks (in which delays and rewards are not experienced, and large rewards and delays are typically used), is not highly correlated (Scheres et al., 2010a). These differences in discounting behavior when using different types of tasks might be due to the fact that distinct cognitive and affective processes are involved.
in each type of task. It might be hypothesized that behavior in real TD tasks is strongly influenced by affective processes (e.g., reward sensitivity and delay aversion), while behavior in TD tasks with long delays and large rewards (which are typically used in hypothetical tasks) also depends on more cognitive processes (e.g., subjective time perception and working memory) which follow a protracted developmental trajectory (Casey et al., 2008; Crone & Dahl, 2012). Differential involvement of these processes might account for the distinct age-related differences that are observed when using different TD tasks. Moreover, adolescents might display different behavior in real and hypothetical tasks, even when reward and delay magnitudes are matched. These hypotheses need to be tested in future research, by administering a real TD task, a hypothetical TD task with long delays and large rewards and a hypothetical TD task with small rewards and short delays to individuals of a large age range.

Gender Differences in TD

Young adult males discounted delayed rewards less steeply than females, while there were no gender differences in TD in adolescents. A similar gender difference in young adults has also been observed in one recent study (Ramos, Victor, Seidl-de-Moura, & Daly, 2013), but it has been reported that women discount delayed rewards less steeply than men as well (Peper et al., 2013c). The increased preference for larger delayed rewards in young adult males in the present investigation might suggest that men were more motivated than women to maximize their own rewards. It must be noted though, that due to the relatively small sample of males, one should be careful in interpreting this finding. Future research should explore gender differences in TD and their underlying mechanisms in more detail.

Age-related differences in Risk-taking

In line with previous research using the Cake Gambling Task (van Leijenhorst et al., 2008), risky decision-making was not correlated with age in the present study. Studies in which other risky decision-making tasks were employed also did not find differences in risk-taking between adolescents and young adults (Cauffman et al., 2010; Overman et al., 2004). In contrast, van Leijenhorst and colleagues (2010) reported that 12-14-year-olds made less high-risk decisions than 19-26-year-olds on trials of the Cake Gambling Task in which the high- and low-risk options were matched on expected value. Although we matched all low- and high-risk options on expected value in the present study, the 12-14-year olds in our sample did not differ from the 19-26-year-olds regarding the percentage of high-risk decisions. When closely comparing the findings across these studies, it becomes apparent that the 12-14-year-olds showed similar levels of risk-taking in both studies, while the 19-26-year-olds engaged in higher levels of risk-taking in the present study relative to the van Leijenhorst et al. (2010) study. Differences in sample sizes (n =93-113 per age group in the current study vs. n =15 per age group in the van Leijenhorst et al. study) and settings
and procedures (our behavioral study conducted in classrooms/groups vs. an fMRI study) between studies might have contributed to these different results.

Contrary to the findings of the current study, many studies did demonstrate either decreased risk-taking with age (Crone & van der Molen, 2004; Crone & van der Molen, 2007; Hooper et al., 2004; Mitchell et al., 2008; Steinberg et al., 2008; van Duijvenvoorde et al., 2012), or a peak in risky decisions in (mid) adolescence (Burnett et al., 2010; Smith et al., 2012). The majority of these prior studies used (modified versions of) the Iowa Gambling Task, which draws heavily upon working memory (van Duijvenvoorde et al., 2012) and other complex executive functions which are still developing during adolescence. A decline in risky decisions with age in this task might therefore partially reflect the increased maturation of executive functions during adolescent development. In the present study, demands on executive functioning were reduced by using a gambling task in which all information on the rewards and probabilities associated with each choice was presented visually during each trial. This explicit presentation of the probabilities might have also contributed to the lack of age effects in this study. It has been reported that adolescents do not take more risks than adults when the probabilities of potential outcomes are known, but they do take more risks compared to adults when the probabilities are ambiguous (Tymula et al., 2012).

The non-linear age-related differences in risk-taking which were observed in other studies (Burnett et al., 2010; Smith et al. 2012), could indicate the effect of the emotional salience of the task on decision-making. Brain areas involved in the processing of (positive) emotions and rewards have been found to show an inverted u-shaped development, with a peak in activation in (mid) adolescence (Casey et al., 2008; Crone & Dahl, 2012). This enhanced reward sensitivity could promote increased risk-taking in tasks with a strong affective component, such as dynamic tasks in which the level of risk increases after each risky decision (Figner et al., 2009), or tasks that are performed in the presence of peers (Gardner & Steinberg, 2005). In this light, it would be interesting to administer the Cake Gambling task to adolescents in both neutral and emotionally salient contexts, and to compare the age-related differences in both versions.

Relation between risk-taking and TD

In this study, TD and risk-taking were not correlated, and their age-related differences during adolescence and young adulthood were distinct. These findings are congruent with prior research (Olson et al., 2007; Prencipe et al., 2011; Scheres et al., 2006) and suggest that impulsivity and risk-taking are not necessarily similar constructs in adolescence and young adulthood. While the neural correlates of risky and impulsive decision-making partly overlap, there are also distinct neural systems involved in both types of decision-making. Specifically, the lateral PFC and parietal cortex are more active during risky choices relative to choices between immediate and delayed rewards (Weber & Huettel, 2008). The posterior cingulate cortex (Weber & Huettel, 2008) and middle occipital areas (Peters & Buechel, 2009) are more active during choices between immediate and delayed rewards,
compared to risky choices. These distinct neural systems involved in both types of decision-making could partly contribute to the lack of a correlation between TD and risk-taking.

It might be hypothesized that the different age-related differences in TD and risk-taking could be attributed to some extent to the different demands of the tasks that were used to assess these constructs in the present study. For instance, being able to wait for a reward that is delayed up to 1 year in time requires not only self-control, but also the ability to accurately estimate extended time intervals and to project oneself into the future, which in turn depends on working memory. These higher-order cognitive functions are thought to depend on brain regions which show a relatively protracted development during adolescence, such as the DLPFC (Casey et al., 2008; Crone & Dahl, 2012). However, in the Cake Gambling task, all information that is needed to make a decision was presented visually, thereby reducing demands on working memory and cognitive control.

**Reward valuation**

Interestingly, we found that valuation of the monetary rewards that were used in the TD task and gambling task was not related to the decisions in these tasks. As a consequence, the linear decrease in TD with age remained significant after controlling for individual differences in reward valuation. These findings argue against the hypothesis that age effects in decision-making tasks in which monetary rewards are used could be attributed to age differences in reward valuation. To our knowledge, this is the first study to systematically compare age differences in monetary reward valuation, and its relation with discounting and risk-taking behavior.

**Pubertal development**

Contrary to our hypotheses, pubertal development was not related to risk-taking and TD in adolescent boys and girls. Two previous studies did find a relation between advanced pubertal development and sensation-seeking in experimental tasks (Peper et al., 2013b; Steinberg et al., 2008). Differences between the experimental tasks used in these prior studies and the task employed in the current study could explain these discrepant findings. Peper et al. (2013b) administered the BART, in which participants could gain money by pumping a balloon, but would lose the money if the balloon exploded. Steinberg et al. (2008) administered a driving task, in which participants would crash with other cars if they took too many risks. In our Cake Gambling Task, risky decisions could lead to not gaining a monetary reward. These differences in the intensity of the potential negative consequence of a risky choice across studies might have contributed to different findings. It could be hypothesized that advanced pubertal development is particularly associated with a greater enjoyment of thrills, and the potentially large negative consequences following a risky choice in tasks used by Steinberg et al. (2008) and Peper et al. (2013b) provide an arguably larger thrill than the task used in the present study.

The lack of an association between pubertal development and TD could suggest
that TD is not related to puberty. Nonetheless, it could also be argued that we might have found significant associations if we would have used more objective measures of pubertal status, such as levels of pubertal hormones (e.g., testosterone). Future studies should therefore include both self-report and hormonal assessments of pubertal development.

**Limitations**

It should be noted that the current study also has some limitations. Even though we controlled for the potentially confounding effects of reward valuation and Raven score, there are still other factors which might have contributed to the observed positive relation between age and the ability to wait for a delayed reward. These include possible age differences in subjective time perception, working memory and delay aversion. Future studies should investigate the role of each of these factors in TD and its development.

Moreover, while the present study included a large number of participants from a wide age range, the design was cross-sectional and therefore perhaps less sensitive to subtle developmental changes than a longitudinal design (e.g., Audrain-McGovern et al., 2009). Nevertheless, our findings of stable discounting behavior between the ages of 16 and 20 were strikingly similar to the findings of the longitudinal Audrain-McGovern et al. (2009) study.

In line with prior research (van Leijenhorst et al., 2008, 2010), the exact reward magnitude associated with the options in the Cake Gambling task was not made explicit to participants, but instead presented visually as a stack of coins. While this minimized the information that needed to be processed by participants, it might have been difficult for them to confirm that both options were equal in expected value. Future studies could make the reward magnitude associated with the options more explicit, by presenting the actual number of the reward that can be obtained.

The reward valuation questions were administered after completion of the TD and risk-taking tasks in all participants. Counterbalancing the order of the reward valuation questions is recommended to ascertain whether valuation of rewards before performing TD and risk-taking tasks impacts the results differently as compared to valuation of rewards after completing these tasks.

Finally, the TD task and the risk-taking task differed in the dynamic nature of the choices, in that the immediate rewards were adjusted based on participants’ choices in the TD task, while the rewards and risk levels were fixed (or static) in the risk-taking task. To circumvent this issue, dynamic risk-taking tasks, such as the Columbia Card Sorting Task (Figner et al., 2009) could be administered in addition to the TD task in future investigations.
Conclusions

In conclusion, we found that TD declined linearly with age in adolescents, even when controlling for individual differences in reward valuation. A particularly sharp decline in discounting was observed from 15 to 16 years. Risk-taking behavior was stable across ages, and discounting and risk-taking were not correlated. These findings suggest that temporal discounting and risk-taking are two separate constructs in adolescence and young adulthood, and that age-related differences in both constructs might be accounted for by different underlying (neural) mechanisms.
CHAPTER 3

Neural Mechanisms of Individual Differences in Temporal Discounting of Monetary and Primary Rewards in Adolescents

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Abstract

Adolescents are generally characterized as impulsive. However, impulsivity is a multidimensional construct that involves multiple component processes. Which of these components contribute to adolescent impulsivity, is currently unclear. Focusing on an important aspect of impulsivity, this study examined the neural mechanisms underlying individual differences in distinct components of temporal discounting (TD), or the preference for smaller immediate rewards over larger delayed rewards. Participants were 58 adolescents (12-16 years) who performed an fMRI TD task with both monetary and snack rewards. Using a mixed-effects model, TD choices were decomposed into: 1) average impatience; 2) amount sensitivity (unique contribution of the magnitude of the immediate reward); and 3) delay sensitivity (unique contribution of delay duration). Adolescents’ average impatience was positively correlated with frontoparietal and ventral striatal activity during delayed reward choices, and with ventromedial prefrontal cortex activity during immediate reward choices. Adolescents’ amount sensitivity was positively associated with ventral striatal and dorsal anterior cingulate cortex activity during immediate reward choices. Delay sensitivity was positively correlated with inferior parietal cortex activity during delayed reward choices. As expected, snacks were discounted more steeply than money, and TD of both rewards was associated with overlapping activation in the inferior parietal cortex. Exploring whether testosterone or estradiol were associated with TD and its neural correlates revealed no significant associations. These findings indicate that distinct components contribute uniquely to TD choice and that individual differences in amount sensitivity are uniquely associated with activation of reward valuation areas, while individual differences in delay sensitivity are uniquely associated with activation of cognitive control areas.
Adolescents are typically characterized as impulsive. For instance, compared to children and adults, they show increased levels of substance use and other reckless behaviors (Steinberg, 2008). However, not all adolescents are equally impulsive. Importantly, adolescents who are highly impulsive are at a heightened risk to develop behavioral problems, such as substance abuse (Audrain-McGovern et al., 2009), with substantial costs across all domains of life (i.e., social, financial, health) (Mertens, Lu, Parthasarathy, Moore, & Weisner, 2003). Therefore, it is important to understand the underlying mechanisms of individual differences in adolescent impulsivity, as this could inform prevention and intervention programs to reduce such behavioral problems.

A key component of impulsivity, namely the preference for smaller, more immediate rewards over larger delayed ones has been widely studied with temporal discounting (TD) tasks (see Scheres, de Water, & Mies, 2013, for a review). TD refers to the decrease in subjective value of a reward as the delay preceding its delivery is increased. TD tasks involve choices between smaller, more immediate rewards (e.g., $2 today) and larger, delayed rewards (e.g., $10 in 90 days). Adolescents with psychiatric disorders whose core symptom includes impulsivity (e.g., ADHD, substance abuse, gambling, and conduct disorders) have been found to show steeper discounting of delayed rewards than typically developing adolescents (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2012; Jackson & MacKillop; MacKillop et al., 2011; Patros et al., 2016; Scheres, Tontsch, Thoeny, & Kaczkurkin, 2010; White et al., 2014). Typically developing adolescents also show steeper discounting of delayed rewards than adults (de Water, Cillessen, & Scheres, 2014; Olson, Hooper, Collins, & Luciana, 2007; Scheres et al., 2006; Steinberg et al., 2009; van den Bos, Rodriguez, Schweitzer, & McClure, 2015; but see Scheres, Tontsch, Thoeny, & Sumiya, 2014).

Studies investigating the neural correlates of TD have implicated both frontoparietal and limbic brain areas in TD, including the lateral PFC, parietal cortex, ventral striatum (VS), medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC) (Scheres et al., 2013). However, little is known about the neural mechanisms underlying individual differences in TD, particularly in adolescents. The individual variation in impulsivity in adolescents is reflected in a wide range of individual differences in TD. Few studies have explored the neural mechanisms of these individual differences (Benningfield et al., 2014; Ripke et al., 2012; Stanger et al., 2013), and found that differential functioning of both frontoparietal and limbic areas contributes to these individual differences. One study reported that adolescents who exhibit relatively steep discounting of delayed rewards in TD tasks show increased activation of lateral prefrontal and parietal brain areas during delayed reward choices, and increased activation of the VS and ventromedial PFC (vmPFC) during immediate reward choices (Stanger et al., 2013). However, other studies reported decreased VS activation during decision-making (Ripke et al., 2012) or reward processing (Benningfield et al., 2014) in adolescents who show relatively steep discounting of delayed rewards.
Previous studies on the neural mechanisms of individual differences in TD have used outcome measures that reflect the *average* preference for smaller, more immediate rewards over larger, delayed rewards, such as the area under the curve (AUC; Myerson, Green, & Warusawitharana, 2001) and *k* rate (Mazur, Stellar, & Waraczynski, 1987). Both measures reflect the average preference for immediate rewards, but do not enable the investigation of processes underlying steep TD (van den Bos & McClure, 2013), such as sensitivity to the immediate reward amount and to the delay preceding the larger reward. It can be hypothesized that there are individual differences in how strongly the amount of the immediate reward and delay preceding the larger reward influence TD choice. Here, we refer to these individual differences as *amount sensitivity* and *delay sensitivity*, respectively. That is, someone who is highly sensitive to amount would show a relatively sharp increase in immediate reward choices as the magnitude of the immediate reward increases, while someone who is highly sensitive to delay would show a steep decrease in delayed reward choices as the delay duration increases. Delineating these underlying components of TD choice might provide a more detailed understanding of individual differences in TD. It also could help interventions aimed at reducing steep TD in adolescents with impulse-control problems, by targeting interventions to adolescents who are primarily driven by amount sensitivity versus adolescents who are primarily driven by delay sensitivity (see Neef, Bicard, & Endo, 2001, for an example of an intervention that improves tolerance to delays).

One approach that makes it possible to separate the unique contribution of reward amount from delay duration to TD choice is to systematically vary the amount of the immediate reward and the length of the delay preceding the larger reward, and using mixed-effects models to analyze the resulting complex data (Baayen, Davidson, & Bates, 2008). In the present study, we used mixed-effects modeling to determine individual differences in distinct components of TD choice: 1) *average impatience*, reflecting the effects of both immediate reward amount and the delay preceding the larger reward. This component is conceptually similar to traditional measures such as the AUC and the *k* rate, in that it is a proxy of participants’ overall tendency to select the immediate reward option, in which the unique contributions of immediate reward amount or delay duration to TD choice are not distinguished; 2) *amount sensitivity*, or the unique effect of the amount of the immediate reward; and 3) *delay sensitivity*, or the unique effect of the length of the delay preceding the larger reward. This approach allowed us to study individual variation in TD choices, as well as the mechanisms underlying these choices.

The first goal of this study was to investigate the neural mechanisms underlying individual differences in these three components of TD choices in typically developing adolescents. Prior studies that used mixed-effects modeling to analyze TD choices (Decker, Figner, & Steinglass, 2015; Figner et al., 2010; Foerde et al., 2016), did not examine the neural correlates of the components of TD choice. Therefore, we based our hypotheses of the neural correlates of the three TD choice components on fMRI studies that used conceptually similar measures, such as the AUC and *k* rate for average impatience (Benningfield et
al., 2014; Figner et al., 2010; Gianotti, Figner, Ebstein, & Knoch, 2012; McClure, Laibson, Loewenstein, & Cohen, 2004; Ripke et al., 2012; Stanger et al., 2013), return sensitivity (expected value) (van Duijvenvoorde et al., 2015) and subjective value (Kable & Glimcher, 2007) for amount sensitivity, and anticipating delays of different lengths (Lemiere et al., 2012; Wilbertz et al., 2013) for delay sensitivity. We hypothesized that average impatience would be positively associated with activation of the dorsolateral PFC (DLPFC) and superior parietal cortex during delayed reward choices (Stanger et al., 2013). Alternatively, a negative association between average impatience and DLPFC activity during delayed reward choices could also be predicted (Figner et al., 2010; Gianotti et al., 2012). Further, we predicted that average impatience would be positively associated with activation of the vmPFC (McClure et al., 2004; Stanger et al., 2013) and that it would be associated with differential recruitment of the VS (Benningfield et al., 2014; Ripke et al., 2012) during immediate reward choices. We expected that amount sensitivity would be positively associated with VS and vmPFC activity during immediate reward choices (Kable & Glimcher, 2007; van Duijvenvoorde et al., 2015). We anticipated that delay sensitivity would be positively associated with amygdala and insula activation during delayed reward choices (Lemiere et al., 2012; Plichta et al., 2009; Wilbertz et al., 2013).

The second goal of this study was to directly compare the neural correlates of TD of money and snacks in adolescents. Most prior developmental studies have used monetary rewards to study individual differences in TD (Benningfield et al., 2014; Ripke et al., 2012; Stanger et al., 2013). However, most health-related choices between immediate and delayed rewards involve directly consumable, primary rewards (e.g., snacks or alcohol). Further, primary rewards, such as candy, but not monetary rewards, are discounted by young adults in a manner similar to alcohol (Estle et al., 2007). TD of primary rewards may therefore better mirror daily life choices to engage in unhealthy behaviors (e.g., alcohol use and overeating) than TD of money (Jimura et al., 2011). Thus, in the same TD task, we collected choices between immediate and delayed monetary rewards, and between immediate and delayed snack rewards. Primary rewards are discounted more steeply than monetary rewards in adolescents (Demurie, Roeyers, Baeyens, & Sonuga-Barke, submitted) and young adults (Estle, Green, Myerson, & Holt, 2007; Jimura et al., 2011). Little is known about the underlying cognitive and neural mechanisms of this domain-dependence of TD. We explored whether the neural mechanisms of TD of monetary and primary rewards differed, and whether amount sensitivity and delay sensitivity contributed differently to TD of both reward types. The neural correlates of TD of money and primary rewards have not yet been compared directly. Aggregating across two separate studies with adults, McClure et al. (2004, 2007) found high overlap for TD of money and juice in a frontoparietal network, and to a lesser extent in the VS and medial orbitofrontal cortex (mOFC). Based on previous studies, we expected that adolescents would discount delayed snack rewards more steeply than monetary rewards (Demurie et al., submitted; Estle, Green, Myerson, & Holt, 2007; Jimura et al., 2011). We also expected that TD choices for money and snacks would both
activate frontoparietal regions (McClure et al., 2007). Based on a meta-analysis (Sescousse, Caldu, Segura, & Dreher, 2013), we hypothesized that monetary choices would activate the mOFC more than snack choices, whereas snack choices would activate the anterior insula more than money choices.

The third goal of this study was to explore whether testosterone and estradiol levels were associated with TD and its neural correlates. When investigating the neural mechanisms underlying individual differences in TD in adolescence, it is important to account for pubertal hormone levels (e.g., testosterone and estradiol), as they are rapidly increasing in adolescence and stimulate impulsive behaviors by influencing brain activity in reward-related brain areas (Peper & Dahl, 2013). Higher testosterone levels, for example, have been associated with increased VS responses during reward processing (Braams, van Duijvenvoorde, Peper, & Crone, 2015; Op de Macks et al., 2011). Higher testosterone and estradiol levels in adolescent boys have been associated with increased alcohol use (de Water, Braams, Crone, & Peper, 2013), which is considered an impulsive behavior. Behavioral findings on the relation between TD and puberty are inconclusive: recent studies have found no association between TD and self-reported pubertal development (de Water et al., 2014) or a non-significant trend toward increased TD in adolescents with higher testosterone levels (Bromberg, Wiehler, & Peters, 2015). Further, the association between pubertal hormone levels and brain activity during TD choices has not yet been explored. We expected that higher testosterone and estradiol levels would be associated with increased discounting of delayed rewards (Bromberg et al., 2015), and increased VS activation during decision-making (Braams et al., 2015; Op de Macks et al., 2011).

In summary, the aims of the present study were: 1) to examine the neural mechanisms of individual differences in three components of TD choice in adolescents (average impatience, amount sensitivity, and delay sensitivity); 2) to compare TD of monetary and primary rewards at the neural and behavioral level; and 3) to explore whether pubertal hormones (testosterone and estradiol) are associated with TD and its neural mechanisms.

Methods

Participants

Participants were 61 adolescents (all but one right-handed) who completed a functional magnetic resonance imaging (fMRI) session. Three participants were excluded from subsequent analyses, due to head motion > 3 mm, a brain anomaly, or limited field-of-view coverage. Thus, data from 58 adolescents (31 girls; \( M_{\text{age}} = 14.47 \) years, \( SD = 1.15 \), range = 12-16 years) were reported. IQ (\( M = 109, SD = 13, \) range 80-135) was estimated from the Vocabulary and Block Design subtests of the WISC-III (Wechsler, 1991). The Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) was filled out by a parent. No participant scored in the clinical range (T-score > 70) for internalizing or externalizing problems.
Temporal Discounting Task

Each participant performed a temporal discounting (TD) task in the MRI scanner (see Figure 3.1). The TD task included two blocks with monetary rewards, and two blocks with snack rewards. The task was potentially real, in that one choice was randomly selected for each reward type and given to participants. If the participant chose an immediate reward, they received the respective outcome (money and snack) immediately. If the participant chose a delayed reward, the money was transferred to their bank account, and the snack was mailed or delivered to their home at the corresponding delay. A potentially real task relies on the assumption that each choice will be made as if it has real consequences, since participants do not know which choice will be selected and paid (Scheres et al., 2013).

A total of 80 choices were administered for each reward type between a small reward available on the day of testing (“today”), and a larger reward available after a delay. In snack trials, participants chose between different amounts of their favorite snack, selected from a list of 14 types (see Table S3.1). The delayed reward was always €10 or 10 snacks for the monetary or snack task, respectively. The immediate reward was €2, €4, €6, or €8 or 2, 4, 6 or 8 snacks. There were five delays: 2, 14, 30, 90, and 180 days. For each trial type, each immediate reward-delay combination was presented four times. In addition to money and snack choices, there were 20 control trials in which participants chose the larger of two circles. These control trials allowed us to compare brain activity between TD choices and choices not requiring consideration of reward amounts or delays but only a perceptual decision and motor response.

Participants indicated their preference by pressing a button on a button box with their right index finger (for the option presented on the left) or their right middle finger (for the option on the right). The position of the options on the screen was counterbalanced across trials.

Each participant completed 22 practice trials (10 money choices, 10 snack choices, and 2 control choices) before entering the scanner. In the scanner, the TD task was administered in 4 blocks of 45 choices (40 TD choices and 5 control choices). Money and snack choices were administered in four separate, alternating blocks (counterbalanced across participants). The TD task lasted approximately 20 minutes.

Participants were asked to refrain from eating snacks 24 hours before the experiment. The experimenter weighed and measured each participant in order to compute their Body Mass Index (BMI; weight in kg/height in cm²). Participants also reported the time since their last meal (in hours and minutes), and how hungry they felt on a 10-point scale, immediately before the TD task. None of these variables correlated significantly (all p’s >.12) with TD choices (neither money nor snack choices).
Figure 3.1. Trial procedure of the Temporal Discounting task.
Note. Participants had to indicate their choice within 8000 ms. After indicating their choice by pressing a button, they immediately continued to the next trial.

Reward Valuation
Participants rated on a 10-point scale how much they would enjoy receiving each reward that was used in the task (see Figure S3.1). Participants’ average rating across the rewards of each type (money, snacks) was taken as an index of subjective reward valuation of that reward type. Participants also indicated how much money they were willing to pay for each snack amount (see Figure S3.2). These reward valuation questions were administered before the task for half the participants, and after the task for the other half.

Subjective Delay Perception
We assessed participants’ subjective delay perception by presenting them with a 180 mm visual analogue scale, with the anchors “very short” and “very long” below the left and right ends of the scale, respectively (Zauberman, Kyu Kim, Malkoc, & Bettman, 2008). For each delay used in the task, participants indicated how long they considered it by placing a pencil mark on the line. The length (in mm) from the left end of the line to the mark was taken as an index of subjective delay perception (see Figure S3.3).

Quick Delay Questionnaire
To assess participants’ delay aversion and delay discounting in daily life, they filled out the Quick Delay Questionnaire (QDQ; Clare, Helps, & Sonuga-Barke, 2010; Hsu, Benikos, & Sonuga-Barke, 2015), which has high test-retest reliability ($r = .81$); QDQ delay aversion and delay discounting scores positively correlate with ADHD symptoms (Clare et al., 2010). The QDQ has 5 items for delay aversion (e.g., “Having to wait for things makes me feel stressed and tense”), and 5 items for delay discounting (e.g., “The future is not important to me, I only consider the immediate consequences of my actions”); participants rated how
well each statement described their behavior in the past 6 months on a 5-point scale (1=not like me at all, 5 = very like me). The five ratings for each scale were averaged to one for delay aversion (Cronbach’s α = .78) and delay discounting (α = .61). Scores for positively phrased questions were reversed, such that higher scores indicated more delay aversion or discounting.

**Pubertal Hormones**

Participants collected saliva samples by passive drool at home on two consecutive days. Girls who had reached menarche collected the samples on days 6 and 7 after the start of their period, or during their stop week if they used oral contraceptives (n =1) (see de Water, Braams, Crone, & Peper, 2013; Peper et al., 2013). On each day, participants collected two saliva samples: directly after waking up, and 15 minutes later. The two daily samples were first combined (Wood, 2009), and testosterone and estradiol levels were subsequently determined using an enzyme-linked immunosorbent assay (ELISA; IBL, Hamburg, Germany) at the Clinical Chemistry Lab of Medical Centre Alkmaar, the Netherlands. The lowest detectable levels were 0.4 pg/mL for estradiol, and 4.7 pg/mL for testosterone. The reliability coefficients of the hormone assays are reported in the supplementary materials.

Given that hormone levels for the two days were highly correlated (testosterone: rho = .77, p<.001; estradiol: rho = .55, p<.001), we used average testosterone and estradiol levels for the two days in analyses. Testosterone level was log-transformed to reduce positive skew. One outlier (>3 SD of the mean within each gender) was excluded from analyses (1 boy for estradiol).

Participants completed the Pubertal Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988), to determine Tanner stages (Carskadon & Acebo, 1993). Consistent with prior studies with participants of the same age (Crockett & Petersen, 1987), all Tanner stages were represented in our sample: prepubertal (6.7 %), early pubertal (10.0 %), midpubertal (31.7%), late pubertal (48.3 %), and postpubertal (3.3 %). As expected, girls reported more advanced Tanner stages than boys (t = 2.95, p = .005), even though they did not differ significantly in age (t = 0.63, p = .53).

**fMRI Data Collection**

Neuroimaging data were collected using a 1.5 T Siemens Avanto scanner with a 32-channel head coil. To minimize head movement, we placed foam inserts around each participants’ head and paper tape across their forehead and the head coil. We collected: (1) a T1-weighted anatomical scan (repetition time = 2250 ms, echo time = 2.95 ms, field of view = 256 mm, 176 slices, slice thickness = 1 mm, slice gap = 0.5 mm, flip angle = 15°, duration = 5 min 14s), and (2) functional images using a multi-echo GRAPPA sequence during four runs of approximately 5 minutes each (repetition time = 2010 ms, echo times = 9.4, 20.9, 33, 44, and 56 ms, field of view = 224 mm, 32 slices collected in ascending order, slice thickness = 3 mm, slice gap = 0.51 mm, flip angle = 90°). Before the first run, we collected
30 volumes (preshans). The first two volumes of runs 2-4 were discarded to allow for steady state magnetization.

**Procedure**

Participants were first familiarized with the scanner environment by performing practice trials of the TD task in a mock scanner. In the MRI scanner, they first watched a movie while the T1-weighted anatomical scan was collected, followed by the TD task. A second task (social exclusion paradigm) and a DTI scan were collected after the TD task, which are not reported in this manuscript. After the MRI session, participants completed the QDQ, PDS and WISC-III subtests. Participants were paid €20 for their participation, and could earn an additional €2-€10 and 2-10 snacks depending on the randomly selected choices in the TD task. Parents gave informed consent, participants gave informed assent. All procedures were approved by the Medical Ethical Committee of the first author’s institute.

**Mixed-Effects Model Analyses**

TD task choices were analyzed with a generalized linear mixed-effects model using the lme4 package (Bates, Maechler, Bolker, & Walker, 2015) in R (version 3.2.0; R Core Team, 2013). The dependent variable was the TD choice (1 = immediate reward choice, 0 = delayed reward choice) (see Figure 3.2 for individual differences in the % of delayed reward choices). The model included a fixed intercept and the following fixed effects: amount of the immediate reward, length of the delay, reward type (snacks, money), the interaction between amount and reward type, and the interaction between delay and reward type. In addition, for each participant, random adjustments to the fixed intercept and to the slopes of all fixed effects (main effects and interactions) were included. Furthermore, all correlation terms among the random effects were estimated, resulting in a model “maximal with respect to the random effects” as suggested by Barr, Levy, Scheepers, and Tily (2013), to avoid inflated Type 1 errors. Amount and delay were standardized (centered and scaled), and reward type was specified by a sum-to-zero contrast (1 = snacks, -1 = money). The model was estimated using the objective amounts and delays, as this model fit better than the model with subjective amounts and delays based on participants’ reward valuation and subjective delay perception ratings (see supplementary materials).

To examine the mechanisms underlying individual differences in TD, we decomposed participants’ overt choices into three components by extracting for each participant three so-called Best Linear Unbiased Predictions (BLUPs; the model’s best estimate for each participant’s intercept and regression coefficients): 1) Average impatience (random intercept), this is each participant’s likelihood to choose the immediate reward for an average amount and delay. Higher values indicate a greater tendency to choose the immediate reward. This component is similar to the frequently used AUC and k rate in that it includes both the influence of delay and amount on choice. Consistent with this point, participants’ random intercept was highly correlated with both their AUC ($rho = -.93, p<.001$).
for money and snacks) and \( k \) rate (money: \( \rho = .77, p < .001 \); snacks: \( \rho = .83, p < .001 \));

2) Amount sensitivity (random amount slope), indexing the unique contribution of the immediate reward amount to TD choice. Higher values indicate an increased likelihood of choosing the immediate reward as its amount increases; 3) Delay sensitivity (random delay slope), indexing the unique contribution of delay to the larger reward to TD choice. Higher values indicate an increased likelihood of choosing the immediate reward as the delay to the delayed reward increases.

We explored gender differences in the three components of TD choice by performing a generalized mixed-effects model analysis that included a fixed intercept and fixed effects for amount of the immediate reward, delay to the delayed reward, gender (sum-to-zero contrast: 1 = girl, -1 = boy), gender by amount, and gender by delay. Again, for each participant, random adjustments to the fixed intercept and to the slopes of amount, delay, gender, gender by amount, and gender by delay were included. All correlation terms among the random effects were explicitly estimated, and amount and delay were standardized.

Finally, we examined whether the components of TD choice were correlated for money and snack choices by performing separate generalized mixed-effects model analyses for the money and snack choices. Both models included a fixed intercept and fixed effects for amount of the immediate reward, and delay. Again, for each participant, random adjustments to the fixed intercept and the slopes of amount and delay were included. All correlation terms among the random effects were explicitly estimated, and amount and delay were standardized.

For the mixed-effects model analyses the optimizer “bobyqa” was used, with a maximum number of \( 1 \times 10^9 \) iterations. \( P \)-values were determined using Likelihood Ratio Tests as implemented in the mixed function of the afex package (Singmann, Bolker, & Westfall, 2015).

We used SPSS version 22.0 to compute Spearman rank-order correlations (\( \rho \)) of the participant-specific BLUPs with hormone levels, QDQ scale scores, and age. We also computed Spearman rank-order correlations (\( \rho \)) of the participant-specific BLUPs for money and snack choices, to examine the correlations of the TD components between both reward types.
fMRI Data Analyses

fMRI data were preprocessed and analyzed in SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). From the 30 prescans, optimal weights were calculated for each of the five echo times and used to combine them to one image per volume (Poser, Versluis, Hoogduin, & Norris, 2006). Data were realigned using a rigid body transformation and slice time corrected. The T1-weighted anatomical scan was segmented, and functional images were coregistered to the segmented gray matter image. Finally, data were normalized to an MNI template (ICBM152) and smoothed with a 5mm FWHM Gaussian kernel.

Three event types were modeled in the general linear model implemented in SPM8: Delayed reward choice, Immediate reward choice, and Control task choice. Events were modeled separately for each block. Events were modeled at the onset of the presentation of the choice (duration = response time of that choice), and convolved with a hemodynamic response function and its first-order temporal derivative. Trials in which participants responded faster than 300 ms or failed to respond within 8000 ms, were not included in the model (to eliminate trials in which participants likely did not process the options sufficiently) (cf. Lansu, Cillessen, & Karremans, 2012). Additional regressors were included to model head motion (18 parameters: 3 translation and 3 rotation parameters plus the square and first-order derivative of each of these six motion parameters), and to model the objective amount of the immediate reward and delay (parametric regressors, linear trend). To avoid removing low-frequency task-induced effects, we applied a high-pass filter with a 320s cutoff (the maximum duration of a run).
Whole-brain analyses

Pairwise contrast images were first computed at the participant level, and subsequently entered in group level one-sample t-tests. First, we examined brain regions that were involved in TD choices, independent of individual differences. The following contrasts were computed: TD choice > Control choice, Delayed reward choice > Immediate reward choice, Immediate reward choice > Delayed reward choice (the latter two contrasts could not be computed for 4 participants: 3 participants always chose the delayed reward, while 1 participant always selected the immediate reward). These contrasts were computed combined for the money and snack runs.

Second, we examined how individual differences in TD choice components and hormone levels were associated with brain activity during TD choices. We performed one-sample t-tests on the contrast Delayed reward choice > Immediate reward choice, with as covariate of interest either the TD choice components or hormone levels. Specifically, in order to examine the neural mechanisms of individual differences in TD choice components, three one-sample t-tests were run: one with average impatience (random intercept) as a covariate, one with amount sensitivity (random amount slope) as a covariate, and one with delay sensitivity (random delay slope) as a covariate. Two one-sample t-tests were run to examine the associations between hormone levels and brain activity: one with estradiol as a covariate, and one with log-transformed testosterone as a covariate. Given the gender-specific nature of pubertal hormones, the hormone analyses were performed for boys and girls separately, with age as an additional covariate.

Third, we compared brain activity during money TD choices versus snack TD choices in two ways. We first examined the neural overlap, that is regions that were active during TD of money and snacks, using a conjunction analysis under the conjunction null hypothesis (Nichols, Brett, Andersson, Wager, & Poline, 2005). We examined the neural overlap for money and snacks: 1) during TD choices compared to Control choices (conjunction: TD money choice > Control choice & TD snack choice > Control choice); 2) during delayed reward choices compared to immediate reward choices (conjunction: money delayed reward choice > money immediate reward choice & snack delayed reward choice > snack immediate reward choice) and; 3) during immediate reward choices compared to delayed reward choices (conjunction money immediate reward choice > money delayed reward choice & snack immediate reward choice > snack delayed reward choice).

Second, we directly compared brain activity during TD choices for money versus snacks by examining brain areas that were more active for TD of money than TD of snacks, and vice versa. We computed pairwise contrast images at the participant level, which were subsequently entered in one-sample t-tests at the group level. The difference in mean reward valuation ratings of the money and snack rewards were included as a covariate, to account for differences in valuation between them. We compared activity during TD choices for money versus snacks, independent of whether participants chose the immediate or delayed reward (contrasts: TD choice money > TD choice snacks, TD choice snacks > TD
choice money). We further compared activity during delayed reward choices for money versus snacks (contrasts: Delayed reward choice money > Delayed reward choice snacks, Delayed reward choice snacks > Delayed reward choice money), and during immediate reward choices for money versus snacks (contrasts: Immediate reward choice money > Immediate reward choice snacks, Immediate reward choice snacks > Immediate reward choice money).

All whole-brain analyses were corrected for multiple comparisons using FWE-correction (p < .05 at the cluster level, with a cluster-forming threshold of p < .001).

Region of Interest (ROI) analyses

In order to further investigate the neural mechanisms underlying individual differences in TD, we selected ROIs based on prior fMRI studies that focused on TD in adolescents or conceptually similar constructs (e.g., anticipating delays and return sensitivity). We used MarsBar 0.43 (Brett, Anton, Valabregue, & Poline, 2002) to extract parameter estimates centered on peak voxels (spheres with a 6-mm radius) reported in these studies. We extracted parameter estimates for the contrast Delayed reward choice > Immediate reward choice. Note that this contrast was unbiased in that it probes brain activity during TD choices, independent of the individual differences in TD choice components and hormone levels with which we subsequently correlated the brain activity (see below). The MNI coordinates of the ROIs and the studies from which they were derived are reported in Table S2.

The right and left VS were selected to study associations with average impatience (random intercept), amount sensitivity (random amount slope) and hormones. The right and left vmPFC were chosen to examine associations with average impatience (random intercept), and amount sensitivity (random amount slope). The right DLPFC and superior parietal cortex were selected for associations with average impatience (random intercept). The right amygdala and insula were used to study associations with delay sensitivity (random delay slope).

Spearman rank-order correlations examined associations between activation in these ROIs and average impatience, amount sensitivity, and delay sensitivity. We computed partial correlations, controlling for age, to examine the associations of testosterone and estradiol levels with ROI activation and the TD choice components. Due to the sex-specific nature of these hormones, these analyses were performed separately for boys and girls.

A false discovery rate (FDR) correction was applied to control for multiple testing (see Benjamini & Hochberg, 1995, for the procedure of computing an FDR-corrected p-value), resulting in a significance threshold of p < .013.
Results

Behavioral Results

Correlations

We examined correlations between the three TD choice components, and whether they were associated with self-reported daily life discounting and delay aversion (QDQ; to examine the ecological validity of the TD choice components) and age. All correlations are presented in Table 3.1, while we focus here on those correlations surviving FDR-correction for multiple comparisons. Self-reported delay discounting in daily life (QDQ) was positively correlated with average impatience, indicating that participants who were highly impatient in the TD task, also reported increased discounting of delayed rewards in daily life. The TD choice components were all highly correlated with each other, but in opposite directions. As expected, average impatience and delay sensitivity were positively correlated, indicating that participants who frequently selected the immediate reward, selected it particularly frequently as the delay preceding the delayed reward increased. Unexpectedly, amount sensitivity was negatively correlated with both average impatience (see Figure 3.3) and delay sensitivity, indicating that participants who rarely selected the immediate reward, selected it when its magnitude was high. This is shown in Figure S3.4, in which the number of immediate reward choices is plotted as a function of reward magnitude for the participant with the highest amount sensitivity score in this study. As can be seen in Figure S3.4, this participant only selected the immediate reward in 10% of trials, but when she did select it, it was always when its magnitude was highest (8 Euros). Together, these correlations suggest that the TD choices of adolescents who are relatively impatient, are driven by a strong sensitivity to delay preceding the larger reward, and a relative insensitivity to amount of the immediate reward. In contrast, TD choices of adolescents who are relatively patient seem to be driven by a strong sensitivity to amount, and a relative insensitivity to delay.

We examined whether the three TD components were correlated between money and snack choices. There were strong positive correlations between money and snacks for average impatience \( (\rho = .78, \ p < .001) \), delay sensitivity \( (\rho = .71, \ p < .001) \), and amount sensitivity \( (\rho = .55, \ p < .001) \).
Table 3.1
Correlations (rho) between the study variables

<table>
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<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5.</th>
<th>6.</th>
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</thead>
<tbody>
<tr>
<td>1. Average impatience</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Amount sensitivity</td>
<td>-.67**</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Delay sensitivity</td>
<td>.87**</td>
<td>-.50**</td>
<td>-</td>
<td></td>
<td></td>
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<tr>
<td>4. QDQ–DD</td>
<td>.34*</td>
<td>-.27*</td>
<td>.22</td>
<td>-</td>
<td></td>
<td></td>
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<tr>
<td>5. QDQ- DA</td>
<td>.23†</td>
<td>-.10</td>
<td>.06</td>
<td>.20</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>6. Age</td>
<td>-.12</td>
<td>.25†</td>
<td>-.03</td>
<td>-.24†</td>
<td>-.18</td>
<td>-</td>
</tr>
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</table>

** p < .001 * p < .05 † p < .10

Note. QDQ-DD = Quick Delay Questionnaire- Delay Discounting scale, QDQ-DA = Quick Delay Questionnaire- Delay Aversion scale. Only correlations printed in bold survive FDR-correction for multiple comparisons.

Figure 3.3. Correlation between participants’ average impatience and amount sensitivity.
Note. A linear smooth function was fitted in R (ggplot2 package), the shaded area around the blue line indicates the 95% confidence interval.

Gender Differences

There was a main effect of gender on TD choice (B = 2.36, SE = 0.98, χ²(1) = 5.69, p = .02), indicating that girls were more impatient than boys. The gender by delay sensitivity interaction was significant, indicating that girls were more sensitive to delays than boys (B = 2.07, SE = 0.96, χ²(1) = 9.92, p = .002). Gender and amount sensitivity did not show a significant interaction (B = -0.15, SE = 0.12, χ²(1) = 1.42, p = .23).
Mixed-effects model analysis of TD task choices

The delay preceding the delayed reward, the amount of the immediate reward, reward type (snacks vs. money), and the reward type by delay interaction all significantly influenced participants’ TD choices. Participants were more likely to choose the immediate reward as the delay to the delayed reward increased ($B = 6.36$, $SE = 1.06$, $\chi^2(1) = 27.34$, $p < .001$), and as the amount of the immediate reward increased ($B = 1.54$, $SE = 0.15$, $\chi^2(1) = 60.89$, $p < .001$). Participants showed a stronger preference for immediate rewards when making choices involving snacks than money ($B = 1.58$, $SE = 0.30$, $\chi^2(1) = 22.97$, $p < .001$). There was a significant interaction between reward type and delay ($B = 0.79$, $SE = 0.33$, $\chi^2(1) = 5.89$, $p = .02$) (see Figure 3.4), indicating that delay contributed more strongly to TD choice for snack rewards than money. Reward type did not significantly interact with amount ($B = -0.07$, $SE = 0.08$, $\chi^2(1) = 0.72$, $p = .39$).

Figure 3.4. Interaction between reward type and delay to the larger reward.

Note. Error bars represent the standard error of the mean.

fMRI results

Neural regions involved in TD choices

Consistent with prior TD studies (see Scheres et al., 2013, for a review), a frontoparietal network was more strongly activated during TD choices than control task choices. This network included the angular gyrus, mOFC, DLPFC, VLPFC, dACC, and anterior PFC (see Table S3.3 and Figure 3.5).

Delayed reward choices, compared to immediate reward choices, activated the superior parietal cortex (see Table S3.4). There were no regions more active for immediate reward choices than for delayed reward choices.
There were no significant age or gender differences (all \( p’s > .22 \)) in brain activity during TD choices for any contrast (TD choice > Control choice, Delayed reward choice > Immediate reward choice, and Immediate reward choice > Delayed reward choice).

**Individual differences**

*Whole-brain analyses.* Average impatience was positively associated with activation of frontoparietal regions (lateral PFC, inferior parietal cortex and dACC) during delayed reward choices, compared to immediate reward choices (see Table S3.5 and Figure 3.6A). This means that participants who frequently chose the immediate reward, activated frontoparietal brain areas more during delayed reward choices than during immediate reward choices.

Amount sensitivity was positively correlated with dACC activity during immediate reward choices, compared to delayed reward choices (see Table S3.5 and Figure 3.6B).
This means that participants who chose the immediate reward more often as its amount increased, activated the dACC more during immediate reward choices than during delayed reward choices.

Delay sensitivity was positively correlated with activation of the parietal cortex during delayed reward choices, compared to immediate reward choices (see Table S3.5 and Figure 3.6C). This means that participants who selected the immediate reward more frequently as the delay preceding the larger reward increased, activated the parietal cortex more during delayed reward choices than immediate reward choices.

ROI analyses. Average impatience was positively correlated with activity of the left VS (\(\rho = .38, p = .004\)), right VS (\(\rho = .40, p = .003\)), and DLPFC (\(\rho = .46, p < .001\)) during delayed reward choices (contrast: delayed reward choice > immediate reward choice) (see Figure 3.7A). Average impatience was also positively correlated with activation of the left vmPFC (\(\rho = -.40, p = .003\)) during immediate reward choices (contrast: immediate reward choice > delayed reward choice). Amount sensitivity was positively correlated with activation of the left VS (\(\rho = -.40, p = .003\)) and right VS (\(\rho = -.37, p = .005\)) during immediate reward choices (contrast: immediate reward choice > delayed reward choice) (see Figure 3.7B). Delay sensitivity was not correlated with activity in the selected ROIs.

For the contrast TD choice > Control choice, there were no significant correlations that survived correction for multiple comparisons.
Figure 3.6. Associations between brain activity, identified by whole-brain analyses (FWE-corrected p<.05), and A) average impatience; B) amount sensitivity; C) delay sensitivity.
Comparison of TD of Money and Snacks

First, we performed conjunction analyses to examine brain areas that showed overlap for money and snack TD choices, independent of whether the delayed or immediate reward was selected. TD choices for money and snacks (compared to control task choices) both activated areas in the parietal cortex (see Table S3.6 and Figure 3.8). When we examined brain areas that showed overlap for money and snack TD choices during delayed reward choices or immediate reward choices specifically, no overlapping regions were found.

Second, we directly compared brain activity during TD choices for money and snacks. No regions were more active for one reward type or the other. To control for Type II error, we also compared activity during choices for money and snacks using a more lenient threshold ($p < .001$, uncorrected), but there were no significant differences then either.
Hormone Analyses

Testosterone and estradiol levels were not significantly associated with any TD choice component in boys or girls (all $p$'s > .19). Hormone levels also were not correlated with brain activity during TD choices, neither at the whole-brain level nor the ROI level. Hormone levels also were not significantly correlated with brain activity when we used a more lenient threshold ($p < .001$, uncorrected).

Discussion

This study examined in adolescents: 1) the neural mechanisms underlying individual differences in TD; 2) overlap and differences between TD of money and snacks; 3) the association between testosterone and estradiol levels and (neural activation during) TD choices. In order to study individual differences, we used a mixed-effects model approach to decompose TD choices into three components: 1) average impatience; 2) amount sensitivity; and 3) delay sensitivity. This approach allowed us to delve into the distinct factors underlying the neural mechanisms responsible for individual differences in TD choices.

Individual differences in TD

In line with our hypotheses, we found that individual differences in TD were associated with differential activation of frontoparietal brain areas, the VS and vmPFC during TD choices. Consistent with prior research, adolescents who where on average highly impatient engaged the lateral PFC, inferior parietal lobule and dACC more strongly during delayed reward choices compared to immediate reward choices (Stanger et al., 2013). These frontoparietal regions are involved in cognitive control, conflict monitoring and attention (Bunge & Wright, 2007). It is plausible that more impulsive adolescents recruited these areas preferentially during delayed reward choices because these choices require more effortful
control to delay gratification, consistent with the finding that highly impulsive adolescents were also highly sensitive to delay. Alternatively, the enhanced delayed choice-related frontoparietal activation in participants who were highly impatient might reflect decreased neural efficiency and frontoparietal maturity in more impulsive adolescents, relative to their less impulsive peers. Consistent with this interpretation, a recent longitudinal study in adolescents reported decreased VLPFC activation over time, and those adolescents who showed the strongest reductions also showed the largest declines in risk-taking (Qu, Galvan, Fuligni, Lieberman, & Telzer, 2015).

In addition, participants who were on average highly impatient in the TD task also engaged the vmPFC more strongly during immediate reward choices and the VS more strongly during delayed reward choices. These findings are consistent with prior studies reporting increased VS and vmPFC activity in individuals who showed a stronger preference for immediate rewards (Hariri et al., 2006; Stanger et al., 2013). While the finding that more impatient adolescents exhibited greater VS activity during delayed reward choices is in line with a recent study (Stanger et al., 2013), it does not fit with the notion that the VS is uniquely sensitive to the immediacy of rewards (McClure et al., 2004). Nevertheless, the VS has multiple functions, and has been shown to play an important role in the regulation of emotions and of impulsive behavior in adolescents and adults as well (Hare, Tottenham, Davidson, Glover, & Casey, 2005; Masten et al., 2009; Pfeifer et al., 2011). Highly impatient adolescents were also highly sensitive to delay, as indicated by the strong positive correlation between average impatience and delay sensitivity in this study. Thus, it may be speculated that the increased VS activity during delayed reward choices might reflect the fact that more impatient adolescents needed to regulate their emotions more strongly than their less impatient peers when they made these choices.

In line with our hypotheses, participants who were more sensitive to immediate reward amount demonstrated more VS activity during immediate reward choices. Unexpectedly, adolescents who were more sensitive to immediate reward amount also engaged the dACC more during immediate reward choices. This region has been shown to encode for increasing subjective value of rewards in adults (Kable & Glimcher, 2010). Increased activity might reflect the emotional salience of immediate rewards for adolescents who are more sensitive to immediate reward amount (Liu, Hairston, Schrier, & Fan, 2011).

Adolescents who were more sensitive to delay in the TD task activated the inferior parietal cortex more during delayed reward choices. This region has been implicated in cognitive control functions, such as attention and inhibition (Cavanna & Trimble, 2006). Adolescents who are more sensitive to delay may show increased inferior parietal lobule activation during delayed reward choices, because they require more effortful control during these choices. Contrary to our hypotheses, delay sensitivity was not associated with limbic brain areas such as the amygdala and insula. In prior research, enhanced amygdala and insula responses to anticipated delays were observed in individuals with ADHD (Lemiere et al., 2012; Plichta et al., 2009; Wilbertz et al., 2013). This discrepancy with our findings...
might be because these responses are specific to individuals with ADHD, or to tasks in which all delays are actually experienced (experiential TD tasks). Experiential tasks are arguably highly emotionally salient (Scheres et al., 2014), and might tap into an affective component of delay sensitivity (i.e., the subjective feeling of distress induced by the experience of a delay). The TD task we used may have tapped into a more cognitive component of delay sensitivity (i.e., imagining how one would feel if one would experience a delay). Consistent with this interpretation, delay sensitivity as assessed with the TD task was not correlated with self-reported delay aversion in daily life (i.e., negative feelings that are experienced during imposed delays). Future studies should test this possibility by using experiential TD tasks.

Collectively, our decomposition of TD choices into its underlying components has also provided unique and novel insights into the underlying mechanisms of individual differences in TD in adolescents. At the behavioral level, we showed that both amount sensitivity and delay sensitivity contributed to adolescents’ average impatience, but in opposite directions. Delay sensitivity was positively correlated with average impatience, while amount sensitivity was negatively correlated with average impatience. This indicates that the two extremes of the continuum of impulsivity are driven by different underlying factors. That is, adolescents who are on average highly impatient, are particularly driven by a heightened sensitivity to the delay preceding the delayed reward, and less by their sensitivity to the amount of the immediate reward. Conversely, adolescents who are on average highly patient, seem to be primarily driven by a heightened sensitivity to the amount of the immediate reward (i.e., they only select this reward when its magnitude is high), and less by sensitivity to delays. It can be hypothesized that highly patient adolescents strongly prefer the delayed reward because it is higher in magnitude than the immediate rewards. Future studies should test this hypothesis by systematically varying the magnitude of the delayed reward as well. Further, at the neural level, we showed that distinct neural mechanisms are associated with distinct underlying components of TD choice. Consistent with prior studies, we demonstrated that both frontoparietal and limbic brain areas were hyperactive during TD choices in adolescents who were on average highly impatient. In addition, we showed that activity of the parietal cortex was uniquely associated with delay sensitivity, while activity of the VS and dACC was uniquely associated with amount sensitivity.

Our findings on the neural mechanisms underlying individual differences in TD in typically developing adolescents could serve as a template for aberrant neural functioning in adolescents with impulse-control disorders (e.g., ADHD, substance abuse, gambling), and may inspire interventions to reduce impulsivity. Steep discounting of delayed rewards is characteristic of individuals with a wide variety of impulse-control disorders (Bickel, Jarmolowicz, Mueller, Koffarnus, & Gatchalian, 2012). Therefore, the findings of this study can serve as a model for aberrant neural functioning in adolescents with impulse control problems (e.g. ADHD or substance abuse). While steep TD has been observed across
different impulse-control disorders (Bickel et al., 2012), the mixed-effects model approach we used may reveal subtle differences between adolescents with different impulse-control disorders, as they may show differences in particular components of TD choice (i.e., amount sensitivity and delay sensitivity) (cf. Figner et al., 2010; Foerde et al., 2016). The findings of the current study have implications for interventions as well. We showed that highly impatient adolescents are particularly driven by a heightened sensitivity to delays, suggesting that interventions targeting delay tolerance may be particularly effective (Neef et al., 2001). We have further identified frontoparietal and limbic (i.e., VS) brain areas that are associated with steep discounting of delayed rewards, and activation of these brain areas could be altered by recently developed neurofeedback training programs, such as real time fMRI neurofeedback (Cohen Kadosh et al., 2016). Further, we showed that differential recruitment of the lateral and medial PFC is related to steep TD, and several cognitive interventions have been shown to alter activation of these regions and reduce TD in young adults, including working memory training (Bickel, Yi, Landes, Hill, & Baxter, 2011; Wesley & Bickel, 2014) and episodic prospection training (Benoit, Gilbert, & Burgess, 2011; Peters & Buechel, 2010).

Comparison of TD of money and snack rewards
Consistent with our hypotheses and prior studies (Estle et al., 2007; Jimura et al., 2011), snack rewards were discounted more steeply than monetary rewards. Despite this behavioral difference, there were no brain areas more active for one reward type or the other. This might be due to the fact that TD of money and snacks were highly correlated, more highly than in adult studies (Jimura et al., 2011), possibly because many adolescents use the money they earn or receive from their parents to buy snacks (anecdotally, several participants indicated that they used their money to buy snacks). Consistent with McClure et al.’s findings (2004, 2007), choices for both reward types showed neural overlap in the parietal cortex. Given the role of the parietal cortex in cognitive control, the overlap between TD of money and snacks in this region may reflect that exerting effortful control to guide decisions involving rewards and delays is important for TD choices in general, independent of the type of reward.

Pubertal hormones
Testosterone and estradiol levels were surprisingly neither associated with TD choices, nor with neural activity during these choices. Previous behavioral studies, however, also did not find statistically significant associations between testosterone levels and TD (Bromberg, Wiehler, & Peters, 2015; Peper et al., 2013), although Bromberg et al. found a non-significant trend towards a positive association between testosterone and a preference for immediate rewards in adolescent boys. Two previous neuroimaging studies showed that testosterone levels were positively correlated with VS responses to reward processing (Braams, van Duijvenvoorde, Peper, & Crone, 2015; Op de Macks et al., 2011). In contrast
with the present study, these investigations employed gambling tasks in which participants received or lost real rewards. It has been proposed that pubertal hormones particularly influence brain areas involved in motivational or emotional tendencies towards sensation-seeking behavior (e.g., the VS) (Crone & Dahl, 2012). Thus, it might be that associations between hormone levels and brain activation will only be observed when emotionally salient tasks that draw on sensation-seeking tendencies are used, such as gambling tasks involving real money, that include elements of uncertainty and surprise. The TD task of this study and most prior studies might be less emotionally salient than such gambling tasks, since participants do not experience all rewards and delays. Future studies should examine whether associations between hormones and brain activity are observed in experiential TD tasks, in which all rewards and delays are experienced, making these tasks more emotionally salient than the TD task of the present study. Additionally, the relatively modest sample size for the pubertal hormone analyses might have obscured significant associations between hormone levels and (neural activity underlying) TD.

Limitations and future directions

This study had some limitations. Some participants could not be included in the analyses, because they showed no variability in their TD choices. This issue could be reduced by using designs in which the amount of the immediate reward is adjusted based on participants’ choices (Christakou, Brammer, & Rubia, 2011), or in which participant-specific choice sets are presented based on a pre-test outside of the scanner (van den Bos et al., 2015). Further, we used a potentially real TD task, in which one choice was randomly selected and paid to participants at the corresponding delay, under the assumption that participants would choose as if every choice might have real-life consequences. The effects of amount sensitivity and delay sensitivity on TD choices could have been even stronger if all rewards and delays were experienced, such as in experiential or “real” TD tasks (cf. Scheres et al., 2013; Scheres et al., 2006).

Future studies could extend the current study in several ways. First, longitudinal studies could examine how changes in the underlying components of TD choices are associated with changes in brain activity, they could elucidate whether functional maturation of frontoparietal areas is delayed in adolescents who are more impatient, and whether brain activation at one time predicts impatience at a later time. Second, although the current study could serve as a template for neural mechanisms of components of impulsivity in adolescents with impulse-control problems (e.g., ADHD and substance abuse), they need to be included in future studies in order to directly compare their brain activity to typically developing adolescents.

Conclusions

In summary, individual differences in TD were associated with differential activity of brain areas implicated in cognitive control (lateral PFC and parietal cortex) and...
reward valuation (VS and vmPFC) during TD choices. We used mixed-effects modeling to decompose TD choices into three components: average impatience, amount sensitivity and delay sensitivity. Different underlying components contributed to two extremes of the continuum of impulsive choice: highly impatient adolescents were particularly driven by delay sensitivity, while highly patient adolescents were particularly driven by amount sensitivity. Distinct brain areas were associated with distinct components of TD choice. Both cognitive control and reward valuation areas were associated with average impatience, while reward valuation areas were uniquely implicated in amount sensitivity, and cognitive control areas were uniquely involved in delay sensitivity. Snack rewards were discounted more steeply than money, and TD of money and snacks showed overlap in the parietal cortex. Pubertal hormones were not correlated with TD choices and neural activity. These findings underscore the value of using models designed to disentangle how underlying components of impulsive choice contribute to a seemingly identical behavioral outcome, and should be extended to adolescents with impulse-control problems.
Supplement Chapter 3

Figure S3.1. Reward valuation ratings of money and snack rewards used in the TD task.

Figure S3.2. Amount of euro’s participants were willing to pay for the amount of snacks.
Figure S3.3. Participants’ subjective delay perception as a function of the delays.

Figure S3.4. Number of delayed and immediate reward choices as a function of immediate reward magnitude for the participant with the highest amount sensitivity score in this study.

Note. Each panel depicts one immediate reward amount (2, 4, 6 or 8 Euros, respectively).
Mixed-effects model with subjective amounts and delays

Participants’ reward valuation ratings and delay perception ratings were used to determine the subjective amounts and delays for each participant separately, following a procedure explained by Figner and colleagues (2010). Participants’ subjective value of an immediate reward amount and delay was computed as: Objective amount $^k$ (1)

We performed linear regression analyses in R in which participants’ reward valuation ratings and delay perception ratings were regressed against these subjective amounts and delays, for 20 values of $k$, ranging from 0 to 1 in increments of 0.005. For each value of $k$ and for each participant separately, the variance ($R^2$) in the ratings explained by the subjective amounts and delays was computed, and the value of $k$ for which the explained variance was the highest for each participant was used to compute the subjective amounts and delays of all immediate rewards and delays of that participant using Equation 1. We formally compared the fit of the mixed-effects model reported in the main text (with the objective amounts and delays) with a mixed-effects model in which these subjective immediate rewards and delays were used. We used the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) as fit indices. Smaller AIC and BIC values indicate a better model fit. The fit of the model with objective amounts/delays (AIC = 5052, BIC = 5244) was better than the fit of the model with the subjective amounts/delays (AIC = 7023, BIC = 7216).

Reliability of hormone assays

Intra-assay coefficient of variation (CV) was 6.4% at 4.6 pg/mL, and 2.6% at 77.2 pg/mL for estradiol. Intra-assay CV was 7.0% at 10.9 pg/mL, and 8.9% at 620.3 pg/mL for testosterone. Inter-assay CV was 3.8% at 2.1 pg/mL, and 4.3% at 20.8 pg/mL for estradiol. Inter-assay CV was 13.3% at 19.01 pg/mL, and 12.7% at 350.6 pg/mL for testosterone.

Table S3.1

<table>
<thead>
<tr>
<th>Chocolate</th>
<th>Sweets</th>
<th>Salty</th>
<th>Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mars (mini) *</td>
<td>Sweet liquorice</td>
<td>Salty liquorice</td>
<td>Cucumber slices</td>
</tr>
<tr>
<td>Bounty (mini) *</td>
<td>Haribo peaches *</td>
<td>Pringles (Paprika flavor) *</td>
<td>Baby carrots</td>
</tr>
<tr>
<td>Twix (mini) *</td>
<td>Fruttella*</td>
<td>Cheese cubes</td>
<td></td>
</tr>
<tr>
<td>Milky Way (mini) *</td>
<td>Winegums</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snickers (mini) *</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The most frequently selected type of snack was Pringles (22.4% of participants), followed by Haribo peaches (17.2%), Twix (12.1%), Winegums (10.3%), Snickers (8.6%), Mars (6.9%), Bounty (5.2%), Fruttella/cheese cubes/milky way/cucumber slices (all 3.4%), and sweet and salty liquorice (both 1.7%).
### Table S3.2
MNI coordinates of regions of interest used to examine individual differences

<table>
<thead>
<tr>
<th>Region</th>
<th>MNI coordinates (X Y Z)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>VS (left)</td>
<td>-9 6 -6</td>
<td>Ripke et al. (2012)</td>
</tr>
<tr>
<td>VS (right)</td>
<td>9 6 -3</td>
<td>Ripke et al. (2012)</td>
</tr>
<tr>
<td>vmPFC (left)</td>
<td>-10 26 -12</td>
<td>van Duijvenvoorde et al. (2015)</td>
</tr>
<tr>
<td>vmPFC (right)</td>
<td>14 38 -16</td>
<td>van Duijvenvoorde et al. (2015)</td>
</tr>
<tr>
<td>DLPFC</td>
<td>18 26 52</td>
<td>van den Bos et al. (2015)</td>
</tr>
<tr>
<td>Superior parietal cortex</td>
<td>29 -54 59</td>
<td>Stanger et al. (2013)</td>
</tr>
<tr>
<td>Insula</td>
<td>45 14 -11</td>
<td>Wilbertz et al. (2013)</td>
</tr>
<tr>
<td>Amygdala</td>
<td>27 -1 -20</td>
<td>Wilbertz et al. (2013)</td>
</tr>
</tbody>
</table>

*Converted into MNI from Talairach coordinates, using a Matlab script (tal2mni)*

### Table S3.3
Brain activity during temporal discounting (TD) task choices, relative to control task choices

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates (X Y Z)</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TD (money + snacks) &gt; Control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angular gyrus</td>
<td>48 -58 42</td>
<td>471</td>
<td>5.43</td>
</tr>
<tr>
<td>Medial orbital frontal cortex</td>
<td>10 66 -6</td>
<td>101</td>
<td>5.34</td>
</tr>
<tr>
<td>Cuneus</td>
<td>-10 -60 20</td>
<td>890</td>
<td>5.12</td>
</tr>
<tr>
<td>Middle occipital cortex</td>
<td>-36 -68 40</td>
<td>283</td>
<td>4.96</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>26 18 56</td>
<td>192</td>
<td>4.92</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>-40 50 4</td>
<td>246</td>
<td>4.69</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>-16 32 38</td>
<td>140</td>
<td>4.23</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>32 64 4</td>
<td>81</td>
<td>3.87</td>
</tr>
</tbody>
</table>

*All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported.*
### Table S3.4

Brain activity associated with delayed and immediate reward choices

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Delayed reward choice (money+snacks) > Immediate reward choice (money+snacks)**

Superior parietal lobule 28 -52 40 102 4.88

*Note.* All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported.

### Table S3.5

Brain activity associated with individual differences in temporal discounting

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Average impatience (random intercept of mixed-effects model)**

*Positive correlation*

Inferior parietal lobule 48 -54 48 270 4.83

Dorsal anterior cingulate cortex 12 36 42 91 4.39

Middle frontal gyrus 42 36 20 76 3.96

**Amount sensitivity (random amount slope of mixed-effects model)**

*Negative correlation*

Dorsal anterior cingulate cortex 10 30 34 95 3.98

**Delay sensitivity (random delay slope of mixed-effects model)**

*Positive correlation*

Inferior parietal lobule 38 -50 48 100 4.23

*Note.* All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported. The contrast *Delayed reward choice (money + snacks) > Immediate reward choice (money + snacks)* was used.
Table S3.6
Conjunction of brain activity involved in money and snack temporal discounting choices

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>-34</td>
<td>-66</td>
<td>40</td>
</tr>
<tr>
<td>Angular gyrus</td>
<td>50</td>
<td>-60</td>
<td>32</td>
</tr>
</tbody>
</table>

*Note.* All reported activations are FWE-corrected (*p* < .05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported.
CHAPTER 4

LONGITUDINAL CHANGES IN TEMPORAL DISCOUNTING IN ADOLESCENTS: A COMBINED fMRI AND sMRI STUDY

In preparation as:
de Water, E., Koolschijn, P.C.M.P., Mies, G.W., Yoncheva, Y., Figner, B.,
van den Bos,
W., Castellanos, F.X., Cillessen, A. H. N., & Scheres, A.
Longitudinal changes in temporal discounting in adolescents: a combined fMRI and sMRI study.
Abstract

Cross-sectional studies have shown that adolescents show a stronger preference for immediate rewards than adults in temporal discounting (TD) tasks, which involve choices between smaller, immediate rewards and larger delayed rewards. In addition, there are large individual differences in discounting of delayed rewards in adolescents, and these individual differences are correlated with daily life impulsive behaviors, such as substance use. We carried out a 1-year longitudinal MRI study, in which adolescents (n = 41) aged 12-17 years twice completed a TD task with money and snack rewards while they were scanned with fMRI. Further, we collected MRI data on cortical thickness and gray matter volume. We examined: 1) the stability of TD choices and brain activity underlying these choices; 2) longitudinal changes in brain activity during TD choices; 3) whether longitudinal changes in activity and structure of brain areas implicated in cognitive control and reward valuation were associated with changes in TD. We found that TD choices showed excellent test-retest reliability, while brain activity during these choices showed poor reliability. Longitudinal declines in dorsolateral prefrontal cortex (DLPFC) and medial orbitofrontal cortex (mOFC) activity were observed. Longitudinal decreases in DLPFC activity were associated with increases in the ability to wait for delayed rewards, while longitudinal increases in superior parietal cortex activity were associated with increases in the ability to wait for delayed rewards. These findings indicate that longitudinal changes in the function of brain regions involved in cognitive control underlie increases in the ability to wait for delayed rewards in adolescence, and that the direction of these neural changes (i.e., increases or decreases over time) differs by brain region.
Adolescents are typically characterized as impulsive, in that they engage in behaviors that have short-term benefits but that might be detrimental to their health in the long run (e.g., substance use) (Steinberg, 2008). This preference for immediate rewards is often assessed by temporal discounting (TD) tasks, in which individuals choose between smaller, more immediate rewards (e.g., €2 today) and larger, delayed rewards (e.g., €10 in 90 days) (see Scheres, de Water, & Mies, 2013 for a review). TD tasks have high ecological validity; a relatively strong immediate reward preference in these tasks has been observed in many psychiatric disorders in which impulsivity is a core symptom, including ADHD (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2012; Scheres, Tontsch, Thoeny, & Kaczkurkin, 2010), substance use and gambling (Reynolds, 2006), and conduct disorder (White et al., 2014).

The ability to wait for delayed rewards develops with age, and both linear and non-linear age-related differences have been reported. Several studies have shown that adolescents show a stronger preference for immediate rewards than young adults (Olson, Hooper, Collins, & Luciana, 2007; Steinberg et al., 2009), even when controlling for age differences in monetary reward valuation (de Water, Cillessen, & Scheres, 2014). However, one recent study found that mid-adolescents (14 years old) actually showed a stronger preference for delayed rewards, compared to late adolescents (18-19 years old) and children (6-12 years old) (Scheres, Tontsch, Thoeny, & Sumiya, 2014).

Age-related differences in TD are associated with differential functioning of brain areas implicated in cognitive control and reward valuation. Specifically, adolescents show decreased activation of the ventromedial prefrontal cortex (vmPFC), dorsolateral PFC (DLPFC) and parietal cortex during decision-making, compared to adults (Christakou, Brammer, & Rubia, 2011; Ripke et al., 2012). Additionally, adolescents engage the ventral striatum (VS) less during decision-making than adults (Christakou et al., 2011; van den Bos, Rodriguez, Schweitzer, & McClure, 2015), while adults show increased negative functional connectivity between the DLPFC and VS compared to adolescents (van den Bos et al., 2015).

Even though adolescents on average show steeper discounting of delayed rewards than adults, there are large individual differences in TD in adolescents (Benningfield et al., 2014; Ripke et al., 2012; Stanger et al., 2013). These individual differences are associated with functional and structural differences in the same brain areas that contribute to age differences in TD. Adolescents who show relatively steep TD, show increased activation of the VS during delayed reward choices (de Water et al., 2016; Stanger et al., 2013) and increased vmPFC activity during immediate reward choices (de Water et al., 2016), although decreased VS activation during decision-making has been reported as well (Ripke et al., 2012). Adolescents who show relatively steep TD further exhibit increased activation of the DLPFC and superior parietal cortex during delayed reward choices (de Water et al., 2016), but decreased activation of these areas during immediate reward choices (Stanger et al., 2013).

Steep discounting of delayed rewards is associated with increased gray matter volume (Cho et al., 2013) but decreased cortical thickness (Bernhardt et al., 2014) of the
medial PFC and anterior cingulate cortex (ACC) in young adults. Moreover, TD is correlated with gray matter volume of the VS in young adults: both positive (Cho et al., 2013) and negative correlations (Tschernegg et al., 2015) have been reported. To our knowledge, the structural neural correlates of individual differences in TD have not yet been explored in adolescents.

Furthermore, all studies on individual and age-related differences in TD in adolescence have been cross-sectional. While these studies have certainly been highly valuable, longitudinal studies are more sensitive to detect subtle developmental changes and can address additional research questions (Crone & Elzinga, 2015). For instance, longitudinal studies allow one to examine both stability and changes, and to investigate whether changes in brain activity and structure are associated with changes in TD over time.

The goals of the present study were to examine: 1) stability of TD choices and neural activity during these choices; 2) longitudinal changes in TD choices and in neural activity during these choices; 3) the associations between longitudinal changes in TD and longitudinal changes in the function and structure of the lateral PFC, parietal cortex, vmPFC and VS. To investigate these research questions, we carried out a longitudinal MRI study, consisting of two assessments approximately 1 year apart. Adolescents (n = 41) aged 12-17 years completed a TD task with money and snack rewards while being scanned with fMRI, and a structural MRI scan was collected to assess cortical thickness of the lateral and medial PFC and parietal cortex, and gray matter volume of the VS.

Methods

Participants

A 1-year longitudinal study was carried out, in which adolescents completed two magnetic resonance imaging (MRI) sessions. The baseline sample (timepoint 1; T1) (de Water et al., 2016; Chapter 3) consisted of 60 adolescents aged 12-16 years, of which 42 (70%) adolescents (21 girls) completed the follow-up MRI session (timepoint 2; T2) approximately 1 year later (range = 0.91-1.70 years, M = 1.17 years, SD = 0.15 years). One participant did not complete the T2 MRI session due to feelings of claustrophobia, meaning that longitudinal MRI data could be analyzed for 41 participants. At T2, participants were aged between 13 and 17 years (M = 15.63 years, SD = 1.18 years). Participants’ IQ (M = 109, SD = 13, range = 80-135) was estimated at T1 using the Block Design and Vocabulary subtests of the WISC-III (Wechsler, 1991). Parents completed the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) to screen for behavioral problems. At T1, none of the participants scored in the clinical range (T > 70) for internalizing or externalizing problems. At T2, again none of the participants scored in the clinical range for externalizing problems, but one participant scored in the clinical range for internalizing problems (T = 70).

Participants who completed both assessments did not differ from participants who only completed the first assessment regarding age, gender or IQ (all p’s > .20). However,
participants who completed both assessments showed less discounting of delayed rewards (as measured by the area under the curve; see methods) than participants who only completed the first assessment \( (p = .022) \).

Participants completed the Pubertal Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988) at both timepoints, which was used to examine their distribution across Tanner stages (Carskadon & Acebo, 1993). At T1, all Tanner stages were represented in our sample: prepubertal (6.7 %), early pubertal (10.0 %), midpubertal (31.7 %), late pubertal (48.3 %), and postpubertal (3.3 %). At T2, all Tanner stages except the prepubertal stage were represented: early pubertal (4.8 %), midpubertal (23.8 %), late pubertal (66.7 %), and postpubertal (4.8 %).

Temporal Discounting (TD) task

A temporal discounting (TD) task (see Figure 4.1) was administered at T1 and T2 while participants underwent an fMRI scan. This task consisted of choices between a small reward that was available today, and a larger reward that was available after a delay. Participants made choices for monetary rewards \((n = 80)\), and their favorite snack \((n = 80)\), which they selected from a list of 14 at each timepoint (see Table S4.1). The delayed reward was always €10 or 10 snacks. The immediate reward was either €2, €4, €6 or €8, or 2, 4, 6 or 8 snacks. Five delays were used: 2, 14, 30, 90 and 180 days. Each immediate reward-delay combination was presented 4 times. In addition to the money and snack reward choices, 20 control trials were included in the TD task. In these trials, participants had to indicate which of two circles was bigger.

Participants indicated their preference by pressing a button on a button box with their right index finger (for the option presented on the left) or their right middle finger (for the option on the right). The position of the options on the screen was counterbalanced across trials. Before the task started, outside of the scanner, participants completed 22
practice trials (10 money choices, 10 snack choices, and 2 control choices). The TD task was administered in 4 blocks of 45 choices (40 TD choices and 5 control choices). Money and snack choices were administered in separate blocks. Two different orders were used: 1) money – snack – money – snack; 2) snack – money – snack – money. These orders were counterbalanced across participants, but each participant received the same order at both timepoints.

After participants completed the TD task, the experimenter randomly selected one of the choices of the money and the snack task. If that choice was for an immediate reward, participants’ received the money and snack immediately. If the choice was for a delayed reward, the money was transferred to their bank account, and the snack was mailed or delivered to their home at the corresponding delay.

The main outcome measure was the area under the curve\(^1\) (AUC; Myerson, Green, & Warusawitharana, 2001) (see supplementary materials for more details on the calculation procedure). AUC ranges from 0 to 1, where larger values indicate a stronger preference for delayed rewards. We originally computed the AUC separately for the money and snack choices, but we chose to use the mean of the money and snack AUCs in the analyses, since they were highly correlated (\(\rho = .82, p < .001\) at T1; \(\rho = .86, p < .001\) at T2).

Participants were asked to refrain from eating candy 24 hours before the experiment. We measured several variables that might affect participants’ choices in the TD task, such as their reward valuation, body mass index, time since their last meal and how hungry they felt. The correlations between these variables and participants’ AUC are reported in the supplement.

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\(^1\) In Chapter 3, we didn’t use the AUC. Instead, we performed a mixed-effects model analysis on the TD task choices to determine participant-specific coefficients for three TD choice components: 1) average impatience (conceptually similar to AUC); 2) amount sensitivity; 3) delay sensitivity. However, since the sample mean contributes to the values of these coefficients and sample means differed at T1 and T2, coefficients for these components could not be used to examine longitudinal changes in TD. Therefore, we used the AUC, which is a normalised measure that can be directly compared at both timepoints. AUC and the coefficients for the 3 TD choice components were nonetheless highly correlated at T1 (\(\rho = .64-.96, p’s < .001\)) and T2 (\(\rho = .57-.95, p’s < .001\)).
MRI Data Collection

Neuroimaging data were collected using a 1.5 T Siemens Avanto scanner. A 32-channel head coil was used, and participants viewed the screen through a mirror mounted on the head coil. We placed foam inserts around the head of each participant, and placed a piece of paper tape across their forehead and the head coil to minimize head movement. We collected the following neuroimaging scans at both timepoints: (1) a T1-weighted anatomical scan (repetition time = 2250 ms, echo time = 2.95 ms, field of view = 256 mm, 176 slices, slice thickness = 1 mm, slice gap = 0.5 mm, flip angle = 15°, duration = 5 min 14s). (2) A multi-echo GRAPPA sequence to obtain functional images during four runs of approximately 5 minutes each (repetition time = 2010 ms, echo times = 9.4, 20.9, 33, 44, and 56 ms, field of view = 224 mm, 32 slices collected in ascending order, slice thickness = 3 mm, slice gap = 0.51 mm, flip angle = 90°). Before the first run started, we collected 30 volumes (prescans). The first two volumes of runs 2-4 were discarded to allow for a steady state magnetization.

Behavioral Data Analyses

We computed an intraclass correlation coefficient (ICC; two-way mixed model with absolute agreement) in SPSS version 22.0 to examine the reliability of the AUC derived from the choices in the TD task across timepoints. Reliability was quantified as poor (<0.4), fair (0.41–0.59), good (0.60–0.74) or excellent (>0.75) (Cicchetti, 2001).

We performed linear mixed-effects model analyses using the lme4 package (Bates, Maechler, Bolker, & Walker, 2015) in R (version 3.2.0; R Core Team, 2013) in order to examine the effects of timepoint and age on TD. Two models were estimated: a model with AUC (at both timepoints) as dependent variable and timepoint (T1 or T2) as predictor, and a model with AUC (at both timepoints) as dependent variable and the standardized linear and quadratic age trends (at both timepoints) as predictors. Both models included a fixed intercept and fixed effects for the predictors, and a random per-participant adjustment to the fixed intercept was included to model the repeated measures nature of the data. The optimizer “bobyqa” was used, with a maximum number of 1x10⁹ iterations. P-values were determined using Likelihood Ratio Tests as implemented in the mixed function of the afex package (Singmann, Bolker, & Westfall, 2015).

fMRI data analyses

fMRI data were preprocessed and analyzed in SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). Based on the 30 prescans collected at each timepoint, optimal weighting parameters for each of the five echo times were calculated and used to combine the echo times into one image per volume at each timepoint (Poser, Versluis, Hoogduin, & Norris, 2006). Data were realigned using a rigid body transformation and slice time corrected. The T1-weighted anatomical scan was segmented, and functional images at each timepoint were coregistered to the segmented gray matter image of that timepoint. Finally,
data were normalized to an MNI template (ICBM152), and smoothed with a full-width at half maximum Gaussian kernel of 5 mm.

Three event-types were modeled in the general linear model implemented in SPM8: Delayed reward choice, Immediate reward choice, and Control task choice. Events were modeled at the onset of the presentation of the choice (duration = response time of that choice), and convolved with a hemodynamic response function and its temporal derivative. Trials in which participants failed to respond within 8000 ms, or in which they responded faster than 300 ms (to eliminate trials in which participants likely did not process the options sufficiently; cf. Lansu, Cillessen, & Karremans, 2012), were not included in the model. Additional regressors were included to model the realignment parameters (18 parameters: 3 translation and 3 rotation parameters, and their square and first-order derivative), and parametric regressors (linear trend) were included to model the amount of the immediate reward and delay to the delayed reward. We applied a high-pass filter (cutoff = 320s).

**Whole-brain analyses**

First, we examined whether brain activity during TD choices and correlations between TD and brain activity at T1 could be replicated at T2. In order to examine brain activity during TD choices, independent of individual differences in these choices, we computed pairwise contrast images for each participant separately, and entered them in a one-sample t-test at the group-level. Two contrasts were computed: TD choice > Control choice, and Delayed reward choice > Immediate reward choice (note that the latter contrast could not be computed in 10 participants due to a lack of variability in choices, meaning that this contrast could be computed for 31 participants). These t-tests were performed on the T2 data, and also on the T1 data of all participants who completed both assessments, in order to determine brain activity during TD choices at both timepoints. We further examined correlations between TD and brain activity during TD choices by performing a one-sample t-test, with AUC as covariate for the contrast Delayed reward choice > Immediate reward choice (since the TD choice > Control choice contrast did not yield significant findings at T1). This analysis was again performed on T2 data, and on T1 data of participants who completed both assessments.

Second, we directly tested for longitudinal decreases or increases in brain activity during TD choices, by performing a flexible factorial analysis with subject and timepoint (T1, T2) as factors, for the contrasts TD choice > Control choice and Delayed reward choice > Immediate reward choice. These analyses were first performed without covariates, and subsequently with either age or AUC as covariate, to control for the potential effects of age and AUC at T1 on longitudinal changes in brain activity.

All whole-brain analyses were controlled for multiple testing by applying a FWE-correction (p < .05 at the cluster level, with a cluster-forming threshold of p < .001).
Region of Interest (ROI) analyses

First, we examined the reliability of brain activation in task-based ROIs by computing ICCs. We computed the intravoxel reliability on individual contrast values (for the contrast TD choice > Control choice) for each ROI, using the ICC toolbox developed by Caceres and colleagues (2009). Again, reliability was quantified as poor (<0.4), fair (0.41–0.59), good (0.60–0.74) or excellent (>0.75) (Cicchetti, 2001). The ROIs were defined as all regions that were significantly activated at T1 for the contrast TD choice > Control, based on a one-sample t-test (FWE-corrected \( p < .05 \)) that included all T1 participants for whom fMRI data could be analyzed (\( n = 58 \); including participants that did not complete the second assessment). These functional clusters were masked by the corresponding anatomical region from the automated anatomical labeling (AAL) toolbox. The following 7 ROIs were included (see Table S4.2 for the MNI coordinates corresponding to the peak voxel of each ROI): right angular gyrus, right medial orbitofrontal cortex, left precuneus, left inferior parietal lobule, right middle frontal gyrus, left middle frontal gyrus and left superior frontal gyrus.

Second, we examined longitudinal changes in activation of these task-based ROIs. Parameter estimates (contrast TD choice > Control Choice) were extracted for each ROI using Marsbar version 0.43 (Brett, Anton, Valabregue, & Poline, 2002). ROIs were defined as clusters that were significantly active based on the whole-brain one-sample t-test (see previous paragraph), masked by the corresponding anatomical region from the AAL toolbox. We performed linear mixed-effects model analyses with standardized ROI activation (at both timepoints) as dependent variable and timepoint (T1 and T2) as predictor. The model included a fixed intercept, a fixed effect for the predictor, and a participant-specific random adjustment to the fixed intercept. Separate models were estimated for each ROI. The same R packages and optimizer that are described in the behavioral data analysis section were used to run the models and determine \( p \)-values.

Third, we examined whether longitudinal changes in AUC were associated with changes in brain activity. For these analyses, we selected 6 ROIs based on prior studies on individual differences in TD in adolescents, consistent with our analyses of the T1 data (de Water et al., 2016; Chapter 3). We used Marsbar to extract parameter estimates (contrast: Delayed reward choice > Immediate reward choice) from spherical ROIs (6-mm radius) centered on peak voxels reported in these studies (see Table S4.3 for the MNI coordinates). The selected ROIs included the right dorsolateral prefrontal cortex, right superior parietal cortex, right and left ventral striatum, and right and left ventromedial prefrontal cortex. We performed linear mixed-effects model analyses with AUC (at both timepoints) as dependent variable and standardized ROI activation (at both timepoints) as predictors. All ROIs were included in a single model. The model included a fixed intercept, fixed effect for AUC, and a participant-specific random adjustment to the fixed intercept. The same R packages and optimizer that are described in the behavioral data analysis section were used to run the models and determine \( p \)-values.
Structural MRI Data Analyses

Cortical reconstruction was measured automatically using FreeSurfer 5.3 (http://surfer.nmr.mgh.harvard.edu). Details of the surface-based cortical reconstruction and subcortical volumetric segmentation procedures have been extensively documented previously (Fischl, 2012). To extract volume and thickness estimates, images were automatically processed with the longitudinal stream in FreeSurfer (Reuter, Schmansky, Rosas, & Fischl, 2012). Specifically, an unbiased within-subject template space and image (Reuter and Fischl, 2011) was created using robust, inverse consistent registration (Reuter et al., 2010). Several processing steps, such as skull stripping, Talairach transforms, atlas registration as well as spherical surface maps and parcellations were then initialized with common information from the within-subject template, significantly increasing reliability and statistical power (Reuter et al., 2012).

ROI selection for gray matter morphological assessment was based on 1) functional ROIs from T1: right angular gyrus, right medial OFC, bilateral middle frontal gyrus, left superior frontal gyrus, left inferior parietal cortex, left precuneus; 2) a priori selection of ROIs based on the TD literature: bilateral VS and vmPFC. Given that FreeSurfer does not provide vmPFC and VS parcellations, we used an alternative procedure to create these ROIs. An unbiased vmPFC ROI was created based on a cytoarchitectonic atlas (http://www.bic.mni.mcgill.ca/ServicesAtlases/VmPFC (Mackey & Petrides, 2014) and the VS was extracted from the Oxford-GSK-Imanova Striatal Connectivity Atlas in FSL (Tziortzi et al., 2014). To extract average cortical thickness from the ROIs, we performed the following steps: 1) Each anatomical ROI was registered automatically to the FreeSurfer “fsaverage” template with normalized mutual information and inspected for accuracy of registration. 2) Individual cortical thickness data was mapped to the “fsaverage” template. 3) Average cortical thickness in mm was extracted for each ROI and individual separately. For the VS, gray matter volume was extracted using the following steps: 1) the VS was converted to a FreeSurfer label and registered to the FreeSurfer “fsaverage” template with normalized mutual information and inspected for accuracy of registration. 2) VS labels were mapped to native space, and 3) VS gray matter volumes in ml were extracted per hemisphere for each individual.

We examined whether longitudinal changes in brain structure were associated with longitudinal changes in AUC. We performed linear mixed-effects model analyses with AUC (at both timepoints) as dependent variable and cortical thickness (for the right angular gyrus, right medial OFC, bilateral middle frontal gyrus, bilateral vmPFC, left superior frontal gyrus, left inferior parietal cortex, and left precuneus) and gray matter volume (for the bilateral VS) (at both timepoints) as predictors. All ROIs were included in a single model. The model included a fixed intercept, fixed effect for the predictors, and a participant-specific random adjustment to the fixed intercept. The same R packages and optimizer that are described in the behavioral data analysis section were used to run the models and determine p-values.
Results

All reported findings are based on analyses including all participants who completed both the first and second assessment (n = 41).

Behavioral results

The AUC was highly stable across the two assessments, as indicated by an ICC of 0.85, which signifies excellent test-retest reliability. There was no significant effect of timepoint on AUC (p=.34). Age was not associated with AUC, neither the linear (p=.55) nor the quadratic age trend (p=.52).

Neuroimaging results

Whole-brain findings

First, we examined neural activity during TD choices at T1 and T2 separately. When participants made TD task choices (compared to control task choices) at T1, they activated a frontoparietal network that included the mOFC, VLPFC and inferior parietal cortex (see Table 4.1). At T2, participants again activated the inferior parietal cortex, but the prefrontal activation during TD task choices was more dorsal and activity was less widespread at T2 compared to T1 (see Figure 4.2). At both timepoints, there were no brain areas more active during delayed reward choices than immediate reward choices, or vice versa.

Second, we examined the neural mechanisms of individual differences in TD at both timepoints. At T1, participants who showed relatively steep discounting of delayed rewards exhibited increased activation of the mOFC, lateral PFC, VS and parietal cortex during delayed reward choices, compared to immediate reward choices (see Table 4.2). At T2, participants who showed relatively steep discounting of delayed rewards again showed increased activation of the lateral PFC, VS and parietal cortex during delayed reward choices, compared to immediate reward choices, although the exact subregions were slightly different compared to T1 (see Table 4.2).

Finally, we directly compared brain activity at T1 and T2. There were no brain areas more active at T1 than T2, or vice versa, for any of the contrasts examined (TD choice > Control choice, Delayed reward choice > Immediate reward choice). Adding age and AUC as covariates did not change these findings.
Figure 4.2. Neural activity during temporal discounting choices, compared to control task choices (FWE-corrected $p < .05$) at timepoint 1 (T1) and timepoint 2 (T2).
### Table 4.1
Comparison of brain activity during timepoint 1 (T1) and timepoint 2 (T2) of participants who completed both assessments (n = 41)

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td>T1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TD choice &gt; Control choice</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial orbitofrontal cortex</td>
<td>10</td>
<td>66</td>
<td>-4</td>
</tr>
<tr>
<td>Angular gyrus</td>
<td>50</td>
<td>-60</td>
<td>42</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>-34</td>
<td>-70</td>
<td>42</td>
</tr>
<tr>
<td>Precuneus</td>
<td>-10</td>
<td>-56</td>
<td>14</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>-40</td>
<td>50</td>
<td>4</td>
</tr>
<tr>
<td>T2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TD choice &gt; Control choice</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precuneus</td>
<td>-8</td>
<td>-60</td>
<td>22</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>-20</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Middle occipital cortex</td>
<td>-30</td>
<td>-64</td>
<td>36</td>
</tr>
</tbody>
</table>

*Note. All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported.*
Table 4.2
Negative associations between brain activity during delayed reward choices and temporal discounting (area under the curve) during timepoint 1 (T1) and timepoint 2 (T2) of participants who completed both assessments (n = 31)

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td>T1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Delayed reward choice &gt; Immediate reward choice</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle temporal cortex</td>
<td>68</td>
<td>24</td>
<td>-12</td>
</tr>
<tr>
<td>Caudate</td>
<td>14</td>
<td>12</td>
<td>-2</td>
</tr>
<tr>
<td>Lateral orbitofrontal cortex</td>
<td>20</td>
<td>60</td>
<td>-4</td>
</tr>
<tr>
<td>Angular gyrus</td>
<td>42</td>
<td>-64</td>
<td>46</td>
</tr>
<tr>
<td>Dorsal anterior cingulate cortex</td>
<td>10</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>44</td>
<td>40</td>
<td>16</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>24</td>
<td>24</td>
<td>54</td>
</tr>
<tr>
<td>Precuneus</td>
<td>4</td>
<td>-64</td>
<td>32</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>48</td>
<td>24</td>
<td>42</td>
</tr>
<tr>
<td>Medial orbitofrontal cortex</td>
<td>-40</td>
<td>56</td>
<td>-4</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>-48</td>
<td>-58</td>
<td>52</td>
</tr>
<tr>
<td>Middle occipital cortex</td>
<td>-34</td>
<td>-66</td>
<td>38</td>
</tr>
<tr>
<td>T2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Delayed reward choice &gt; Immediate reward choice</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Putamen</td>
<td>34</td>
<td>14</td>
<td>-4</td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>-42</td>
<td>16</td>
<td>26</td>
</tr>
<tr>
<td>Posterior cingulate cortex</td>
<td>-6</td>
<td>-46</td>
<td>22</td>
</tr>
</tbody>
</table>

Note. All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported.

ROI findings
First, we computed ICCs to examine the intravoxel reliability of 7 ROIs during TD choices, compared to control choices. All ROIs showed poor test-retest reliability (see Table 4.3). Second, we directly compared activation during TD choices (compared to control choices) in these 7 ROIs at T1 and T2. Two prefrontal regions showed a significant decline in activation from T1 to T2: the left DLPFC (B = -2.09, SE = 0.84, χ²(1) = 6.11, p = .01) and mOFC (B = -1.43, SE = 0.67, χ²(1) = 4.44, p = .04). Finally, we examined whether changes in brain activity were associated with changes in TD. Longitudinal increases in the ability to wait for delayed rewards were associated with longitudinal decreases in DLPFC activity (B = -0.10,
SE = 0.03, χ²(1) = 13.50, p <.001), and longitudinal increases in superior parietal cortex (B = 0.06, SE = 0.02, χ²(1) = 5.09, p =.02) activity during delayed reward choices.

Table 4.3
Intraclass correlation coefficients (ICCs) of regions of interest for contrast TD choice > Control choice

<table>
<thead>
<tr>
<th>Region</th>
<th>median ICC (S.E.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angular gyrus</td>
<td>0.24 (0.05)</td>
</tr>
<tr>
<td>Medial orbitofrontal cortex</td>
<td>0.19 (0.10)</td>
</tr>
<tr>
<td>Precuneus</td>
<td>0.24 (0.05)</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>0.34 (0.09)</td>
</tr>
<tr>
<td>Middle frontal gyrus (right)</td>
<td>0.13 (0.05)</td>
</tr>
<tr>
<td>Middle frontal gyrus (left)</td>
<td>0.12 (0.09)</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>0.19 (0.05)</td>
</tr>
</tbody>
</table>

Note. S.E. = standard error of the mean

Structural MRI findings
There were no significant associations between longitudinal changes in brain structure and changes in TD (all p’s > .13).

Discussion
We carried out a 1-year longitudinal multimodal neuroimaging study consisting of two assessments, in which adolescent participants completed a TD task while being scanned with fMRI, and structural MRI data was collected. The goals of the study were to examine: 1) test-retest reliability of TD choices and neural activity during these choices; 2) longitudinal changes in neural activity during TD choices; 3) whether changes in TD choices were associated with changes in brain function and structure (cortical thickness and gray matter volume).

TD choices were highly stable, as indicated by a test-retest reliability of 0.85. This finding is consistent with two recent studies reporting high test-retest reliability (ranging from 0.54 to 0.76) of TD choices in adolescents, with an interval that was 1 year longer than the one in this study (Achterberg, Peper, van Duijvenvoorde, Mandl, & Crone, 2016; Anokhin, Golosheykin, & Mulligan, 2015). The high stability of TD choices has led some researchers to argue that the degree to which an individual discounts delayed rewards could be considered a personality trait (Odum, 2011).
Contrary to the stability of TD choices, brain activity during these choices showed poor test-retest reliability in all ROIs we examined. A recent longitudinal fMRI study in adolescents also reported poor test-retest reliability of neural activity in partly overlapping regions (van den Bulk et al., 2013). Poor test-retest reliability of brain activation might reflect ongoing maturational process, as test-retest reliability is lower in children than in adults (Koolschijn, Schel, de Rooij, Rombouts, & Crone, 2011). Indeed, we found significant longitudinal declines in mOFC and DLPFC activity, consistent with other longitudinal studies in children and adolescents (Durston et al., 2006; Qu, Galvan, Fuligni, Lieberman, & Telzer, 2015). These decreases in activity may be caused by neuronal maturation processes, such as pruning of synapses and elimination of connections (Casey, Tottenham, Liston, & Durston, 2005).

**Individual differences**

At both the first and second timepoint, participants who showed relatively steep discounting of delayed rewards exhibited increased activation of the lateral PFC, parietal cortex and VS during delayed reward choices, compared to immediate reward choices. These findings are consistent with a study of Stanger and colleagues (2013), and the brain-behavior associations at the second timepoint largely replicated the associations in the full baseline sample at the first timepoint (de Water et al., 2016; Chapter 3). The lateral PFC and parietal cortex are involved in cognitive control processes, such as inhibition and attention (Bunge & Wright, 2007), while the VS is implicated in reward prediction and processing (Galvan, 2010). Therefore, our findings indicate that adolescents who show relatively steep TD may be more sensitive to rewards, and require an increased need for cognitive control during delayed reward choices.

Longitudinal increases in the ability to wait for delayed rewards were associated with longitudinal changes in activation of the DLPFC and superior parietal cortex during delayed reward choices. The direction of these changes differed by brain area: increases in the ability to wait for delayed rewards were associated with decreases in DLPFC activation, but increases in super parietal cortex activation. The finding that a decline in DLPFC activity is associated with an increased ability to wait for delayed rewards is in line with the findings of Qu and colleagues (2015), who demonstrated that a decline in lateral PFC activity was associated with decreased risk-taking in adolescents. Given that we observed longitudinal decreases in PFC activity during TD choices, one could argue that a longitudinal decline in DLPFC activity reflects increased maturation of this area. Following this reasoning, the DLPFC may have matured more in those individuals who showed the strongest increase in their ability to wait for delayed rewards. Nevertheless, increases in superior parietal cortex activity were associated with increases in delayed reward preferences, indicating that (in the context of the TD task) neural maturation might be reflected by decreases in DLPFC activity over time, but increases in superior parietal cortex activity.
Contrary to our hypotheses, there were no significant associations between longitudinal changes in brain structure and changes in TD in this study. Several other studies did report associations between cortical thickness of the mPFC and gray matter volume of the VS on the one hand, and TD on the other hand (Bernhardt et al., 2014; Cho et al., 2013; Tschernegg et al., 2015). However, these cross-sectional studies only included young adults, while we examined how changes in brain structure were associated with changes in TD in adolescents. Future longitudinal research in individuals from a wide age range (from adolescents to adults) is needed to examine whether associations between brain structure and TD are limited to certain developmental stages (i.e., adulthood).

Together, our findings are partly in line with dual-system models of adolescent impulsivity. These models postulate that adolescents are impulsive because of an imbalance between relatively mature reward-related brain areas, such as the VS, and immature cognitive control areas, such as the PFC (Somerville & Casey, 2010; Steinberg, 2008). Few studies have examined how longitudinal changes in impulsive behavior are associated with changes in the function and structure of these brain areas. We showed that (longitudinal changes in) the activity of the DLPFC and VS was associated with (changes in) TD, a component of impulsivity, in adolescents. Both increases and decreases of lateral PFC activity have been interpreted as reflecting increased maturity (Crone & Dahl, 2012). In this study, we observed longitudinal decreases in DLPFC activity, and longitudinal declines in DLPFC activity were correlated with increases in the ability to wait for a delayed reward. Thus, in the context of a TD task, decreases in DLPFC activity may confer more functional maturity. Moreover, we found that increased VS activity was associated with steep TD at both timepoints. Further, we also observed that increases in superior parietal cortex activity were associated with increases in the ability to wait for a delayed reward. This underscores the need to move beyond simple neurobiological models of adolescent impulsivity, by including multiple brain networks in these models (Casey, 2015).

Strengths and limitations

We are the first to examine how longitudinal changes in brain function and structure are related to changes in immediate reward preferences in a TD task with money and snack rewards in adolescents. This longitudinal design allowed us to examine the test-retest reliability of TD choices and of brain activity during these choices. These reliability statistics are useful for intervention studies, in which the effects of cognitive training (Bickel, Yi, Landes, Hill, & Baxter, 2011) or other manipulations (e.g., episodic prospection) (Benoit, Gilbert, & Burgess, 2011; Peters & Buechel, 2010) on TD and its neural correlates are investigated. Additionally, our study of normative brain development and its associations with impulsive behavior in typically developing adolescents provides an important template for studies focusing on adolescents with disorders characterized by impulse control problems, such as ADHD, substance abuse and conduct disorder.
Several limitations of the present study deserve to be mentioned as well. Our sample size was relatively modest, particularly for the associations between brain activity and TD choices, as we contrasted delayed and immediate reward choices and several participants almost exclusively preferred one of these two options. Future studies could reduce this issue by using adaptive task designs in which the amount of the immediate reward is adjusted based on participants’ choices (Christakou et al., 2011), or by administering participant-specific choice sets based on a pre-test outside of the scanner (van den Bos et al., 2015). In this study, we focused on adolescents, as adolescence is considered a developmental period characterized by both heightened impulsivity and rapid brain development (Somerville & Casey, 2010). Nonetheless, impulsivity and brain development are certainly not limited to adolescence, and other researchers should be encouraged to include individuals from a wider age range, such as children and young adults, in their studies. Future researchers should also investigate longitudinal changes in functional and structural connectivity of different networks implicated in TD choices (see Achterberg et al., 2016; van den Bos et al., 2015), and extend our research to adolescents with impulse control problems (i.e., ADHD, substance abuse, conduct disorder).

Conclusions

TD choices are highly stable across a 1-year interval in adolescents, while brain activity during these choices shows poor test-retest reliability. During choices in a TD task, adolescents show longitudinal declines in DLPFC and mOFC activity, and decreases in DLPFC activity are associated with increases in the ability to wait for a delayed reward. Longitudinal increases in superior parietal cortex activity were further associated with increases in the ability to wait for a delayed reward. These findings could serve as a template for adolescents with impulse control disorders, and could aid the development of interventions designed to reduce impulsivity in adolescents.
Supplement Chapter 4

Computation of area under the curve

As a first step, we determined the subjective value (SV) of the delayed reward for each delay that was used in the TD task for each participant (and separately for the money and snack choices). As an index of participants’ SV, we computed the proportion of delayed reward choices at each delay separately (cf. Boettiger et al., 2007; Eppinger, Nystrom, & Cohen, 2012; Wittmann, Lovero, Lane, & Paulus, 2010). In order to obtain an SV that is on a meaningful scale, one could multiply this proportion by the value of the delayed reward (i.e., 10). An individual who has chosen the delayed reward exclusively at a certain delay, would then receive an SV of 10, while someone who has chosen the immediate reward exclusively, would receive an SV of 0. However, these SV values are not theoretically plausible, since an SV of 10 would indicate that someone is indifferent regarding a choice between receiving 10 euros now or 10 euros after a delay, while an SV of 0 would suggest that a reward can lose its value completely when a delay precedes its delivery. Therefore, we multiplied the proportion of delayed reward choices by the range of theoretically plausible SV values instead. We defined the highest plausible SV as the mean of the delayed reward and the highest immediate reward (10+8/2 = 9 in this study), and we defined the lowest plausible SV as the mean of 0 and the lowest immediate reward (0+2/2 = 1 in this study). Further, in order to ensure that participants who have exclusively chosen the immediate reward receive a SV equal to the lowest plausible SV (instead of 0), this lowest plausible SV was added to the number resulting from multiplying the proportion of delayed reward choices by the range of plausible SVs.

In sum, we used the following equation to compute participants’ SV for each delay:

\[
\text{SV} = \frac{\text{the number of delayed reward choices at the delay}}{\text{the total number of choices at the delay}} \times \text{the range of plausible SVs} (8) + \text{the lowest plausible SV} (1)
\]

As a second step, we normalized these SV’s by dividing them by the magnitude of the delayed reward (i.e., 10), and we normalized the delays by dividing them by the magnitude of largest delay (180 days). Subsequently, we computed the area under the curve (AUC) using the equation described by Myerson and colleagues (2001). AUC ranged between 0 and 1, where smaller values indicate steeper discounting of delayed rewards.

Snack rewards in the TD task

The list of snack rewards from which participants selected their favorite is presented in Table S4.1.
Table S4.1
List of snack rewards from which participants selected their favorite

<table>
<thead>
<tr>
<th>Chocolate</th>
<th>Sweets</th>
<th>Salty</th>
<th>Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mars (mini)</td>
<td>Sweet liquorice</td>
<td>Salty liquorice</td>
<td>Cucumber slices</td>
</tr>
<tr>
<td>Bounty (mini)</td>
<td>Haribo peaches *</td>
<td>Pringles (Paprika flavor) *</td>
<td>Baby carrots</td>
</tr>
<tr>
<td>Twix (mini)</td>
<td>Fruittella®</td>
<td>Cheese cubes</td>
<td></td>
</tr>
<tr>
<td>Milky Way (mini)</td>
<td>Winegums</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snickers (mini)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

At the first timepoint, the most frequently selected type of snack was Pringles (22.4% of participants), followed by Haribo peaches (17.2%), Twix (12.1%), winegums (10.3%), Snickers (8.6%), Mars (6.9%), Bounty (5.2%), Fruittella/cheese cubes/milky way/cucumber slices (all 3.4%), and sweet and salty liquorice (both 1.7%).

At the second timepoint, the most frequently selected type of snack was Twix (16.7% of participants), followed by Snickers (14.3%), Haribo peaches (11.9%), Pringles/Bounty/winegums (all 9.5%), Mars (7.1%), cheese cubes/milky way/salty liquorice (all 4.8%) and Fruittella/cucumber slices/sweet liquorice (all 2.4%).

Half of the participants selected the same type of snack as their favorite at both timepoints.

**TD task control variables**

We assessed several factors that might influence participants’ choices in the TD task. *Reward valuation* was assessed by asking participants to rate on a 10-point scale how much they would enjoy receiving each reward amount (2, 4, 6, 8, 10 euros and snacks). The mean rating for the money rewards and for the snack rewards was used as an index of reward valuation. In addition, we asked participants how much they were willing to pay (in euros) for each snack reward that was used in the task. At the second timepoint, we additionally asked participants how much money (in euros) they earned (or received from their parents) per month.

Directly before we administered the TD task at both timepoints, we asked participants to rate on a 10-point scale how hungry they felt, and the time (in hours and minutes) since their last meal. Further, we weighed and measured each participant at both timepoints to compute their *Body Mass Index* (BMI: weight in kg/height in cm²).

At T1, none of these variables were significantly correlated with participants’ AUC for money or snack choices (all p’s > .10). At T2, participants who reported to be more hungry, showed steeper discounting of snack rewards (*rho* = -.33, *p* = .033), but not of monetary rewards (*rho* = -.29, *p* = .061). Participants’ reward valuation, the amount of
money they earned or received per month, their BMI and the time since their last meal were not significantly correlated with their AUC for money or snack choices at T2 (all $p's > .18$).

**Table S4.2**

MNI coordinates of peak voxels of regions of interest that were used to examine intravoxel reliability

<table>
<thead>
<tr>
<th>Region</th>
<th>MNI coordinates</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angular gyrus</td>
<td>48 -58 42</td>
<td></td>
</tr>
<tr>
<td>Medial orbitofrontal cortex</td>
<td>10 66 -6</td>
<td></td>
</tr>
<tr>
<td>Precuneus</td>
<td>-10 -20 60</td>
<td></td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>-36 -68 40</td>
<td></td>
</tr>
<tr>
<td>Middle frontal gyrus (right)</td>
<td>26 18 56</td>
<td></td>
</tr>
<tr>
<td>Middle frontal gyrus (left)</td>
<td>-40 50 4</td>
<td></td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>-16 32 38</td>
<td></td>
</tr>
</tbody>
</table>

**Table S4.3**

MNI coordinates of regions of interest used to examine individual differences

<table>
<thead>
<tr>
<th>Region</th>
<th>MNI coordinates (X Y Z)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>VS (left)</td>
<td>-9 6 -6</td>
<td>Ripke et al. (2012)</td>
</tr>
<tr>
<td>VS (right)</td>
<td>9 6 -3</td>
<td>Ripke et al. (2012)</td>
</tr>
<tr>
<td>vmPFC (left)</td>
<td>-10 26 -12</td>
<td>van Duijvenvoorde et al. (2015)</td>
</tr>
<tr>
<td>vmPFC (right)</td>
<td>14 38 -16</td>
<td>van Duijvenvoorde et al. (2015)</td>
</tr>
<tr>
<td>DLPFC</td>
<td>18 26 52</td>
<td>van den Bos et al. (2015)</td>
</tr>
<tr>
<td>Superior parietal cortex</td>
<td>29 -54 59*</td>
<td>Stanger et al. (2013)</td>
</tr>
<tr>
<td>Insula</td>
<td>45 14 -11</td>
<td>Wilbertz et al. (2013)</td>
</tr>
<tr>
<td>Amygdala</td>
<td>27 -1 -20</td>
<td>Wilbertz et al. (2013)</td>
</tr>
</tbody>
</table>

**Note.** VS = ventral striatum, vmPFC = ventromedial prefrontal cortex, DLPFC = dorsolateral prefrontal cortex

* Converted into MNI from Talairach coordinates, using a Matlab script (tal2mni)
CHAPTER 5

SUBSTANCE USE AND DECISION-MAKING IN ADOLESCENT BEST FRIENDSHIP DYADS: THE ROLE OF POPULARITY

Published as:
Abstract

In adolescent best friendship dyads, we examined: 1) similarity in substance use and decision-making; 2) associations between participants’ decision-making and their own and best friend’s substance use, 3) the influence of relative popularity within the dyad on these associations. Participants (n = 172; 12-18 years) named their best friend, completed popularity ratings and a substance use questionnaire. Computer tasks were administered to assess risk-taking and immediate reward preferences. Reciprocated same-sex best friendship dyads (n = 49) were distinguished on their popularity, and we controlled for age differences between dyads in the analyses. Best friends were similar in substance use and risk-taking preferences. More popular friends’ risk-taking preferences were positively associated with alcohol use of less popular friends. These findings underscore best friendship similarity in risky behaviors, and the influence of popular friends.
Adolescents engage in heightened levels of risky behaviors, such as substance use, relative to children and adults (Steinberg, 2008). The peer group becomes highly important during adolescence (Steinberg & Morris, 2001), and adolescents prioritize being popular with their peers over many other goals in life (LaFontana & Cillessen, 2010). Therefore, it is not surprising that peers strongly influence adolescents’ risky behavior (Gardner & Steinberg, 2005).

Best friends are particularly potent sources of peer influence. Adolescent best friends are highly similar in their alcohol, tobacco and marijuana use (Burk, van der Vorst, Kerr, & Stattin, 2012; Kiuru, Burk, Laursen, Salmela-Aro, & Nurmi, 2010). This similarity is due to selection processes (choosing friends who are similar to oneself) and socialization processes (adopting the behaviors of one’s best friend over time) (Lubbers, 2007; Male, 2004).

Adolescents are not only strongly influenced by their best friends, but also by their peers who have a high social status. In a series of experiments using a chat room paradigm, it has been demonstrated that adolescents increased their willingness to drink alcohol when popular classmates displayed pro-alcohol norms, compared to when unpopular classmates displayed the same norms (Cohen & Prinstein, 2006; Teunissen et al., 2012). Interestingly, adolescents’ social status also determines the direction of influence within best friendship dyads. Laursen, Hafen, Kerr, and Stattin (2012) examined alcohol intoxication frequency in best friendship dyads, that were distinguished based on their acceptance by their peers. Laursen and colleagues (2012) found that in stable friendships, the more accepted friends’ intoxication frequency positively predicted increases in the intoxication frequency of the less accepted friends over time. In contrast, the less accepted friends’ intoxication frequency did not predict the intoxication frequency of the more accepted friends over time. Similarly, Tucker et al. (2014) reported that adolescents were more likely to adopt the marijuana use of their more popular friends as compared to their less popular friends.

Even though the literature on similarity and influence regarding substance use in best friendship dyads is substantial, very little is known about the potential role of underlying dispositions leading to this similarity in risky behavior. Prior research has shown that adolescents can be indirectly influenced by psychological characteristics and dispositions of their best friends (Giletta, Burk, Scholte, Engels, & Prinstein, 2013). These dispositions might exert their influence by acting as potential reinforcers of certain behaviors (e.g., friends with strong risk-taking preferences could reinforce risky behaviors, such as substance use), or by making certain norms in the peer group salient (e.g., risky behavior is cool) (Rambaran, Dijkstra, & Stark, 2013). Additionally, adolescents might select best friends who are similar in dispositions that are associated with risky behavior, and these similarities might predate the establishment of the friendship (Lubbers, 2007; Male, 2004).

Decision-making preferences could be dispositions that lead to best friendship similarity in substance use. Adolescents’ decision-making abilities are still developing, which is thought to contribute to their risky behavior, such as substance use (Boyer, 2006).
Therefore, it could be hypothesized that adolescent best friends are not only similar in their substance use behavior, but also in decision-making preferences that are contributing to this behavior. Further, adolescents’ decision-making might be associated with their own and their best friends’ substance use. One recent study provided support for this hypothesis, by showing that adolescents reported similar risk-taking preferences as their friends, and also adjusted their risk-taking in a simulated driving task to match the risk-taking preferences of their friends who were watching and commenting on participants’ driving performance (Centifanti, Modecki, MacLellan, & Gowling, 2016). We aimed to extend these findings by: 1) including other decision-making preferences that might also contribute to similarity and influence in substance use; 2) using experimental tasks to assess decision-making preferences; 3) exploring the role of popularity in peer influence on substance use.

Two types of decision-making preferences have been consistently linked to substance use in adolescents: risk-taking preferences and the preference for immediate rewards. Risk-taking preferences are assessed by administering gambling tasks, in which individuals make choices between risky and safe options. The risky options are usually associated with the possibility of obtaining a larger monetary reward than the safe options, but they are also associated with a higher probability of losing or not gaining money. Adolescents who display stronger risk-taking preferences in these gambling tasks relative to their peers, also report more alcohol and tobacco use (Lejuez et al., 2005; Xiao et al., 2009).

The preference for smaller, immediate rewards over larger, but delayed rewards is also associated with substance use (MacKillop et al., 2011). This preference is most often investigated by administering a temporal discounting (TD) task (see Scheres, de Water, & Mies, 2013 for a review), in which individuals are asked to choose between receiving a small monetary reward (e.g., €2) today, or receiving a larger monetary reward after a delay (e.g., €10 in 30 days). The magnitude of the immediate reward and the delay preceding the delayed reward are varied, to determine the extent to which the subjective value of the delayed reward decreases with increasing delay for each individual. Adolescents who show a stronger preference for immediate rewards in TD tasks relative to their peers, also report higher levels of alcohol and tobacco use (Field, Christiansen, Cole, & Goudie, 2007; Reynolds & Fields, 2012).

Even though risk-taking preferences and immediate reward preferences are both positively associated with substance use, they have been proposed to be distinct constructs that are not necessarily correlated (Romer, 2010). Indeed, risk-taking preferences and immediate reward preferences are not significantly correlated in adolescents and young adults (de Water, Cillessen, & Scheres, 2014; Loughran, Paternoster, & Weiss, 2012; Olson, Cooper, Collins, & Luciana, 2007; Scheres et al., 2006).

Distinct neural systems might underlie risk-taking preferences and immediate reward preferences. Dual-system models propose that adolescent risk-taking is caused by reduced connectivity between socio-emotional brain areas (e.g. the ventral striatum), and
cognitive control regions (e.g., the prefrontal cortex) (Crone & Dahl, 2012; Luciana, 2013). In line with these models, Steinberg and colleagues (2008) showed that the development of sensation-seeking (i.e., the willingness to take risks to attain highly stimulating experiences) mirrored the development of the socio-emotional neural system, while the development of self-control (conceptually similar to delayed reward preferences) mirrored the development of the cognitive control neural system.

Moreover, different components of impulsivity, TD and response inhibition, were found to be differentially associated with health-risk behaviors and criminal behaviors in adolescents (Nagin & Pogarsky, 2004). Together, these findings suggest that risk-taking preferences and immediate reward preferences should be treated as separate constructs that might be differentially associated with substance use in adolescents.

Thus, the first goal of the current study was to investigate whether adolescent best friends are not only similar in their substance use behavior, but also in their decision-making preferences associated with these behaviors, such as risk-taking and immediate reward preferences. In addition, we examined whether adolescents’ risk-taking and immediate reward preferences were associated with their own and their best friends’ substance use. To our knowledge, these questions have not yet been explored.

Moreover, the handful of studies that have been conducted on the role of social status in peer influence effects on substance use within adolescent best friendships (Laursen et al., 2012; Tucker et al., 2014), have used measures of popularity that might be more strongly related to peer acceptance. For instance, Laursen and colleagues (2012) asked participants to name peers with whom they spend time and hang out with, while Tucker et al. (2014) used the number of received friendship nominations as a proxy for popularity. While popularity and acceptance are correlated in adolescents, this correlation is only moderate (Mayeux, Sandstrom, & Cillessen, 2008), leading some researchers to argue that acceptance and popularity reflect different types of social status in adolescence (Cillessen & Rose, 2005).

Popular adolescents are dominant, influential and highly visible and central in the peer group. They not only engage in pro-social behaviors, but also display negative behaviors, such as heightened levels of relational aggression and substance use (Cillessen & Mayeux, 2004; Tucker et al., 2012). This mixed profile of behaviors is also reflected in the attitudes of peers towards popular adolescents; while popular adolescents are liked by their peers on the explicit level (i.e., based on peer nominations), they evoke avoidance reactions on the implicit level, as measured by an Approach-Avoidance task (Lansu, Cillessen, & Karremans, 2012). Given that popular adolescents are dominant and visible, and engage in heightened levels of substance use themselves, they could influence the substance use of their best friends even more than accepted adolescents.

Therefore, the main aim of the present study was threefold. We examined: 1) whether adolescent best friends were similar in their alcohol, tobacco and marijuana use, and in their decision-making, which included risk-taking and immediate reward preferences; 2) whether adolescents’ own decision-making was associated with their own substance use;
and 3) the associations between adolescents' own decision-making and their best friend's substance use, and whether the relative popularity of the friends affected these associations. Actor-Partner Interdependence Models (API; Kenny, Kashy, & Cook, 2006) were used to test these associations. These models control for the interdependence of the data within best friendship dyads, caused by the high degree of similarity between best friends. We controlled for age differences between the dyads in these analyses.

We predicted that adolescent best friends would be similar in their substance use and decision-making (Burk et al., 2012; Kiuru et al., 2010). We hypothesized that adolescents who showed stronger risk-taking preferences and a stronger immediate reward preference, would report enhanced substance use (Field et al., 2007; Lejuez et al., 2005; Reynolds & Fields, 2012; Xiao et al., 2009). We expected that stronger risk-taking preferences and a stronger preference for immediate rewards of the most popular friends would be associated with increased substance use of the least popular friends (Cohen & Prinstein, 2006; Laursen et al., 2012; Teunissen et al., 2012; Tucker et al., 2014).

Method

Participants

A total of 172 adolescents aged 12 to 18 years participated in the present study (48% female, $M_{age} = 15.22$, $SD = 1.51$). Most participants were Dutch (85.5%), with the remaining 14.5% from various ethnic backgrounds (e.g., Turkish, Moroccan, Surinamese, and Indonesian). Participants were drawn from eight classrooms of a high school in The Netherlands. Classrooms ranged in size from 20 to 29 students ($M = 23.88$, $SD = 3.04$).

Prior to the study, parents of the participants were sent an information letter describing the goals and procedures of the study. If they did not want their child to participate, they were asked to notify the experimenter before the start of the study. The parents of only one of the contacted participants denied participation of their child in the current study. Moreover, absenteeism on the days of testing was relatively low, in that on average 91.4% ($SD = 6.0%$; range = 80-100%) of the students in each class participated in the present study. All procedures were approved by the Internal Review Board at the authors' research institute.

Measures

Population. Participants rated the popularity of each of their classmates on a 7-point scale (ranging from 1 = not popular at all to 7 = extremely popular). The mean of all classmates’ ratings for each participant was used as a measure of popularity for each adolescent. We also asked participants to nominate classmates they thought were most popular and least popular. The popularity score computed from these peer nominations (number of most popular nominations received minus least popular nominations received, both standardized within the classroom) correlated highly with the popularity score derived...
from the popularity ratings ($\rho = .90$). Given that ratings might be more sensitive to subtle inter-individual differences, we used the popularity ratings to distinguish the dyad members on their popularity.\(^1\)

**Best friendships.** In order to determine best friendship dyads, participants were asked to name their best friend in their classroom, and they were allowed to name only one friend. Based on this information, 54 unique reciprocated best friendship dyads (i.e., two adolescents who have both named each other as their best friend) were identified. These dyads consisted of 49 same-sex dyads, and 5 mixed-sex dyads. To keep the sample as homogeneous as possible, only the same-sex dyads were included in the dyadic analyses ($n = 98$ participants in 49 dyads; 50 girls and 48 boys). Note however, that by including all 54 dyads, the results of the dyadic analyses were unchanged. Dyads were distinguished based on their popularity, with each best friendship dyad consisting of a more popular and a less popular peer. For one dyad, the rating-based popularity score was identical for both members, but they could be distinguished based on the peer nominations, since one dyad member did have a slightly higher popularity score derived from the peer nominations. For the other participants, the difference in popularity between the dyad members ranged from 0.04 to 2.44 ($M = 0.57, SD = 0.53$).

\(^1\) Note that when the popularity score derived from the peer nominations was used to distinguish the dyad members on their popularity, 6 dyads (12.2%) were distinguished differently compared to the ratings-based popularity score. However, when we distinguished the dyads based on the popularity score derived from the peer nominations, and repeated the APIM analyses, the findings were similar to the reported findings.

**Substance use.** The Youth Risk Behavior Survey (YRBS; Brener et al., 2002) was used to measure substance use. The YRBS has high test-retest reliability in adolescents (Brener et al., 2002). Alcohol use ($\alpha = .87$) was assessed by two items: one item on the frequency of recent (past 30 days) alcohol use, and one item on the frequency of binge drinking (5 or more alcoholic drinks within a couple of hours) in the past 30 days. Tobacco use ($\alpha = .87$) was indexed by four items: one item on the number of days tobacco was used in the past 30 days, one item on the number of cigarettes smoked per day in the past 30 days, one item on whether participants had ever smoked cigarettes daily, and one item on the frequency of smoking on school property in the past 30 days. Marijuana use was measured by one item on the number of times marijuana was used in the past 30 days.

Skewness and kurtosis statistics indicated that alcohol use was positively skewed (Skewness = 1.13, S.E. = .24; Kurtosis = .33, S.E. = .48). Applying a square root transformation to the alcohol use data reduced the skewness (.33, S.E. = .24), but not the kurtosis (-1.32, S.E. = .48). Further, given that results were the same when the transformed alcohol use scores were used compared to the raw scores, we chose to report the results with the untransformed alcohol use scores in the present paper. Tobacco use (Skewness = 2.25, S.E. = .24; Kurtosis = 3.56, S.E. = .48) and marijuana use (Skewness = 3.16, S.E. = .24; Kurtosis...
were strongly positively skewed. Even after applying a square root transformation, the skewness and kurtosis remained high for tobacco use (Skewness = 1.60, S.E. = .24; Kurtosis = 1.35, S.E. = .48) and marijuana use (Skewness = 2.21, S.E. = .24; Kurtosis = 3.67, S.E. = .48). Therefore, we used dichotomous measures of tobacco and marijuana use in the analyses (0 = no past month use; 1 = past month use).

**Cake Gambling Task.** Risk-taking preferences were assessed with an adapted version of the Cake Gambling (CG) Task (de Water et al., 2014), in which participants made repeated choices between a high-risk option with a 33.3% probability of obtaining a relatively large monetary reward, and a low-risk option with a 66.7% probability of obtaining a smaller monetary reward. The trial procedure of the CG task is illustrated in Figure 5.1A. Participants viewed a cake consisting of six wedges, which were either pink or brown in a 4:2 ratio (the majority color was counterbalanced across trials). Underneath the cake, a pink square and a brown square were presented on the left and right sides (counterbalanced across trials), each containing a stack of 50 cent coins to indicate the reward associated with each color. Participants were told to choose one of the two colors by pressing the corresponding computer key, after which the computer would randomly select 1 of the 6 wedges of the cake. If the color of the selected wedge matched the color chosen by the participant, the reward associated with that color would be gained, if not, no reward would be gained. Thus, choosing the majority color is considered a low-risk choice, while choosing the minority color is considered a high-risk choice. Gain feedback was presented by showing the stack of coins, while no gain feedback was depicted by this stack of coins with a cross through them.

The rewards associated with the high-risk and low-risk choices were varied over trials (4 reward magnitudes: €1-€4 for the low-risk options, and €2-€8 for the high-risk options). The mean percentage of high-risk choices across rewards was taken as the measure of risk-taking preference. Participants first performed 8 practice trials of the task, followed by 72 experimental trials (18 repetitions of each reward magnitude), with a total duration of approximately 7 minutes. The trials were presented in a random order across participants.

Risk-taking preferences were internally consistent across the four reward types used in the CG task (Cronbach’s α = .93). Consistent with prior research (van Leijenhorst et al., 2008, 2010), a repeated measures ANOVA revealed that participants made more high-risk decisions as the reward associated with the high-risk option increased ($F(3, 169) = 13.49, p < .001, \eta^2_p = .19$). The CG task was shown to be externally valid, in that individuals who made more high-risk decisions in this task, also reported greater sensation-seeking in daily life (van Leijenhorst et al, 2008).

**Temporal Discounting Task.** In order to assess the preference for immediate rewards, a temporal discounting (TD) task was administered (see Figure 5.1B). In each trial of this task (see de Water et al., 2014 for a detailed description), participants were required to choose between an immediate monetary reward they would receive today, or a larger reward they would receive after a delay. Five delays were used: 2, 14, 30, 180, and 365 days. The delayed reward was always €10. The magnitude of the immediate reward was
always smaller than the delayed reward, and was adjusted based on participants’ choices (Du, Green, & Myerson, 2002). The adjustments of the immediate reward magnitude continued until participants had made six choices at a delay. After these six choices, a new delay was introduced, and participants were again presented with six choices at this delay. The separate delays were presented in a random order across participants. The subjective value of the delayed reward at each delay was defined as the magnitude of the immediate reward on a hypothetical seventh trial (Du et al., 2002). These subjective values were subsequently used to calculate the main outcome measure: area under the curve (AUC), using a procedure described by Myerson, Green, and Warusawitharana (2001). AUC ranges from 0 (in case the immediate reward is always selected) to 1 (in case the delayed reward is always selected). Thus, smaller values indicate a stronger preference for immediate rewards, while larger values indicate a stronger preference for delayed rewards. A total of 30 trials were administered. Six practice trials were administered, at a delay that was not used in the actual task (1 day). The TD task had a total duration of approximately 5 minutes.

Participants’ subjective values of the delayed rewards were internally consistent across the five delays (Cronbach’s $\alpha = .87$). A repeated measures ANOVA further revealed that participants showed TD: the subjective value of the delayed reward decreased significantly as the delay increased ($F(4, 168) = 78.59, p < .001, \eta^2_p = .65$). TD tasks have excellent test-retest reliability in adolescents (r’s up to .76 with a 2-year interval; Anokhin, Golosheykin, & Mulligan, 2015). The TD task has high external validity as well, in that adolescents with impulse-control problems—including substance abuse, ADHD and conduct disorder—show increased preferences for immediate rewards in the TD task, compared to typically developing controls (Field et al., 2007; Patros et al., 2016; White et al., 2014).

**Procedure**

Participants were tested in their school classroom, one class at a time, using computers (notebooks). Partitions were placed at each side of the screen, to make sure that participants could not view each other’s screens. A teacher was present, and a team of research assistants was available to answer questions of participants. At the beginning of the experiment, participants were ensured that all of their answers would remain confidential, in that their answers would not be disclosed to their teachers, parents or classmates. Participants first completed a sociometric questionnaire (which included the best friendship question) and the popularity ratings, followed by the YRBS, the CG task, and the TD task. The experiment had a total duration of 50 minutes (one classroom period).

To increase motivation and ecological validity, participants were told that at the end of the CG and TD tasks, one of their outcomes of each task would be randomly selected by the computer, and that they would receive the combined outcome. In reality, to keep differences in earnings between participants minimal, their earnings were based on a random computer selection from a fixed and narrow range of rewards (€6-€9).
Figure 5.1. (A) Trial procedure of the Cake Gambling task; (B) Trial procedure of the Temporal Discounting task.

Note. The time indicated underneath the decision phase of both tasks is the maximum amount of time allowed to make a decision. When participants indicated their preference within this time period, the trial continued immediately after they pressed the button corresponding to their preference.

Analysis Plan

Mean differences between friends’ popularity, substance use, risk-taking preference and immediate reward preference were tested using paired-samples t-tests. Similarity between the best friends in decision-making and substance use was examined by computing Pearson correlations.

The primary analyses include a series of Actor-Partner Interdependence Models (APIM; Kenny et al., 2006) with distinguishable dyads, estimated within a structural equation modeling framework, using Mplus version 7 (Muthén & Muthén, 1998-2012). Dyads were distinguished based on their popularity, with each dyad consisting of a more popular and a
less popular friend. The primary advantage of APIMs over conventional statistical methods (e.g., regression or ANOVA), is that the APIMs account for interdependence between dyad member’s reports. This is important for this study because best friends are similar, particularly on substance use (Burk et al., 2012). Figure 5.2 presents a conceptual APIM. **Actor effects** are represented by the horizontal lines, and describe associations between adolescents’ decision-making and their own substance use. **Partner effects** are represented by the diagonal lines and describe associations between adolescent’s decision-making and their best friend’s substance use. These effects are estimated in a single model, such that the partner effects are controlled for the actor effects and vice versa. The correlation between predictors (friends’ decision-making preferences), and the correlation between outcomes (friends’ substance use) are estimated (but not depicted in the figures) to account for similarities between friends. All measures were centered by subtracting the grand mean of all participants included in the APIM analyses, as recommended by Kenny et al. (2006). Saturated models were separately estimated for alcohol, tobacco, and marijuana use. Given that we used dichotomous variables for tobacco and marijuana use, the actor and partner effects for these variables were denoted by odds ratios. Further, in order to ensure adequate statistical power, separate models were estimated for risk-taking preferences, and immediate reward preferences. However, note that the results were the same when both predictors were included in a single model. The mean age of the dyads was included as predictor in all APIMs, to control for age differences between the dyads.

Chi square difference tests were used to test whether actor or partner effects differed for the more and less popular dyad members, by individually constraining each effect to be equal across the dyad members. Significant differences between dyad members are demonstrated when the fit of the model significantly decreases after a constraint is included, as indicated by a $\chi^2$-statistic $\geq 3.84$ and associated $p$-value $<.05$.

There were no significant differences between participants who were included in the dyadic analyses and those who could not be matched up in reciprocated dyads, in terms of age, popularity, risk-taking preference on the gambling task, immediate reward preference on the TD task, and substance use (all $p$’s $\geq .079$).

**Results**

**Descriptive Statistics**

**Frequency of substance use.** Substance use frequency was explored for the adolescents who were included in the dyadic analyses ($n = 98$). Past month alcohol use was reported by 58.2% of adolescents, and 35.7% engaged in binge drinking (i.e., >5 alcoholic beverages within a couple of hours) in the past month. Regarding tobacco use, 18.4% smoked cigarettes during the past month, and 10.2% indicated that they smoked cigarettes daily. Past month marijuana use was reported by 10.2% of adolescents.
**Dyadic differences.** The popularity ratings of the best friends were highly correlated ($\rho = .84$). Nonetheless, the more popular dyad members were significantly more popular than the less popular dyad members (see Table 5.1). There was a trend towards more popular friends showing a stronger risk-taking preference on the gambling task ($p = .06$) than the less popular friends. The dyad members did not differ in their age, substance use or preference for immediate rewards.

<table>
<thead>
<tr>
<th>Table 5.1</th>
<th>Descriptive Statistics of the Participants Included in the APIM analyses (n = 98)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>More Popular Friend</strong></td>
</tr>
<tr>
<td></td>
<td>Range</td>
</tr>
<tr>
<td>Popularity rating</td>
<td>1.65 - 6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>12.49-18.56</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0 - 5</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>0 - 1</td>
</tr>
<tr>
<td>Marijuana use</td>
<td>0 - 1</td>
</tr>
<tr>
<td>Risk-taking preference</td>
<td>1.39 - 100</td>
</tr>
<tr>
<td>Delayed reward preference</td>
<td>.01-.99</td>
</tr>
</tbody>
</table>

**Correlations.** In Table 5.2, the correlations between the study variables are shown. Popularity was positively correlated with alcohol, tobacco and marijuana use. Age was positively correlated with alcohol use, and age was negatively correlated with the preference for immediate rewards at a trend level ($p = .054$).

**Gender differences.** Boys reported greater alcohol use than girls ($t = 3.68, p < .001$). There were no significant gender differences in tobacco use, marijuana use, risk-taking preferences or immediate reward preferences (all $p$'s > .16).

<table>
<thead>
<tr>
<th>Table 5.2</th>
<th>Correlations Between the Study Variables for the Participants Included in the APIM analyses (n = 98)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>1. Popularity rating</td>
<td>-</td>
</tr>
<tr>
<td>2. Age (years)</td>
<td>.11</td>
</tr>
<tr>
<td>3. Risk-taking preference</td>
<td>.04</td>
</tr>
<tr>
<td>4. Delayed reward preference</td>
<td>.03</td>
</tr>
<tr>
<td>5. Alcohol use</td>
<td>.33***</td>
</tr>
<tr>
<td>6. Tobacco use</td>
<td>.36***</td>
</tr>
<tr>
<td>7. Marijuana use</td>
<td>.27**</td>
</tr>
</tbody>
</table>

*Note. Tobacco and marijuana use were coded as 0 = no use, 1 = use.*

† $p < .10$ * $p < .05$ ** $p < .01$ *** $p < .001$
Similarity in Substance Use and Decision-Making

Best friends were similar in their alcohol use ($r = .52, p < .001$), and tobacco use ($r = .37, p = .01$). In addition, best friends were similar in their risk-taking preferences ($r = .31, p = .028$), but not in their preference for immediate rewards ($r = .18, p = .227$) or marijuana use ($r = .12, p = .427$).

APIM Analyses

The results of the APIM analyses are presented in Figure 5.2 for alcohol use, and Figure 5.3 for tobacco and marijuana use. The APIMs were estimated to examine: 1) The association between adolescents own decision-making and their own substance use (actor effects); and 2) the association between adolescents own decision-making and their best friend’s substance use (partner effects).

![Figure 5.2. The Actor-Partner Interdependence Models for alcohol use.](image)

Note. Standardized actor and partner effects are reported. Mean age of the dyads was included as predictor (not shown here) to control for age differences between dyads.

* $p < .05$  ** $p < .01$  *** $p < .001$
Actor effects. For the more popular friends, stronger risk-taking preferences were associated with more alcohol use ($p = .025$). For the less popular friends, stronger risk-taking preferences were also associated with a greater likelihood of tobacco use ($p < .05$), but not with alcohol use ($p = .791$). There were no other significant actor effects for tobacco or marijuana use (all $p$'s >.10).

Partner effects. Stronger risk-taking preferences of the more popular friends were associated with greater alcohol use of the less popular friends ($p = .002$). Further, this partner effect was significantly stronger for more popular friends relative to less popular friends ($\chi^2(1) = 8.50, p = .003$). There were no partner effects for tobacco and marijuana use (all $p$'s >.10).

Controlling for popularity We performed additional analyses that included the average popularity scores of both dyad members to account for differences in popularity between dyads, and the absolute difference in popularity scores between dyad members to account for differences in popularity within dyads. When these two additional predictors were
included, the observed actor and partner effects for alcohol use were similar. Specifically, stronger risk-taking preferences of the more popular friends remained associated with higher levels of their own alcohol use, albeit at a trend level ($\beta = .25$, $p = .059$), and with higher levels of their less popular friends’ alcohol use ($\beta = .35$, $p = .003$). This means that the observed actor and partner effects do not differ for dyads in which the difference in popularity between the dyad members is large, compared to dyads in which the difference in popularity is small.

Discussion

The main aim of the current study was threefold. APIM analyses were performed to examine: 1) whether adolescent best friendship dyads are similar in their substance use and decision-making, which included risk-taking and immediate reward preferences; 2) whether adolescents’ decision-making is associated with their own substance use (actor effects); and 3) whether adolescents’ decision-making is associated with their best friend’s substance use (partner effects). Further, we investigated whether the relative popularity of the friends influenced these associations.

Similarity in Substance Use and Decision-Making

Consistent with our predictions and with previous findings (Burk et al., 2012; Kiuru et al., 2010), best friends were similar in their alcohol and tobacco use. In addition, best friends were similar in their risk-taking preferences on a gambling task. This finding is in line with the findings of Centifanti and colleagues (2016), who showed that adolescent friends are similar in their self-reported risk-taking preferences. To our knowledge, we are the first to demonstrate that adolescent best friends are not only similar in their substance use behavior, but also in an experimentally measured (i.e., by a gambling task) decision-making preference that is thought to underpin this behavior.

Two processes have been proposed to account for this similarity within best friendship dyads: selection and socialization (Lubbers, 2007; Male, 2004). Selection takes place prior to the establishment of the friendship, and refers to choosing a friend based on similarities in certain attributes, such as risk-taking preferences (Lubbers, 2007; Male, 2004). Socialization occurs when the friendship has already been established, and refers to friends becoming more similar to each other over time, because they influence each other. For instance, adolescents with relatively strong risk-taking preferences could encourage the alcohol and tobacco use of their best friend, which would make the friends more similar in their substance use over time (cf. Centifanti et al., 2016).

We found that adolescent best friends were similar in their risk-taking preference, but not in their immediate reward preference. This supports the notion that risk-taking and the preference for immediate rewards are distinct constructs (de Water, et al. 2014; Loughran et al., 2012; Olson et al., 2007; Scheres et al., 2006), which may be differentially
related to health-risk behaviors (Pogin & Nagarsky, 2004), and which might have distinct underlying neural systems (Steinberg, 2008). The preference for immediate rewards is highly stable, which has led some researchers to argue that it is akin to a personality trait (Odum, 2011). Therefore, an individual’s preference for immediate rewards may be less likely to be impacted by socialization processes compared to an individual’s risk-taking preference, which could explain the lack of best friendship similarity in immediate reward preferences.

**Decision-Making and Own Substance Use (Actor Effects)**

In line with prior studies (Lejuez et al., 2005; Xiao et al., 2009), we found that adolescents who showed stronger risk-taking preferences on the gambling task also reported higher levels of alcohol use, and a greater likelihood of past month tobacco use. This association was only significant for the more popular friends regarding alcohol use, and for the less popular friends regarding tobacco use.

Contrary to the risk-taking preference findings and previous research (Field et al., 2007; Reynolds & Fields, 2012), the preference for immediate rewards on the TD task was not associated with substance use in the current study. Nevertheless, this finding does fit with a study by Pogin and Nagarsky (2004), who reported that different components of impulsivity are differentially associated with health-risk behaviors. It might be argued that TD tasks are particularly suited for distinguishing individuals at extreme ends of the impulsivity spectrum: those who are highly impulsive from those with excellent self-control. Indeed, Field et al. (2007) found that adolescents who consumed 23 alcoholic drinks per week on average, showed a stronger preference for immediate rewards than adolescents who consumed 3 alcoholic drinks per week on average. Similarly, Reynolds and colleagues (2012) observed that adolescents who smoked at least one cigarette a day during the last 3 months, showed a stronger preference for immediate rewards relative to adolescents who had never smoked. The levels of substance use in the present study might not have been extreme enough to find an association between TD and substance use. For instance, only 10% of the participants in our study reported to have smoked cigarettes daily.

**Decision-Making and Best Friend’s Substance Use (Partner Effects)**

In keeping with our hypotheses, we found that the most popular friends’ risk-taking preferences were positively associated with the alcohol use of their less popular friend. The risk-taking and immediate reward preferences of the least popular friends were not associated with the alcohol use of their more popular friends.

The finding that the relative popularity of best friends influences the association between adolescents’ own risk-taking preferences and their best friends’ alcohol use, is consistent with chat room studies which demonstrated that popular adolescents exert a greater influence on the risky choices of their peers than unpopular adolescents (Cohen & Prinstein, 2006; Teunissen et al., 2012). This finding is also consistent with the results of Laursen et al. (2012), who showed that the intoxication frequency of the more accepted
friend within an adolescent best friendship dyad positively predicted the intoxication frequency of the less accepted friend, while the reverse association was not significant.

There are several potential explanations for the positive association between the risk-taking preferences of the more popular friends and the alcohol use of the less popular friends. First, the more popular friends might actively influence their less popular friends (cf. Centifanti et al., 2016). One form of active peer influence is deviancy training (Dishion, Capaldi, Spracklen, & Li, 1995), in which friends influence each other by positively reinforcing (either verbally or non-verbally) each other’s anti-social behavior, including substance use. Additionally, the more popular friends might bring their less popular friends into environments where there are opportunities to engage in alcohol use, such as parties. Since the more popular friends also showed a stronger risk-taking preference than their less popular friends (at a trend level) in the present study, they might influence the behavior of their best friend passively as well. According to social learning theory (Bandura, 1977), people learn by imitating, or modeling, the behavior of others. It could be that the less popular friends in our study copied the alcohol use of their more popular friends, who served as potent models of this risky behavior.

Contrary to the findings for alcohol use, there were no partner effects for tobacco and marijuana use. In other words, the decision-making of the most popular friends was not associated with the tobacco and marijuana use of the least popular friends. Different motivations for using each substance might contribute to these discrepant findings across substances. Social motivations (e.g., making parties more enjoyable) are the most important reasons for adolescents to engage in alcohol use (Kuntsche, Knibbe, Gmel, & Engels, 2005), while enhanced tobacco use is often indicative of the addictive nature of cigarettes (Kandel, Chen, Warner, Kessler, & Grant, 1997), and experimentation is the primary motive to engage in marijuana use (Lee, Neighbors, & Woods, 2007). The fact that social motivations are linked so strongly to alcohol use, might explain why partner effects were only significant for alcohol use in the present investigation. Alternatively, the lack of partner effects for tobacco and marijuana use could be due to the limited variance in these variables, which might have made it difficult to find an effect. Indeed, Tucker et al. (2014) did find that adolescents were more likely to adopt the marijuana use of their friends, but in their sample past month marijuana use was markedly higher (up to 29.9% of adolescents) compared to our sample (10.2% of adolescents).

Finally, partner effects were only observed for risk-taking preferences, and not for immediate reward preferences. This is consistent with the notion that risk-taking and the preference for immediate rewards are distinct constructs (de Water, et al. 2014; Loughran et al., 2012; Olson et al., 2007; Scheres et al., 2006), which may be differentially related to health-risk behaviors (Pogin & Nagarsky, 2004), and which might have distinct underlying neural systems (Steinberg, 2008). In the present study, only risk-taking preferences were associated with substance use, which may reflect the fact that TD tasks are particularly sensitive to extreme levels of impulsivity, and the substance use in our study was relatively moderate.
Strengths and Limitations

To the best of our knowledge, our study is the first to combine experimental decision-making tasks with measures of popularity and best friendship derived from sociometric questionnaires. By including these experimental tasks, we were able to provide more detailed insights into similarities and influence regarding substance use within best friendship dyads. Furthermore, the use of APIMs allowed us to study how the decision-making of adolescents was related to the substance use of their best friend, while controlling for similarity in both decision-making and substance use. Our finding that the risky decision-making of the more popular friends was associated with the substance use of the less popular friends has important implications for substance abuse prevention and interventions. Risky decision-making can be reduced in adolescents by cognitive interventions (Reyna, Weldon, & McCormick, 2015), and these interventions could be focused particularly on more popular adolescents.

Nonetheless, several limitations of the current study need to be mentioned. The number of dyads in the present study (n = 49) was relatively modest. This number is larger than the 36 dyads needed to test for dyadic similarity with a power > 0.80 (Kenny, Kashy, & Bolger, 1998). Nevertheless, the relatively modest number of dyads limits the generalizability of our findings. Future studies need to replicate our findings in larger samples, which would also allow for the examination of additional moderators, such as gender effects. Due to the cross-sectional design of our study, the direction of the associations between the decision-making of the most popular friend and the alcohol use of the least popular friend could not be determined. Future studies should examine these associations using a longitudinal design, in order to determine whether increases in the most popular friends’ risk-taking preferences over time are also associated with increases in the least popular friends’ alcohol use. Additionally, longitudinal designs would enable researchers to test whether the associations between decision-making and alcohol use are bi-directional, since alcohol use might also affect decision-making. Further, our proposed explanations for the observed partner effects (e.g., active peer influence, modeling) need to be tested in observational or experimental studies. Additionally, we did not assess the duration and quality of the friendships, which could have influenced the strength of the associations. Given that friends in reciprocated friendships are more similar than friends in nonreciprocated friendships (Fujimoto & Valente, 2012; Tucker et al., 2014), it might be argued that friends who report a higher friendship quality or duration are also more similar and influence each other more strongly. This interesting possibility needs to be addressed in future investigations.

Finally, future studies should extend our findings by using different decision-making tasks (e.g., a simulated driving task or a TD task in which all rewards and delays are experienced), to better understand what these tasks are tapping.
Conclusions

We found that adolescent best friends are similar in their alcohol use, tobacco use, and in their risk-taking preferences on a gambling task. The risk-taking preferences of the most popular friends were associated with higher levels of alcohol use of the least popular friends. These findings indicate that adolescent best friends are similar in their substance use behavior and their risky decision-making, and underscore the influence popular adolescents have on the substance use of their peers, including their best friends. These findings may have practical implications as well. Interventions aimed at preventing alcohol abuse in adolescents might benefit from focusing specifically on decreasing the risky decision-making of the more popular friends, or on increasing the resistance to peer influence of the less popular friends. For instance, cognitive training programs have been shown to reduce risky decision-making in adolescents (Reyna et al., 2015). These programs might be administered in combination with resistance to peer influence training, in order to evaluate whether they reduce risky decision-making and the associated substance use in adolescents.
CHAPTER 6

NEURAL RESPONSES TO SOCIAL EXCLUSION IN ADOLESCENTS:
EFFECTS OF PEER STATUS

Submitted as:
de Water, E., Mies, G.W., Ma. I., Mennes, M., Cillessen, A.H.N, & Scheres, A.
Neural Responses to Social Exclusion in Adolescents: Effects of Peer Status
Abstract

We examined whether adolescents’ neural responses to social exclusion and inclusion are influenced by their own popularity and acceptance and by the popularity of their excluders and includers. Accepted adolescents are highly prosocial. In contrast, popular adolescents, who are central and influential, show prosocial as well as antisocial behaviors, such as peer exclusion. Fifty-two 12-to-16 year-old adolescents underwent an fMRI scan while playing the ball-tossing game Cyberball in which they received or did not receive the ball from other virtual players. The other virtual players were described as either highly popular or average in popularity. Participants’ own popularity and acceptance were assessed with peer nominations at school (n = 31). Participants’ acceptance was positively correlated with activity of the dorsal anterior cingulate cortex (ACC) during exclusion. Participants’ popularity was positively associated with ventral striatum and medial prefrontal cortex activity during exclusion, but only when the excluders were popular virtual players. Participants showed increased rostral ACC activation to inclusion by players who were average in popularity. These findings indicate that peer status plays an important role in adolescents’ neural processing of social exclusion and inclusion. Moreover, these findings underscore that popularity and acceptance are distinct types of high peer status in adolescence, with not only distinct behavioral correlates, but also distinct neural correlates.
Adolescents spend a lot of time interacting with peers (Steinberg & Morris, 2001). Not all of these interactions are positive; 41% of adolescents reported exclusion by their peers in the past two months (Wang, Iannotti, & Nansel, 2009). Frequent exclusion by peers can lead to maladaptive outcomes, including poor academic achievement (DeRosier, Kupersmidt, & Patterson, 1994), depression and anxiety (Ladd & Troop-Gordon, 2003), and aggression (Sturaro, van Lier, Cuijpers, & Koot, 2011).

Peer status plays a large role in social exclusion in adolescents’ daily lives. In adolescence, two moderately correlated types of high status in the peer group are distinguished: acceptance and popularity (Cillessen & Rose, 2005; Parkhurst & Hopmeyer, 1998). Sociometric measures are frequently used to assess peer status in adolescents (Cillessen, 2009). Acceptance is measured by asking adolescents which classmates they like most and least, while popularity is measured by asking which classmates they perceive as most and least popular. Accepted adolescents show high levels of prosocial behaviors and low levels of antisocial behaviors (Sandstrom & Cillessen, 2006). In contrast, popular adolescents, who are central and influential in the peer group, show high levels of both prosocial and antisocial behaviors, such as peer exclusion (Cillessen & Mayeux, 2004; Rose, Swenson, & Waller, 2004).

Examining how peer status is associated with adolescents’ responses to social exclusion is highly relevant, given that being popular in the peer group is a priority for many adolescents (LaFontana & Cillessen, 2010). Additionally, socially excluding peers allows adolescents to achieve and maintain popularity (Cillessen & Mayeux, 2004; Rose, Swenson, & Waller, 2004). While sociometric peer status measures have been widely used to study behavioral correlates of peer status (Cillessen, 2009), few studies have combined sociometric peer status measures with experimental paradigms of social exclusion. This interdisciplinary approach has several advantages. First, combining highly controlled experimental paradigms with well-established sociometric measures of peer status provides both excellent experimental control and high ecological validity, since sociometric peer status measures involve asking adolescents’ real life peers (their classmates) about their status in this important peer group. Moreover, experimental paradigms of social exclusion can be combined with neuroimaging methods and sociometric measures of peer status, to investigate whether individual differences in neural responses to exclusion are a function of both the participants’ own peer status and the peer status of the excluders.

The Cyberball paradigm is the most frequently used paradigm to study behavioral and neural responses to social exclusion in adolescents (Bolling et al., 2011; Gunther Moor et al., 2012; Masten et al., 2009; Sebastian et al., 2011; Will, van Lier, Crone, & Güröğlu, 2015b). Cyberball is an online ball-tossing game that participants play with virtual players, whose behavior is preprogrammed (Williams & Jarvis, 2006). Participants are first included, and after a while, the virtual players stop throwing them the ball. Exclusion leads to reduced mood and decreased satisfaction of needs, accompanied by activation of the ventral anterior cingulate cortex (vACC), dorsal ACC (dACC), subgenual ACC (sgACC), medial orbitofrontal
cortex (mOFC), anterior insula and ventrolateral prefrontal cortex (VLPFC) (Bolling et al., 2011; Gunther Moor et al., 2012; Masten et al., 2009; Sebastian et al., 2011; Will et al., 2015b).

While the neural responses to social exclusion are relatively well-established, little is known about how these neural responses are associated with adolescents’ peer status as indexed by sociometric measures (i.e., peer-report). Nevertheless, a handful of studies have explored how neural responses to exclusion are associated with self-reported or parent-reported social functioning or peer status. These prior studies have yielded mixed findings. Some researchers have reported increased activation of both emotion-processing regions (dACC, sgACC, insula) and emotion-regulation regions (dACC, VLPFC) in adolescents with more developed interpersonal skills (Masten et al., 2009). In contrast, other researchers observed reduced activation of emotion-processing regions (dACC, insula, medial prefrontal cortex; mPFC) in response to exclusion, in adolescents who spent more time with friends (Masten, Telzer, Fuligni, Lieberman, & Eisenberger, 2012), in adolescents who reported to be better able to resist peer influence (Sebastian et al., 2011), and in adolescent girls who reported to be stably accepted compared to adolescent girls who reported to be chronically rejected (Rudolph, Miernicki, Troop-Gordon, Davis, & Telzer, 2016).

Will and colleagues (2015b) were the first to use sociometric measures to examine the association between peer status (i.e., acceptance) and neural responses to social exclusion in adolescents. They used an event-related Cyberball design, which allowed them to not only distinguish between exclusion and inclusion events, but also to focus on a third event: incidental exclusion. This refers to not receiving the ball in an inclusion block, in which participants are overall included but sometimes do not receive the ball, when the other players throw the ball to each other. Will et al. (2015b) argued that incidental exclusion might serve as a cue for potential rejection. They found that chronically rejected adolescents showed increased dACC activity during both exclusion and incidental exclusion, compared to stably accepted adolescents.

While the findings of Will and colleagues (2015b) provide intriguing insights into the association between acceptance and neural responses to exclusion, the association between these neural responses and popularity has remained unexplored, even though popularity is most strongly linked to involvement in social exclusion (Cillessen & Mayeux, 2004). Therefore, the first goal of this study was to examine whether participants’ own popularity and acceptance are associated with their behavioral and neural responses to social exclusion. Although popular and accepted adolescents both show high social functioning, they might respond differently to exclusion. Accepted adolescents are highly sensitive to peer relationship problems (Hoglund, Lalonde, & Leadbeater, 2008), and report greater use of emotion-regulation strategies following rejection than less accepted adolescents (Reijntjes, Stegge, Terwogt, Kamphuis, & Telch, 2006). On the basis of these behavioral findings, it may be predicted that participants’ acceptance would be positively associated with activation of brain areas implicated in the processing (i.e., dACC, sgACC, insula, mPFC) and regulation...
(VLPFC, dACC) of social distress (cf. Masten et al., 2009) in response to exclusion and incidental exclusion. Alternatively, a negative association between acceptance and dACC activity during exclusion and incidental exclusion could also be expected (Will et al., 2015; Rudolph et al., 2016). Popular adolescents, however, are influential and well-connected in the peer group (Dijkstra, Cillessen, Lindenberg, & Veenstra, 2010) and might therefore be less affected by occasional peer exclusion. Thus, we expected that participants’ popularity would be negatively associated with activation of brain areas involved in the processing (dACC, sgACC, insula, mPFC) and regulation (VLPFC, dACC) of social distress in response to exclusion and incidental exclusion (cf. Masten et al., 2012; Sebastian et al., 2011).

In prior Cyberball studies, no information was provided on the popularity of the virtual players. Adolescents want to affiliate with popular peers (Adler & Adler, 1998; Dijkstra et al., 2010) and place high value on being popular themselves (LaFontana & Cillessen, 2010). Thus, being excluded by popular peers may be more distressing than being excluded by less popular peers. Therefore, the second goal of this study was to examine whether exclusion and incidental exclusion by popular virtual players, compared to virtual players who were average in popularity, elicited increased social distress and increased activation of brain areas involved in the processing and regulation of this distress. Given that popularity, but not acceptance, is positively associated with involvement in peer exclusion (Cillessen & Mayeux, 2004), we compared exclusion and incidental exclusion by virtual players who differed in popularity, but who were similar in acceptance. We expected that participants would show more activation of the sgACC, vACC, dACC, insula, mOFC and VLPFC in response to exclusion and incidental exclusion by popular virtual players than in response to exclusion and incidental exclusion by virtual players who are average in popularity.

Finally, adolescents’ behavioral and neural responses to exclusion and incidental exclusion may depend on an interaction between their own popularity and the popularity of those who exclude them. Lansu and colleagues (2012) found that popular adolescents have stronger negative implicit responses to each other, probably because they are competing for the same position in the peer group. Being excluded by popular virtual players might therefore be particularly distressing for participants who are more popular themselves. Thus, the third goal of this study was to investigate whether participants’ own popularity interacted with their behavioral and neural responses to exclusion and incidental exclusion by popular virtual players. We anticipated that participants’ popularity would be positively associated with activation of emotion-processing regions (dACC, sgACC, vACC, insula, mOFC) and emotion-regulation regions (VLPFC) in response to exclusion and incidental exclusion by popular virtual players, relative to virtual players who were average in popularity (Lansu et al., 2012).
Methods

Participants

Sixty-one adolescents participated in a functional magnetic resonance imaging (fMRI) session. Nine participants were excluded from the analyses due to head motion > 3 mm (n=2), completion of only one run due to feeling ill (n=1), computer software malfunctioning (n=2), limited coverage of the brain (n= 3; likely due to moving outside the field of view), or a brain anomaly (n=1). Therefore, 52 adolescents (27 girls) aged 12 to 16 years (M = 14.49, SD = 1.14) were included in the analyses. Participants’ IQ was estimated based on the vocabulary and block design subtests of the WISC-III (Wechsler, 1991) (M = 109, SD = 13, range = 80-135). One parent of each participant completed the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001). None of the participants scored in the clinical range (T-score ≥ 70) for internalizing or externalizing problems.

All procedures were approved by the medical-ethical committee at the first author’s institute. All parents of participants gave informed consent, while all participants gave informed assent.

Participants’ Peer Status

We approached all participants’ schools to collect data on popularity and acceptance using classroom peer nominations (Cillessen, 2009). The mean interval between the fMRI scan and the collection of peer nominations was 4.08 months (SD = 2.60 months, range = 0.23 – 8.97 months). Popularity and acceptance are highly stable constructs in adolescence (Cillessen & Mayeux, 2004).

On notebook computers, participants and their classmates indicated which classmates they found most and least popular, and which classmates they liked most and least. Nominations received were counted and standardized within classrooms to control for differences in classroom size. Popularity was computed by taking the difference between the standardized numbers of most popular and least popular nominations received. Acceptance was computed as the difference between the standardized numbers of liked most and liked least nominations received. We were able to collect peer nominations data for 38 of the 61 participants. Teachers of the remaining 23 participants did not allow us to collect peer status data in their classroom, because they already participated in other research studies in the school year, or because they did not want the research to interfere with their time spent on teaching and preparing their students for upcoming exams. The 38 participants for whom we collected peer status data came from 28 different classrooms and 10 different schools. All classmates that were present on the day of testing provided peer nominations. The number of classmates that rated a participant ranged from 16-30, due to differences in classroom size. Of these participants, 7 were excluded from the fMRI analyses for various reasons (see above), meaning that we could test the association between adolescents’ own peer status and their brain activity for 31 participants (17 girls, 12–16 years, M age = 14.49, SD = 1.06). Popularity and acceptance were not correlated in this sample (r = .25, p = .168).
Cyberball

All participants completed two runs of the Cyberball task during scanning. Participants read a standard cover story before they were administered the Cyberball task (Williams & Jarvis, 2006). They were told that they would play an online ball-tossing game with two same-gender peers, and that the goal of the game was to study the effects of mental visualization on task performance. We told participants that the other players were at home, and that participants would be connected to them through an online link. To buttress the credibility, the experimenter told participants right before he started the scanner that he was going to text the players to be ready, and that he was starting the online link. The screen displayed: “waiting for the scanner....” at that time. Participants were told that they would not meet the other players, but that they were of the same age and gender as participants themselves. Unknown to participants, the behavior of the virtual players was preprogrammed, such that participants either received or did not receive the ball during different periods of the game. The Cyberball task was programmed using Presentation® software (Version 16.2, www.neurobs.com).

Participants played two Cyberball games in a counterbalanced order: once with two popular virtual players, and once with two virtual players who were average in popularity (see below for a detailed description). First, participants played a practice block (consisting of 6 ball tosses) outside of the scanner to get acquainted with the game.

Each Cyberball game in the scanner consisted of eight alternating periods (12 ball tosses) of exclusion (E) and inclusion (I), to increase the signal-to-noise ratio, but reduce participants’ fatigue or disengagement (cf. Bolling et al., 2011; Sebastian et al., 2011). Participants received the ball in 33.3% of tosses during inclusion periods, and they never received the ball during exclusion periods. We used an event-related design (cf. Gunther Moor et al., 2012; Will, Crone, & Güröglu, 2015a; Will et al., 2015b) with three event-types: Exclusion (not receiving the ball within an exclusion period), Inclusion Ball (receiving the ball in an inclusion period), and Inclusion No Ball (not receiving the ball in an inclusion period; i.e., incidental exclusion). In order to have enough Inclusion Ball events to reliably distinguish brain activity related to receiving versus not receiving the ball, there were more inclusion periods than exclusion periods, since participants received or did not receive the ball in only 33.3% of the ball tosses of inclusion periods.

Two different orders (counterbalanced across participants) were administered: 1) I-E-E-I-E-I-I; 2) I-E-I-E-E-I-I. Each ball toss lasted two seconds, with a jitter of 250–4000 ms between ball tosses.

After participants completed the task, they were debriefed about the deception used in the task. Finally, all participants signed a secrecy contract, in which they promised not to share this information with classmates.
Manipulation of the Popularity of the Virtual Players

Before playing Cyberball, participants read vignettes of the two players they would be playing with (see Figure 6.1). The players of one team were described as popular adolescents; the players of the other team as adolescents who were average in popularity. Specifically, we created descriptions of the hobbies, number of Facebook friends and classmates’ opinion of the popularity and acceptance of the virtual players (the “classmates’ opinion” was fictitious, as the virtual players obviously did not have classmates). Participants were asked to indicate their number of Facebook friends, hobbies and what they believed their classmates’ opinions were of their popularity (“How popular do you think your classmates find you?”) and acceptance (“How much do you think your classmates like you?”) before they played Cyberball. They were told that the other players would get to see these descriptions before the game started as well. Participants were told that they received these descriptions to help them imagine the game more vividly. Virtual players were always of the same gender as the participant. To ensure that participants had thoroughly read the vignettes, they were presented to participants twice: once outside of the scanner, and once inside the scanner, directly before each Cyberball game started. Vignettes were created in two pilot studies (see supplementary materials).

After reading the vignettes (and before playing the game), participants rated the popularity (“How popular do you find these players?”) and acceptance (“How much do you like these players?”) of the players of the popular and average team on a 10-point scale as a manipulation check. In order to control for potential differences between the popular and average players, participants rated on a 10-point scale how similar the players were to them and how often they expected to receive the ball from each team in 12 ball tosses. Finally, participants rated on a 10-point scale how important it was to them to be popular with peers. They then played the game.
Figure 6.1. Vignettes used to manipulate the popularity of the virtual players in Cyberball, for boys (A) and girls (B).

Note. The upper two panels of each figure display the popular virtual players, the lower two panels the virtual players who were average in popularity.

Self-reported Social Distress

Directly after each of the two Cyberball runs, while still in the scanner, participants answered four questions about their satisfaction of fundamental human needs and two questions about their mood during that game (see Table S6.1). Participants answered these questions separately for the times when they were included and excluded by the other players. Items were rated on a scale from 1 (do not agree at all) to 5 (agree completely). We created a measure of social distress by taking the mean of the responses to these six items (cf. Bolling et al., 2011; Masten et al., 2009, Sebastian et al., 2011). Answers to positively
phrased questions were reversed, so that higher scores indicated more social distress. Internal consistency for the social distress scales was good (Cronbach’s $\alpha = .67$ – $80$).

**fMRI Data Acquisition**

Participants were first familiarized with the scanner environment in a mock scanner. Neuroimaging data were collected using a 1.5 T Siemens Avanto scanner. A 32-channel head coil was used, and participants viewed the screen through a mirror mounted on the head coil. To prevent head motion, we placed foam inserts around each participant’s head and a piece of paper tape across their forehead and the head coil. We collected the following neuroimaging scans: (1) A multi-echo GRAPPA sequence was used to obtain functional images during the two Cyberball runs of approximately 5 minutes each (repetition time = 2010 ms, echo times = 9.4, 20.9, 33, 44, and 56 ms, field of view = 224 mm, 32 slices collected in ascending order, slice thickness = 3 mm, slice gap = 0.51 mm, flip angle = 90°). Before the first run started, we collected 30 volumes (prescans). The first two volumes of the second run were discarded to allow for a steady state magnetization. (2) In addition, we obtained a T1-weighted anatomical scan (repetition time = 2250 ms, echo time = 2.95 ms, field of view = 256 mm, 176 slices, slice thickness = 1 mm, slice gap = 0.5 mm, flip angle = 15°, duration = 5 min 14s). The two runs of the Cyberball task were always administered in succession.

**Behavioral Data Analysis**

In order to test whether the popularity of the virtual players influenced self-reported social distress during Cyberball, we performed a 2 (Popularity of Virtual Players: Popular vs. Average) x 2 (Cyberball Period: Exclusion vs. Inclusion) ANOVA with virtual player popularity and Cyberball period as within-subject factors. In order to investigate whether participants’ own peer status influenced their self-reported social distress, the analysis was repeated with participants’ popularity and acceptance as covariates. Behavioral data analyses were performed using SPSS version 21.

**fMRI Data Analysis**

fMRI data were preprocessed and analyzed in SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). Based on the 30 prescans, optimal weighting parameters for each of the five echo times were calculated and used to combine the echo times into one image per volume (Poser, Versluis, Hoogduin, & Norris, 2006). Data were realigned using a rigid body transformation, and slice time corrected. The T1-weighted anatomical scan was segmented, and functional images were coregistered to the segmented gray matter image. Finally, data were normalized to an MNI template (ICBM152), and smoothed with a full-width at half maximum Gaussian kernel of 5 mm.

The three event-types (Exclusion, Inclusion Ball, Inclusion No Ball) were modeled in the general linear model implemented in SPM8. We included a total of 36 Exclusion events
(3 periods of 12 ball tosses), 20 Inclusion Ball events (5 periods of 12 ball tosses, in which participants received the ball in 33.3% of tosses), and 20 Inclusion No Ball events per run (5 periods of 12 ball tosses, in which participants did not receive the ball in 33.3% of tosses, and in the other 66.7% of tosses, participants either received or threw the ball). Events were modeled at the onset of the ball toss (with a duration of 0s), and convolved with a hemodynamic response function and its temporal derivative. Additional regressors were included to model the realignment parameters (18 parameters: 3 translation and 3 rotation parameters, and their square and first-order derivative). We applied a high-pass filter (cutoff =360s).

Pairwise contrast images were first computed at the participant-level, and subsequently entered in group-level one-sample t-tests. First, we examined which brain areas were activated by Cyberball events, independent of the effects of peer status. We computed the following pairwise contrasts: Exclusion > Inclusion Ball, Exclusion > Inclusion No Ball, Inclusion No Ball > Inclusion Ball, Inclusion No Ball > Exclusion, Inclusion Ball > Inclusion No Ball. These contrasts were computed for both runs combined, for the full sample (n = 52).

Second, to test whether participants’ own peer status was associated with their neural responses to exclusion and incidental exclusion, participants’ popularity and acceptance scores were added as covariates to one-sample t-tests on the following pairwise contrasts (computed for both runs combined): Exclusion > Inclusion Ball and Inclusion No Ball > Inclusion Ball. Popularity and acceptance scores were included in the same regression analysis, in order to examine the unique association between each type of peer status (controlling for the other type) and brain activation. For each contrast, positive and negative correlations with participants’ popularity and acceptance were examined. These analyses included all participants for whom we obtained peer status data (n = 31).

Third, to test whether participants’ neural responses to exclusion and inclusion were affected by the popularity of the virtual players, we computed interaction contrasts at the participant-level, and submitted these to a group-level one-sample t-test. Two interaction contrasts were computed: 1) the interaction between the popularity of the virtual players (2 levels: popular and average) and event-type (2 levels: Exclusion and Inclusion Ball); and 2) the interaction between the popularity of the virtual players (2 levels: popular and average) and event-type within an inclusion period (2 levels: Inclusion No Ball and Inclusion Ball). The exact contrast values entered in SPM are specified in the supplementary materials. In order to interpret significant interactions, we extracted parameter estimates from a region of interest (ROI) (spheres with a 6-mm radius) centered on peak voxels identified by the whole-brain analyses using Marsbar 0.43 (Brett, Anton, Valabregue, & Poline, 2002). To interpret the interactions, these parameter estimates were extracted and plotted for each condition that was modeled in the interaction contrast. These analyses were performed on the full sample (n = 52).
Finally, we examined whether participants’ popularity interacted with the popularity of the virtual players. To this end, participants’ popularity score was added as a covariate to one sample-tests on the contrasts Exclusion Popular > Exclusion Average, and Inclusion No Ball Popular > Inclusion No Ball Average. These analyses included all participants for whom we obtained peer status data (n = 31).

All whole-brain analyses were corrected for multiple comparisons using FWE-correction (p < .05 at the cluster level). We used the Automated Anatomical Labeling (AAL) template as implemented in MRICron to label significant clusters of activation at the whole-brain level.

Results

Behavioral Results

Manipulation Check

Paired t-tests indicated that the popularity manipulation of the virtual players was effective. Participants rated the popular team (M = 8.11, SD = 1.08) as significantly more popular than the team of players that were average in popularity (M = 5.79, SD = 1.24) (t(51) = 10.37, p < .001, d = 2.00). Inconsistent with our design plan, participants also rated the popular team (M = 6.15, SD = 1.55) as less accepted than the team of players that were average in popularity (M = 6.96, SD = 1.05) (t(51) = 3.86, p < .001, d = 0.60).

Participants indicated that they felt comparably similar to the popular players and players who were average in popularity (t(51) = 1.56, p = .126, d = 0.29), and expected to receive the ball more often from the players who were average in popularity than from the popular players (t(51) = 5.68, p < .001, d = 0.50). Participants’ popularity and acceptance did not correlate significantly with how similar they felt to the popular players and players who were average in popularity, or to how many balls they expected to receive from them (all p’s > .13).

Self-reported Social Distress

There was a main effect of Cyberball period (see Figure 6.2), indicating that participants reported more social distress during exclusion than during inclusion periods (F(1,51) = 39.01, p < .001, η² = .43). The popularity of the virtual players, participants’ own popularity and acceptance, and participants’ self-reported importance of being popular were not significantly associated with participants’ self-reported social distress (all p’s > .08).
fMRI Results

Neural Regions Involved in the Processing of Social Exclusion and Inclusion

Exclusion (compared to Inclusion Ball) elicited activation of the VLPFC, among other regions (see Table S6.2 and Figure 6.3). Not receiving the ball in an inclusion period (contrast: Inclusion No Ball > Inclusion Ball) activated similar brain regions as not receiving the ball in an exclusion period (contrast: Exclusion > Inclusion Ball), such as the VLPFC (see Table S6.2 and S6.3). Nevertheless, when we directly compared not receiving the ball in an exclusion period to not receiving the ball in an inclusion period (contrast: Exclusion > Inclusion No Ball), several regions were more active during exclusion (see Table S6.2), including the dACC. Brain regions activated by inclusion are reported in Table S6.4.

Figure 6.2. Self-reported social distress during exclusion and inclusion by the popular and average teams.

*** p<.001

Figure 6.3. Activation of the left VLPFC (MNI -54 32 10) and right VLPFC (MNI 40 34 -14) during exclusion relative to inclusion ball, combined across the popular and average player conditions.
Effects of Participants’ Peer Status

We performed t-tests on the contrasts Exclusion > Inclusion Ball and Inclusion No Ball > Inclusion Ball, with participants’ popularity and acceptance as covariates. Participants who were more accepted, showed increased dACC activity (MNI 14 28 28, 62 voxels, $Z = 4.14$, $df = 28$) during exclusion (contrast: Exclusion > Inclusion Ball), compared to less accepted participants (see Figure 6.4). Participants’ acceptance was not associated with brain activity during incidental exclusion (contrast: Inclusion No Ball > Inclusion Ball), and participants’ popularity was not associated with brain activity during exclusion or incidental exclusion.

Figure 6.4. Association between participants’ acceptance and dACC activity (MNI 14 28 28) during exclusion, compared to inclusion ball (n = 31).
Note. We used MarsBar 0.43 (Brett et al., 2002) to extract parameter estimates from the clusters identified by the whole-brain analyses.

Effects of the Virtual Players’ Popularity

To test whether participants’ neural responses to exclusion and inclusion were affected by the popularity of the virtual players, we computed interaction contrasts at the participant-level, and submitted these to a group-level one-sample t-test. Two interaction contrasts were computed: 1) the interaction between the popularity of the virtual players (2 levels: popular and average) and event-type (2 levels: Exclusion and Inclusion Ball); and 2) the interaction between the popularity of the virtual players (2 levels: popular and average) and event-type within an inclusion period (2 levels: Inclusion No Ball and Inclusion Ball).

There was a significant interaction between the popularity of the virtual players and event-type in the rostral ACC (rACC) (MNI -4 30 14, 71 voxels, $Z = 4.37$, $df = 51$). Figure 6.5 shows the activation of the rACC for each condition separately: the most pronounced activation was observed for inclusion by the players who were average in popularity, and exclusion by the popular players also activated this region. As can be seen in Figure 6.5, being included by the popular players or being excluded by the players who were average in popularity did not activate the rACC.
Exploratory follow-up analyses indicated that the difference in participants’ acceptance ratings of the players who were average in popularity and popular players (i.e., acceptance average - acceptance popular) was associated with a stronger response in the rACC to inclusion by the players who were average in popularity ($\rho = .32, p = .023$).

There were no clusters for which the event-type within an inclusion period (e.g., Inclusion No Ball vs. Inclusion Ball) significantly interacted with the popularity of the virtual players.

![Figure 6.5. Parameter estimates in rostral ACC (MNI -4 30 14) for exclusion and inclusion by the popular virtual players and virtual players who were average in popularity (n = 52).](image)

Note. We used MarsBar 0.43 (Brett et al., 2002) to extract parameter estimates from the cluster identified by the whole-brain analysis.

Interaction Between Participants’ Popularity and the Virtual Players’ Popularity

In order to examine the interaction between participants’ own popularity and the popularity of the virtual players, we performed one-sample t-tests on the contrasts Exclusion Popular > Exclusion Average and Inclusion No Ball Popular > Inclusion No Ball Average, with participants’ own popularity score as a covariate. During exclusion (contrast: Exclusion Popular > Exclusion Average), participants’ popularity interacted with the players’ popularity in two regions: more popular participants showed increased activation, relative to less popular participants, of the VS (MNI 2 6 8, 56 voxels, $Z = 4.58$, $df = 28$) and mPFC (MNI -4 62 18, 82 voxels, $Z = 4.18$, $df = 28$) in response to exclusion by popular players, compared to exclusion by players who were average in popularity (see Figure 6.6). During incidental exclusion (contrast: Inclusion No Ball Popular > Inclusion No Ball Average), there was no significant interaction between participants’ own popularity and the popularity of the virtual players.
Discussion

This study had three goals: 1) to investigate whether adolescents’ own peer status is associated with their behavioral and neural responses to social exclusion; 2) to examine whether adolescents’ behavioral and neural responses to social exclusion and inclusion in Cyberball are influenced by the popularity of the excluders/includers; 3) to examine whether behavioral and neural responses to exclusion and inclusion show an interaction between adolescents’ own popularity and the popularity of the excluders/includers.

The main findings were: 1) adolescents’ acceptance was positively associated with dACC activity during exclusion; 2) Participants showed increased activation of the rostral ACC during inclusion by virtual players who were average in popularity, but rated as more accepted than popular players; 3) Participants’ popularity was positively associated with

Figure 6.6. A) Association between participants’ popularity and VS activity (MNI 2 6 8) during exclusion by the popular virtual players, relative to exclusion by the virtual players who were average in popularity. B) Association between participants’ popularity and mPFC activity (MNI -4 62 18) during exclusion by the popular virtual players, relative to exclusion by the virtual players who were average in popularity.

Note: We used MarsBar 0.43 (Brett et al., 2002) to extract parameter estimates from the clusters identified by the whole-brain analyses.
activation of the VS and mPFC during exclusion by popular virtual players compared to exclusion by players who were average in popularity.

Neural Regions Involved in the Processing of Social Exclusion and Inclusion

Our adaptation of the Cyberball task was effective in eliciting activation of brain areas that have been consistently reported in prior Cyberball studies in adolescents (Bolling et al. 2011; Gunther Moor et al., 2012; Masten et al., 2009, 2012; Sebastian et al., 2011; Will et al., 2015b). Exclusion (relative to Inclusion Ball) activated the VLPFC. Exclusion additionally activated the dACC when it was directly compared to not receiving the ball in an inclusion period. Inclusion (relative to Exclusion) activated the bilateral insula, among other regions, which is consistent with other studies (Achterberg, van Duijvenvoorde, Bakermans-Kranenburg, & Crone, 2016; Gunther Moor et al., 2012) and might reflect the increased emotional salience of processing socially relevant events (Uddin, 2015).

Effects of Participants’ Peer Status

Consistent with our hypotheses and with prior research (Masten et al., 2009), participants’ acceptance was positively associated with activation of the dACC. We used Neurosynth (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011) to support the interpretation of significant activations in this study. Neurosynth is a database that can be used to link terms (e.g., psychological processes, such as regulation) to fMRI activations, based on > 11,000 fMRI studies, > 400,000 activations and > 3000 terms (www.neurosynth.org). The dACC is involved in the processing and regulation of distress (posterior probability = 0.80 for reappraisal, posterior probability = 0.75 for negative affect). This finding suggests that adolescents who are accepted by their peers may be more sensitive to negative social experiences, and better able to regulate their emotions following these experiences, than less accepted adolescents. Social exclusion elicits aggression and suppresses pro-social behavior (Gunther Moor et al., 2012; Twenge, Baumeister, DeWall, Ciarocco, & Bartels, 2007; Twenge, Baumeister, Tice, & Stucke, 2001). In order to remain well liked by their peers, adolescents’ ability to regulate their emotions and behavior following exclusion may be of key importance. Alternatively, it may be that the increased sensitivity to social exclusion of more accepted adolescents requires greater recruitment of emotion-regulation brain areas. Moreover, accepted adolescents’ heightened sensitivity to social exclusion might motivate behaviors that lead to liking by peers.

It must be noted, though, that the increased dACC activity in response to exclusion we observed in more accepted adolescents is inconsistent with two recent studies (Rudolph et al., 2016; Will et al., 2015b), in which stably accepted adolescents showed decreased dACC activity in response to exclusion, compared to chronically rejected peers. Differences in study designs might explain these discrepant findings. We used a continuous measure of acceptance and a Cyberball task in which information about the peer status of the virtual players was provided. These prior studies compared two groups of adolescents (chronically...
rejected vs. stably accepted) who had extreme acceptance scores (e.g., upper and lower 10th percentile in the Will et al. study), while we included participants whose acceptance scores covered the full range of possible scores. Additionally, these studies used a Cyberball task without information about the virtual player’s popularity. Providing information about the characteristics of the virtual players might make participants more engaged in the task, which could influence activation of brain areas implicated in the processing of emotional salience, such as the dACC. Future studies should examine this hypothesis by directly comparing designs in which information about the virtual players is and is not provided.

### Effects of the Virtual Players’ Popularity

Participants’ neural responses to Cyberball events were influenced by the popularity of the virtual players, but not in the direction we hypothesized. There were no differences in neural responses to exclusion by popular players or players who were average in popularity. Instead, we found a difference in the neural response to inclusion. Inclusion by players who were average in popularity was associated with the most pronounced recruitment of the rACC.

The rACC has frequently been implicated in the processing of negative emotions, such as distress (posterior probability = 0.80 for distress). However, it is unlikely that the increased rACC activity during inclusion by players who were average in popularity reflects increased distress, since participants did not report more distress during inclusion by players who were average in popularity than by popular players. In fact, they rated the players who were average in popularity as more accepted than the popular players.

Nevertheless, a recent meta-analysis showed that the rACC is particularly activated by positive feedback (Liu, Hairston, Schrier, & Fan, 2011). Davey and colleagues (2010) found that receiving positive peer feedback activated the rACC in adolescents. Given that participants rated the players who were average in popularity as more accepted than the popular players, the enhanced rACC response to inclusion by the players who were average in popularity may reflect increased emotional salience or positive affect induced by being included by more accepted peers (posterior probability = 0.93 for happy faces, and posterior probability = 0.79 for salience network). This hypothesis needs to be tested in future research by comparing neural responses to inclusion between players who vary in acceptance but are matched on popularity.

### Interaction Between Participants’ Popularity and the Popularity of the Virtual Players

Adolescents’ popularity correlated positively with VS and mPFC activity in response to exclusion by popular players, compared to exclusion by players who were average in popularity. These regions have been implicated in emotional salience processing (VS: posterior probability = 0.74 for distress) and understanding others’ emotions and self-referential processing (mPFC: posterior probability = 0.85 for theory of mind and posterior probability = 0.78 for self-referential). Being excluded by popular players might be more
salient and self-relevant for adolescents who are more popular themselves, as they might see it as a threat to their status (cf. Lansu et al., 2012).

Strengths and Limitations

The current study has several strengths. To our knowledge, we are the first to examine whether the popularity of virtual Cyberball players influences neural responses to social exclusion and inclusion, and whether participants’ own peer status interacts with these responses. Further, we made an important distinction between acceptance and popularity, and showed that these distinct forms of high peer status are differentially associated with neural responses to (incidental) exclusion. The present study included a relatively large sample of adolescents, and used a Cyberball design that allowed us to maximize signal-to-noise ratio.

Nevertheless, limitations need to be mentioned as well. We did not include a third team of highly unpopular virtual players. Future studies could use between-subjects designs to study whether responses to exclusion and inclusion by unpopular players differ from players who are average in popularity and popular players. Further, we used fictitious Cyberball players instead of actual classmates. The use of fictitious players provided optimal experimental control, as participants were not influenced by confounding factors, such as previous (negative) encounters with the other players or differences in popularity between the classmates of different participants. However, it remains an empirical question whether the same findings would be observed with actual classmates.

Even though we used Neurosynth to support our interpretation of the fMRI activations, these interpretations are still speculative. Future studies should test our interpretations more directly, for instance by directly measuring or manipulating the use of emotion-regulation strategies or perspective taking during Cyberball. Finally, in order to better interpret findings associated with the processing of incidental exclusion, future studies could administer social distress questions that specifically distinguish between not receiving the ball during an exclusion period and during an inclusion period.

Conclusions

Two distinct types of high peer status were differentially associated with neural responses to exclusion. Participants’ acceptance was positively associated with activation of the dACC during exclusion. Participants’ popularity interacted with player popularity, in that more popular participants showed increased activation of the mPFC and VS in response to being excluded by popular players, compared to being excluded by players who were average in popularity. The popularity of the virtual players influenced neural responses to inclusion. The rACC response to inclusion by players who were average in popularity but who were rated as more accepted, was stronger than the response to inclusion by popular players. Together, these findings indicate that distinct types of high peer status were differentially associated with neural responses to exclusion. Higher acceptance was associated with
increased activation of a brain area implicated in social distress processing and regulation. Higher popularity, on the other hand, was associated with increased activation of brain areas involved in perspective-taking, self-referential processing and emotional salience processing, but only when the excluders were also popular. These findings underscore that popularity and acceptance are distinct types of high peer status in adolescence, with not only distinct behavioral correlates, but also distinct neural correlates.
Supplement Chapter 6

Creation of Vignettes to Manipulate the Social Status of Excluders

Vignettes were created based on two pilot studies. In the first pilot study, 8 adolescents (6 girls) aged 12 to 15 were asked to indicate the number of Facebook friends and hobbies of their popular and unpopular classmates. Based on this information, 8 vignettes were created for each gender, which were tested in a second pilot study with 24 independent adolescents (9 girls) aged 14 to 16. In this second pilot study, adolescents read the vignettes, and rated these same-gender peers on popularity and acceptance (on a 10-point scale). Based on these ratings, we selected one vignette describing a popular and one vignette describing a player who was average in popularity for boys and girls separately. The vignettes were selected such that the difference in the mean popularity rating between the popular and average players was as large as possible, while there was no significant difference in their mean acceptance rating. Since the Cyberball task involved two other players, we created a description of the second player of the popular and average team by slightly modifying the number of Facebook friends and changing one hobby (which still reflected a hobby that was characteristic of either popular or average peers as indicated in the first pilot study) of the player that was described in the selected vignette.

Interaction contrasts

Two interaction contrasts were computed: 1) the interaction between the popularity of the virtual players (2 levels: popular and average) and event-type (2 levels: Exclusion and Inclusion Ball). The contrast specified in SPM was: Exclusion popular = 1, Inclusion Ball popular = -1, Exclusion average = -1, Inclusion Ball average = 1; and 2) the interaction between the popularity of the virtual players (2 levels: popular and average) and event-type within an inclusion period (2 levels: Inclusion No Ball and Inclusion Ball). The contrast specified was: Inclusion No Ball popular = 1, Inclusion Ball popular = -1, Inclusion No Ball average = -1, Inclusion Ball average = 1.

Effects of Gender and Age

There were no significant gender differences in participants’ popularity and acceptance ratings of the virtual players. There were also no significant gender differences in participants’ self-reported social distress. Age did not correlate significantly with self-reported social distress. Regarding potential gender and age effects on neural responses, we examined all reported contrasts (Exclusion > Inclusion Ball, Exclusion > Inclusion No Ball, Inclusion No Ball > Inclusion Ball, Inclusion No Ball > Exclusion, Inclusion Ball > Exclusion, Inclusion Ball > Inclusion No Ball). Neither age nor gender were associated with neural responses to exclusion or inclusion (all p’s > .09). Thus, in order to maximize statistical power, all analyses were conducted using the total sample (instead of by gender), and age was left out of the reported analyses as well.
Table S6.1
Need and mood satisfaction questions used to assess self-reported social distress

Needs
1. I felt like I belonged to the group during the game (R).
2. I felt like the other players could decide everything.
3. I had a lot of confidence during the game (R).
4. I felt important (R).

Mood
1. I felt happy (R).
2. I felt sad.

Note. Questions were answered on a scale from 1 (do not agree at all) to 5 (agree completely). R = reverse coded.

Table S6.2
Brain activity during exclusion in the Cyberball task (n = 52; df = 51)

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td>Exclusion (popular + average players) &gt; Inclusion Ball (popular + average players)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital cortex</td>
<td>-14</td>
<td>-96</td>
<td>4</td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>-18</td>
<td>-28</td>
<td>60</td>
</tr>
<tr>
<td>VLPFC</td>
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<td>32</td>
<td>10</td>
</tr>
<tr>
<td>Middle temporal gyrus</td>
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<td>-36</td>
<td>2</td>
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<tr>
<td>VLPFC</td>
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<td>34</td>
<td>-14</td>
</tr>
<tr>
<td>Caudate</td>
<td>-18</td>
<td>-4</td>
<td>26</td>
</tr>
<tr>
<td>Rectus gyrus</td>
<td>-4</td>
<td>36</td>
<td>-18</td>
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<tr>
<td>Exclusion (popular + average players) &gt; Inclusion No Ball (popular + average players)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>-42</td>
<td>-22</td>
<td>52</td>
</tr>
<tr>
<td>Cuneus</td>
<td>-6</td>
<td>-90</td>
<td>20</td>
</tr>
<tr>
<td>Rolandic operculum</td>
<td>-46</td>
<td>-22</td>
<td>20</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>-22</td>
<td>-56</td>
<td>-12</td>
</tr>
<tr>
<td>Dorsal anterior cingulate cortex</td>
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<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Midbrain</td>
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<td>-26</td>
<td>-12</td>
</tr>
<tr>
<td>Superior temporal pole</td>
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<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Fusiform gyrus</td>
<td>26</td>
<td>-68</td>
<td>-10</td>
</tr>
</tbody>
</table>

Note. All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported. Inclusion Ball = receiving the ball in an inclusion period.
Table S6.3
Brain activity associated with not receiving the ball in an inclusion period (n = 52; df = 51)

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td>Inclusion No Ball (popular + average players) &gt; Inclusion Ball (popular + average players)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital cortex</td>
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<td>-92</td>
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</tr>
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<td>Postcentral gyrus</td>
<td>24</td>
<td>-26</td>
<td>58</td>
</tr>
<tr>
<td>Middle temporal gyrus</td>
<td>-58</td>
<td>-38</td>
<td>2</td>
</tr>
<tr>
<td>VLPFC</td>
<td>40</td>
<td>36</td>
<td>-14</td>
</tr>
<tr>
<td>Caudate</td>
<td>-18</td>
<td>-4</td>
<td>26</td>
</tr>
<tr>
<td>VLPFC</td>
<td>-54</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>Rolandic operculum</td>
<td>42</td>
<td>-14</td>
<td>20</td>
</tr>
<tr>
<td>Superior medial frontal gyrus</td>
<td>-2</td>
<td>46</td>
<td>32</td>
</tr>
<tr>
<td>Inclusion No Ball (popular + average players) &gt; Exclusion (popular + average players)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>24</td>
<td>-2</td>
<td>52</td>
</tr>
<tr>
<td>Middle temporal gyrus</td>
<td>40</td>
<td>-60</td>
<td>8</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
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<td>Superior frontal gyrus</td>
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<tr>
<td>Medial orbitofrontal cortex</td>
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</tr>
<tr>
<td>Caudate</td>
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<td>Hippocampus</td>
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</tr>
<tr>
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<td>0</td>
<td>38</td>
<td>34</td>
</tr>
<tr>
<td>Caudate</td>
<td>18</td>
<td>12</td>
<td>22</td>
</tr>
</tbody>
</table>

Note. All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported. Inclusion No Ball = not receiving the ball in an inclusion period.
### Table S6.4
Brain activity during inclusion in the Cyberball task (n = 52; df = 51)

<table>
<thead>
<tr>
<th>Brain area</th>
<th>MNI coordinates</th>
<th>Voxels</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
</tr>
<tr>
<td><strong>Inclusion Ball (popular + average players) &gt; Exclusion (popular + average players)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>-36</td>
<td>-24</td>
<td>52</td>
</tr>
<tr>
<td>Insula</td>
<td>32</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>Insula</td>
<td>-30</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>Thalamus</td>
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<td>-22</td>
<td>6</td>
</tr>
<tr>
<td>Rolandic operculum</td>
<td>-52</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Middle cingulate cortex</td>
<td>-12</td>
<td>-22</td>
<td>44</td>
</tr>
<tr>
<td>VLPFC</td>
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<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Medial frontal gyrus</td>
<td>36</td>
<td>38</td>
<td>30</td>
</tr>
<tr>
<td><strong>Inclusion Ball (popular + average players) &gt; Inclusion No Ball (popular + average players)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>-42</td>
<td>-24</td>
<td>50</td>
</tr>
<tr>
<td>Insula</td>
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</tr>
<tr>
<td>Cerebellum</td>
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<td>-2</td>
</tr>
<tr>
<td>Insula</td>
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<td>16</td>
<td>8</td>
</tr>
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<td>Fusiform gyrus</td>
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<tr>
<td>Postcentral gyrus</td>
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<td>Precentral gyrus</td>
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</tr>
<tr>
<td>Middle occipital cortex</td>
<td>32</td>
<td>-76</td>
<td>30</td>
</tr>
</tbody>
</table>

* Z-score was given as “Inf” in SPM output, corresponding T-value = 11.77.

**Note.** All reported activations are FWE-corrected (p<.05) at the cluster-level. MNI coordinates for the peak voxel of each cluster are reported. Inclusion Ball = receiving the ball in an inclusion period.
The overarching aim of this thesis was to examine the factors that contribute to impulsivity in adolescents. Impulsivity is a multifaceted construct that includes excessive risk-taking, a preference for immediate rewards over delayed rewards, and aggression (Dalley, Everitt, & Robbins, 2011). Adolescents typically are characterized as impulsive, although large individual variation in impulsivity has been observed in this age group (Benningfield et al., 2014; Stanger et al., 2013). Importantly, adolescents who are more impulsive than their peers are at greater risk for behavioral problems later in life, such as substance abuse (Audrain-McGovern et al., 2009). Therefore, understanding the factors that contribute to heightened impulsivity in adolescents is critical. In this thesis, I focused on four factors that play an important role in adolescent impulsivity: cognitive (risky decision-making and temporal discounting), neural (brain development), hormonal (testosterone and estradiol), and social (peer status and influence). Four specific aims corresponded with these four factors. First, I will repeat each aim, discuss its main findings, and link the findings to theory and existing literature. Next, I will discuss general implications and future directions of the research presented in this thesis.

Aim 1: Age Differences in Risky Decision-making and Temporal Discounting

The first aim of this thesis was to examine: 1) age-related differences in risky decision-making and temporal discounting (TD); 2) the correlation of risky decision-making with TD; and 3) age differences in monetary reward valuation and their potential contribution to age differences in risky decision-making and TD. I used a gambling task (to assess risky decision-making) and a temporal discounting (TD) task with adolescents and young adults aged 12-27 years. In the gambling task, participants chose between low-risk options (e.g., 67% of winning €4) and high-risk options (e.g., 33% of winning €8). In the TD task, participants made choices between small immediate rewards (e.g., €5 today) and larger delayed rewards (e.g., €10 in 30 days). Reward valuation was assessed by having participants rate how much they would enjoy receiving the rewards. Three main findings emerged: 1) the preference for immediate rewards declined linearly with age from adolescence to adulthood, while risky decision-making was not associated with age; 2) risky decision-making and TD were not significantly correlated; and 3) while adolescents valued smaller monetary rewards more than adults, age differences in reward valuation could not explain the observed age differences in TD.

The linear decrease with age in the preference for immediate rewards is consistent with prior studies (Olson, Hooper, Collins, & Luciana, 2007; Scheres et al., 2006; Steinberg et al., 2009; but see Scheres, Tontsch, Thoeny, & Sumiya, 2014, for an exception). It might reflect maturation of cognitive control functions (i.e., inhibition, working memory) (Huizinga, Dolan, & van der Molen, 2006; Luciana, Conklin, Hooper, & Yarger, 2005) and of brain areas that subserve these functions (e.g., the lateral PFC and parietal cortex; Christakou, Brammer, & Rubia, 2011; Ripke et al., 2012).
The lack of age differences in risky decision-making is consistent with some previous studies (Cauffman et al., 2010; Overman et al., 2004; van Leijenhorst, Westenberg, & Crone, 2008). However, it is inconsistent with a recent meta-analysis (Defoe, Dubas, Figner, & van Aken, 2015) that found more risk-taking in adolescents than in adults with a medium effect size. This was particularly the case for tasks with immediate outcome feedback (albeit at a trend level of significance), such as the gambling task I used.

Differences in specific task characteristics across studies might partially account for the mixed findings in the risky decision-making literature. Two important characteristics of the gambling task I used were: 1) all information relevant to making a decision (reward magnitude and probability of winning the reward) was presented visually, thereby minimizing demands on working memory; 2) the probabilities of obtaining a reward were presented explicitly. In most prior studies reporting more risky decision-making in adolescents than adults, (adaptations of) the Iowa Gambling Task (IGT) was used (Crone, Somsen, van Beek, & van der Molen, 2004; Hooper, Luciana, Conklin, & Yarger, 2004; Mitchell, Schoel, & Stevens, 2008; van Duijvenvoorde, Jansen, Bredman, & Huizenga, 2012). The IGT draws heavily on working memory (van Duijvenvoorde et al., 2012); thus age differences in risky decision-making in this task might partially reflect age differences in working memory. In addition, it has been shown that adolescents make more risky decisions than adults when the probabilities of obtaining a reward are ambiguous, but not when they are explicitly stated (Tymula et al., 2012), as was the case in my study. Future studies should administer different risky decision-making tasks to the same participants, so that it is possible to directly compare age differences between different tasks and to compute a robust latent variable for risky decision-making based on different tasks (Huizinga et al., 2006).

In addition to the distinct age-related differences observed for risky decision-making and TD, I also found that both constructs were not significantly correlated in adolescents and adults. This is consistent with prior research (Olson et al., 2007; Prencipe et al., 2011; Scheres et al., 2006) and with theoretical models that posit that excessive risk-taking and the preference for immediate rewards are distinct components of impulsivity (Dalley et al., 2011). Different neural regions are recruited during risky decision-making and TD, which might contribute to their low correlation. Specifically, the lateral PFC and parietal cortex are more active during risky decision-making than during TD choices (Weber & Huettel, 2008), while the posterior cingulate cortex and middle occipital cortex are more active during TD choices than during risky decision-making (Peters & Buechel, 2009).

Finally, I showed that even though adolescents value smaller rewards more than adults do, age differences in the preference for smaller immediate rewards remained significant after controlling for differences in reward valuation. This is an important insight for studies focusing on age-related differences in decision-making in which monetary rewards are frequently used. It could be argued that age differences in monetary reward valuation confounded the results of these studies. However, my findings clearly indicate that
this was not the case: age differences in monetary reward valuation could not account for age differences in TD.

Aim 2: Neural Mechanisms of Individual Differences in Temporal Discounting

The second aim of this thesis was to examine the neural mechanisms of individual differences among adolescents in TD, a key component of impulsivity, longitudinally across two assessments. At the first assessment, 58 adolescents aged 12-16 years completed a TD task with money and snack rewards while they were scanned with fMRI. I used a mixed-effects model approach to decompose TD choices into 3 components: 1) average impatience, which reflects the contribution of both immediate reward magnitude and delay duration to choice; 2) amount sensitivity, or the unique contribution of immediate reward magnitude to choice; and 3) delay sensitivity, or the unique contribution of delay duration to choice.

I found that the distinct components of TD choice were associated with differential functioning of distinct brain areas. Specifically, participants’ average impatience was positively associated with activation of the lateral PFC, VS, and parietal cortex during delayed reward choices, and positively associated with ventromedial PFC (vmPFC) activity during immediate reward choices. Amount sensitivity was positively associated with VS and dorsal anterior cingulate cortex (dACC) activity during immediate reward choices. Delay sensitivity was positively associated with parietal cortex activity during delayed reward choices. Snacks were discounted more steeply than money, and TD of money and snacks showed overlap in the inferior parietal cortex.

The finding that relatively steep discounting of delayed rewards was associated with increased activation of the VS, vmPFC, lateral PFC, and parietal cortex is in line with previous studies (Benningfield et al., 2014; Ripke et al., 2012; Stanger et al., 2013). I advanced prior research by showing that distinct underlying processes of TD choice have distinct neural correlates: activation of brain areas implicated in using emotional information to guide behavior (i.e., the VS and dACC) (Liu, Hairston, Schrier, & Fan, 2011; Shenhav, Botvinick, & Cohen, 2013) was uniquely associated with amount sensitivity, while activation of a cognitive control area (i.e., the parietal cortex) (Cavanna & Trimble, 2006) was uniquely associated with delay sensitivity.

At the second assessment, 41 participants from the first assessment again completed the TD task with money and snack rewards in the MRI scanner one year later. The longitudinal MRI design made it possible to examine; 1) stability of TD choices and related brain activity; 2) longitudinal changes in brain activity during TD choices; 3) the associations between longitudinal changes in brain activity and structure and changes in TD.

Consistent with other studies (Achterberg, Peper, van Duijvenvoorde, Mandl, & Crone, 2016; Anokhin, Golosheykin, & Mulligan, 2015) and the notion that TD has trait-like stability (Odum, 2011), TD choices were highly stable across the 1-year interval. However, brain activity during these choices was not stable. I observed longitudinal declines in dorsolateral PFC (DLPFC) and medial orbitofrontal cortex (mOFC) activity during TD choices.
Longitudinal decreases in DLPFC activity and increases in superior parietal cortex activity during delayed reward choices were associated with decreases in TD. Changes in brain structure were not associated with changes in TD. The fact that longitudinal declines in PFC activity were associated with decreases in impulsivity is consistent with a recent study of risky decision-making in adolescents (Qu, Galvan, Fuligni, Lieberman, & Telzer, 2015). Longitudinal declines in PFC activity might reflect increased neural efficiency caused by maturational processes such as pruning and elimination of connections (Durston et al., 2006).

Together, my findings on the neural mechanisms underlying individual differences in TD are consistent with neurobiological models of adolescent impulsivity. These models state that adolescent impulsivity is caused by an imbalance between relatively mature reward valuation brain areas (VS) and relatively immature cognitive control areas (PFC) (Casey, Getz, & Galvan, 2008; Shulman et al., 2016; Steinberg, 2008). While a growing number of studies have compared activation of these regions between children, adolescents, and adults (see Casey, 2015; Richards, Plate, & Ernst, 2013, for reviews), few studies have examined associations between impulsivity and activity of these regions longitudinally. My findings are consistent with the neurobiological models in that they show that differential functioning of the VS and PFC contributes to individual differences in (a component of) impulsivity in adolescence.

Nevertheless, my findings also suggest that neurobiological models of adolescent impulsivity may need to be refined and expanded, consistent with recent critiques of them (Crone & Dahl, 2012; Pfeifer & Allen, 2012). First, these models do not distinguish between subregions of the PFC, even though the PFC has many subregions with distinct functions (Miller & Cohen, 2001). I showed that different PFC regions were differentially associated with TD (Chapter 3): adolescents who showed relatively steep TD activated the vmPFC more during immediate reward choices (compared to delayed reward choices), while they activated the lateral PFC more during delayed reward choices (compared to immediate reward choices).

Second, both increased and decreased PFC activity - in adults relative to adolescents, or in more impulsive adolescents relative to less impulsive adolescents - have been interpreted as reflecting increased maturity of this area of the brain (Crone & Dahl, 2012). We found that more impulsive adolescents showed increased DLPFC activity during delayed reward choices (Chapter 3), DLPFC activity during TD choices declined longitudinally (Chapter 4), and adolescents with the greatest declines in DLPFC activity over time also showed the greatest decrease in the ability to wait for delayed rewards (Chapter 4). Together, these findings indicate that examining brain-behavior correlations may aid the interpretation of activation patterns, particularly when a longitudinal design is used. Given that I observed declines in DLPFC activity over time and that these declines were associated with more “adult-like” behavior (i.e., decreased TD; see also Chapter 2), one could argue that in the context of TD, decreased (DL)PFC activity may reflect increased maturity. These
decreases in DLPFC activity could be due to neuromaturational processes, such as the pruning of synapses and elimination of unused connections (Durston et al., 2006).

Third and finally, neurobiological models of adolescent impulsivity focus exclusively on the PFC and VS. However, other regions also play an important role in impulsivity and its development. I demonstrated that the parietal cortex contributes to individual and developmental differences in TD: adolescents who showed relatively steep TD also showed increased inferior parietal cortex activity during delayed reward choices (Chapter 3), while longitudinal increases in superior parietal cortex activity were associated with longitudinal decreases in TD (Chapter 4). These findings are consistent with studies showing differential functioning of the parietal cortex in more impulsive adolescents (Stanger et al., 2013), and more parietal cortex activation during TD choices in adults than in adolescents (Christakou et al., 2011; Ripke et al., 2012).

**Aim 3: Pubertal Development and Hormones**

The third aim of this thesis was to examine whether pubertal development and sex steroid hormones (testosterone and estradiol) are associated with TD and its neural correlates in adolescents. Two studies were conducted. In the first, 12-18 year-old adolescents completed a TD task and reported on their pubertal development. Specifically, adolescents reported to what extent they had experienced the physical changes of puberty, including body hair growth, skin changes, a growth spurt, voice changes, and facial hair growth (for boys) or breast development and menarche (for girls). Self-reported pubertal development was not significantly correlated with TD in adolescent boys and girls. The second study focused on the association of the sex steroid hormones (testosterone and estradiol) that drive the physical changes of puberty with TD and brain activity during TD choices. Consistent with Study 1, sex steroid hormones were not significantly associated with TD or brain activity during TD choices. Together, these studies indicate that pubertal development and sex steroid hormones do not contribute to TD or its neural mechanisms. Two prior studies also did not find significant correlations between testosterone levels and TD in adolescents (Bromberg, Wiehler, & Peters, 2015) and young adults (Peper et al., 2013b).

Contrary to these findings, several behavioral and neuroimaging studies did report associations of pubertal development and hormones with daily-life impulsivity or its underlying neural mechanisms. For instance, advanced pubertal development and relatively high levels of testosterone and estradiol have been linked consistently to increased impulsivity in daily life in adolescents, such as alcohol use (Costello, Sung, Worthman, & Angold, 2007; de Water, Braams, Crone, & Peper, 2013; Eriksson, Kaprio, Pulkkinen, & Rose, 2005). The association between testosterone levels and alcohol use was found to be mediated by functional connectivity between the amygdala and OFC in adolescent boys (Peters, Jolles, Van Duijvenvoorde, Crone, & Peper, 2015). Specifically, boys with relatively
high testosterone levels (compared to peers), showed reduced functional connectivity between the amygdala and OFC, which in turn was related to increased alcohol use.

It might be hypothesized that testosterone and estradiol stimulate daily-life impulsive behaviors by influencing (the neural mechanisms of) a component of impulsivity that I showed to be distinct from TD, namely risk-taking. Indeed, testosterone levels were positively correlated with self-reported risk-taking in adolescent boys (Vermeersch, T’Sjoen, Kaufman, & Vincke, 2008b), and with risky decision-making in a gambling task in adolescent boys and girls (Peper, Koolschijn, & Crone, 2013a). Estradiol levels were positively correlated with self-reported risk-taking in adolescent girls as well (Vermeersch, T’Sjoen, Kaufman, & Vincke, 2008a). Moreover, higher testosterone levels were associated with increased VS activation during reward processing after a risky decision in adolescents (Braams, Peper, van der Heide, Peters, & Crone, 2016; Op de Macks et al., 2011).

Alternatively, it is possible that characteristics of the TD task I used precluded me from finding an association between sex steroid hormones and TD or its neural correlates. I administered a TD task with relatively long delays (up to 180 days) that were not actually experienced (although one randomly selected choice was experienced). Adolescents’ decision-making in this task recruited brain areas implicated in cognitive control (e.g., lateral PFC and parietal cortex), but not subcortical brain areas implicated in affective processing (e.g., the VS or amygdala). These subcortical affective brain areas are particularly rich in sex steroid hormone receptors, leading some to argue that sex steroid hormones only stimulate the activity of these affective brain areas and not the activity of cognitive control areas (Nelson, Leibenluft, McClure, & Pine, 2005). In line with this hypothesis, previous studies have shown that testosterone levels influence VS activity (Braams et al., 2016; Op de Macks et al., 2011) and connectivity between the amygdala and OFC (Peters et al., 2015). Thus, it might be argued that an association between sex steroid hormones and TD and its neural mechanisms would be observed if one were to employ a TD task that is more emotionally salient than the task I used in my studies. For example, experiential TD tasks (cf. Scheres et al., 2006), in which all rewards and delays are actually experienced, have been shown to engage both the VS (Wittmann, Lovero, Lane, & Paulus, 2010) and amygdala (Mies, Ma, de Water, Buitelaar, & Scheres, 2016). Future studies should examine this hypothesis by administering an experiential TD task in combination with fMRI and by correlating TD and its neural mechanisms as measured by this experiential task with sex steroid hormones in adolescents.

Aim 4: Peer Status and Peer Influence Effects on Impulsivity

The fourth and final aim of this thesis was to examine the role of peer status in adolescents’ impulsivity. This aim was twofold: the first sub-aim was to examine the role of peer status and peer relations in risky decision-making and TD. The second sub-aim was to investigate the effects of peer status on neural responses to social exclusion, one of the most common forms of (relational) aggression.
I addressed the first sub-aim in a behavioral study in which adolescents aged 12-18 years completed a gambling task (to assess risky decision-making) and a TD task, and reported on their recent alcohol, tobacco and marijuana use. The participants and their classmates also completed a sociometric instrument in which they rated each other’s popularity and named their best friends. I identified reciprocated best friend dyads (i.e., two adolescents who named each other as their best friend), and identified the more popular friend and the less popular friend in each dyad.

This design allowed me to examine: 1) whether adolescent best friends are similar in their substance use and risky decision-making and TD; 2) whether adolescents’ risky decision-making and TD are associated with their own and their best friend’s substance use; and 3) whether relative popularity within the dyad affected these associations. I found that adolescent best friends were similar in their substance use and risky decision-making. Adolescents’ own risky decision-making was positively associated with their own alcohol and tobacco use. The risky decision-making of more popular friends was positively associated with the alcohol use of their less popular friends, while the decision-making of the less popular friends was not associated with the alcohol use of the more popular friends.

The fact that friends were similar in substance use is consistent with numerous prior studies (Burk, van der Vorst, Kerr, & Stattin, 2012; de Vries, Engels, Kremers, Wetzels, & Mudde, 2003; Knecht, Burk, Weesie, & Steglich, 2011; Mercken, Steglich, Knibbe, & de Vries, 2012; Tucker, de la Haye, Kennedy, Green, & Pollard, 2014). I also found that best friends were similar in risky decision-making, a cognitive mechanism that has been shown to underlie substance use (Lejuez, Aklin, Bornovalova, & Moolchan, 2005; Lejuez, Aklin, Zvolensky, & Pedulla, 2003b; Xiao et al., 2008, 2009). Two processes have been proposed to account for the similarity of best friends: selection and socialization (Kandel, 1978; Lubbers, 2004; Male, 2007). Selection occurs before the friendship is established, and refers to the fact that adolescent select friends with whom they share certain characteristics or dispositions, such as a preference to engage in risky behaviors. Socialization refers to friends becoming more similar over time because they influence each other.

The finding that adolescents’ risky decision-making was positively associated with their own alcohol and tobacco use is also in line with existing literature (Lejuez, Aklin, Zvolensky, & Pedulla, 2003a; Lejuez et al., 2005; Xiao et al., 2008, 2009). The finding that more popular friends’ risky decision-making was positively associated with less popular friends’ alcohol use is consistent with the notion that popular adolescents are dominant and influential (Allen, Porter, McFarland, Marsh, & McElhaney, 2005; Cillessen & Rose, 2005; Parkhurst & Hopmeyer, 1998; Sandstrom & Cillessen, 2006) and with studies showing that popular adolescents influence peers’ risk-taking more than less popular adolescents do (Cohen & Prinstein, 2006; Prinstein, Brechwald, & Cohen, 2011; Teunissen et al., 2012).

Both passive and active peer influence effects might explain why popular adolescents’ risky decision-making affects the alcohol use of their less popular best friends. Passive influence refers to the imitation of risky behaviors of popular adolescents (Bandura,
who show relatively high levels of substance use (Allen et al., 2005; Tucker et al., 2011, 2012, 2013), and whose preference for risk-taking might cause them to bring their less popular friends into environments in which there are increased opportunities to use alcohol (e.g., parties). Popular adolescents also might actively influence their best friends’ drinking by encouraging them to drink verbally and non-verbally (Centifanti, Modecki, MacLellan, & Gowling, 2016; Dishion, Capaldi, Spracklen, & Li, 1995).

Even though this behavioral study provided important insights into the role of peer status in peer influence on risky decision-making and TD, a third component of impulsivity – aggression – is also highly relevant to adolescent peer relations and therefore deserves attention. Specifically, popular adolescents achieve and maintain their high status by engaging in relational aggression, such as excluding others (Cillessen & Mayeux, 2004; Rose, Swenson, & Waller, 2004). Therefore, the second sub-aim was to examine the effects of peer status on behavioral and neural responses to social exclusion.

In order to address this aim, adolescents aged 12-16 years were scanned with fMRI while they played the virtual ball-tossing game Cyberball in which they experienced both inclusion (receiving the ball) and exclusion (not receiving the ball) from two virtual players. I manipulated the popularity of the virtual players by describing them as either highly popular or average in popularity. I further measured participants’ own peer status in terms of their popularity (being “cool”, central, and visible) as well as peer acceptance (being well-liked). Both were again derived from a sociometric test in which participants and their classmates completed peer nominations for popularity (most and least popular) and acceptance (liked most and liked least). This design allowed me to examine whether adolescents’ own peer status as well as the status of excluders and includers influenced their behavioral and neural responses to exclusion and inclusion.

I found that the status of the includers influenced the neural response to inclusion: being included by others who were presented as average in popularity but who were rated by participants as well-liked, elicited a stronger response in the rostral ACC (rACC) than being included by popular virtual players. As the rACC is implicated in processing emotional salience (Davey, Allen, Harrison, Dwyer, & Yucel, 2010; Shenhav et al., 2013), this might indicate that being included by well-liked peers is particularly important for adolescents, perhaps even more so than being included by popular peers. This hypothesis needs to be tested more directly in future research by comparing inclusion by two teams of players who vary in likeability but are similar in popularity.

In addition, the two distinct types of high peer status (popularity vs. acceptance) were differentially associated with neural responses to social exclusion. More accepted adolescents showed more dACC activity during exclusion than less accepted adolescents. More popular adolescents showed increased VS and mPFC activation during exclusion, but only when they were excluded by popular virtual players compared to players who were average in popularity. The dACC is implicated in the processing and regulation of social distress (Eisenberger, 2012). The increased dACC response to exclusion in more accepted
adolescents is therefore consistent with behavioral findings that more accepted adolescents are more sensitive to peer relationship problems (Hoglund, Lalonde, & Leadbeater, 2008) and better able to regulate their emotions following peer rejection than less accepted adolescents (Reijntjes, Stegge, Terwogt, Kamphuis, & Telch, 2006). The VS and mPFC are involved in emotional salience processing and self-referential processing, respectively (Blakemore, 2008; Galvan, 2010). The finding that more popular adolescents engaged these brain areas particularly strongly when they were excluded by popular others, fits with the notion that popular adolescents might see other popular peers as a threat to their own status (Lansu, Cillessen, & Karremans, 2012). This would make exclusion by popular excluders particularly emotionally salient and personally relevant.

Together, my findings on the associations between peer status and impulsivity in adolescents have provided important new insights for theories on peer status in adolescence. In prior research, the behavioral correlates of the two distinct types of high peer status have been well-established. Popular adolescents show not only prosocial behaviors but also higher levels of substance use and relational aggression (Allen et al., 2005; Cillessen & Mayeux, 2004; Mayeux, Sandstrom, & Cillessen, 2008; Rose et al., 2004; Tucker et al., 2011, 2012, 2013), and they influence peers’ risk-taking more than less popular adolescents do (Cohen & Prinstein, 2006, 2011; Teunissen et al., 2012). Accepted adolescents, on the other hand, only engage in high levels of prosocial behaviors (Parkhurst & Hopmeyer, 1998; Sandstrom & Cillessen, 2006). While the behavioral correlates of popularity and acceptance have been extensively studied, little is known about the mechanisms underlying these associations. In this thesis, I focused on how cognitive (i.e., decision-making) and neural mechanisms of impulsive behaviors are associated with popularity and acceptance.

Consistent with prior research, I confirmed the positive association between popularity and substance use in adolescents and showed that more popular friends exerted a strong influence on the alcohol use of their less popular friends (Chapter 5). In addition, I showed that risky decision-making plays an important role in these peer influence effects on substance use. I also observed that popularity and acceptance were differentially associated with neural responses to social exclusion, a form of relational aggression (Chapter 6). To summarize, I confirmed and extended existing theories of peer status by showing that: 1) popularity is positively associated with substance use, more popular adolescents influence the alcohol use of their less popular friends, and popular adolescents’ risky decision-making plays an important role in peer influence on alcohol use; 2) popularity and acceptance are distinct types of high peer status in adolescence with behavioral differences but also neural differences that may reflect differences in the cognitive and emotional strategies used in response to exclusion by peers.
General Implications

Importance of Distinguishing between Different Components of Impulsivity

Impulsivity is a multifaceted construct. Definitions of impulsivity have included a failure of motor inhibition, a preference for smaller immediate rewards over larger delayed rewards, risky decision-making, and aggression (Dalley et al., 2011). Prior studies have shown that these components are not necessarily correlated in children and adolescents. Motor inhibition is not correlated with the preference for immediate rewards (Solanto et al., 2001), nor with risky decision-making (Geurts, van der Oord, & Crone, 2006). I showed that the preference for small immediate rewards over larger delayed rewards (TD) is also not correlated with risky decision-making in adolescents and young adults and that TD and risky decision-making show distinct age-related differences (Chapter 2). I further showed that peer relations and status were differentially associated with risky decision-making and TD in adolescents (Chapter 5). Specifically, best friends were similar in their risky decision-making but not in TD. More popular friends’ risky decision-making, but not their TD, was associated with the alcohol use of their less popular friends. Collectively, these findings support the notion that TD and risky decision-making are separate components of impulsivity. Adolescents may engage in more impulsive behaviors than adults because they value the present more strongly, and not because they are worse at estimating risks than adults.

One could argue that differences in task characteristics contributed to the weak correlation between different components of impulsivity, since such differences can lead to weak correlations, even between tasks measuring the same component of impulsivity, that is, TD (Scheres, Sumiya, & Thoeny, 2010). Nevertheless, the fact that risky decision-making and TD were not correlated and showed different age-related differences cannot be completely explained by the tasks I used. Several prior studies have reported similar findings using tasks that were more closely matched in terms of task characteristics than the ones I used (Olson et al., 2007; Scheres et al., 2006). For instance, in my study there was a difference in the presentation of the choice options of the risky decision-making task (in which the magnitudes and probabilities of the rewards were presented visually as a stack of coins and cake with different flavors, respectively) and TD task (in which the reward magnitudes and delays were simply mentioned on the screen, without visual cues). This may have resulted in different demands on working memory of both tasks. However, in the two prior studies with similar findings as my study, the presentation of the choice options was more similar for both tasks. Scheres et al. (2006) used visual cues to indicate the delays (planes flying at different heights) and reward magnitudes (coins) of the TD task, and to indicate the probabilities (piggybanks with shells that differed in thickness) and reward magnitudes (coins) of the probabilistic discounting task used to assess risky decision-making. Olson et al. (2007) used a TD task and probabilistic discounting task in which all rewards, delays, and probabilities were simply mentioned on the screen, without visual cues.
In addition to demonstrating that TD and risky decision-making are separate components of impulsivity, I also showed that TD can be broken down into distinct subcomponents (e.g., amount sensitivity, delay sensitivity) that have distinct neural mechanisms (Chapter 3). Together, these findings indicate that researchers should carefully consider which component(s) of impulsivity to include in studies aimed at specific questions. Furthermore, decomposing a specific impulsivity component into its subcomponents might be particularly relevant for researchers studying adolescents with impulse-control disorders. This approach could elucidate the specific cognitive and emotional processes that might underlie heightened impulsivity in these adolescents, and may help to develop individualized interventions. For example, adolescents who are highly impulsive due to enhanced sensitivity to the amount of immediate rewards could benefit from different interventions than adolescents who are highly impulsive due to an enhanced sensitivity to delay (see Neef, Bicard, & Endo, 2001, for a delay tolerance intervention for individuals with ADHD).

Importance of Investigating Individual Differences in Impulsivity

Many studies focus on differences in impulsivity between adolescents and adults (Figner, Mackinlay, Wilkening, & Weber, 2009; Olson et al., 2007; Overman et al., 2004; Steinberg et al., 2009). On average, adolescents are more impulsive than adults, as I also found in Chapter 2. However, not all adolescents are highly impulsive or equally impulsive. Indeed, the adolescent participants of the studies in Chapters 3 and 4 varied greatly in a key component of impulsivity, TD. And in the longitudinal study with two assessments of TD one year apart (Chapter 4), there were large individual differences in the longitudinal changes in TD. In fact, there was no overall effect of time on TD, reflecting that some adolescents decreased in TD over time, while others increased or did not change. I believe that these individual differences deserve to be the focus of investigation, instead of being treated mainly as noise. By studying individual differences in impulsivity, researchers could gain more insight into why some adolescents reach adulthood without major problems while others develop behavior problems such as substance abuse and dependence. In Chapters 3 and 4, I identified neural regions that were associated with individual differences in TD. Adolescents who showed relatively steep discounting of delayed rewards activated the lateral PFC, parietal cortex, and VS more during delayed choices than adolescents who discounted delayed rewards less steeply (Chapters 3 and 4). Longitudinal changes in brain activation during TD choices also were associated with individual differences in TD. Overall, participants showed a decline in DLPFC and mOFC activation during TD choices across the 1-year interval (Chapter 4). This decline was the strongest for those who also showed the strongest decreases in TD.

These findings have two main implications. First, the findings of this thesis could serve as a template for the neural mechanisms that contribute to heightened impulsivity in adolescents with impulse-control disorders, such as ADHD or substance abuse. The
participants in my studies were typically developing adolescents who displayed varying levels of impulsivity. However, the notion that psychiatric disorders can be understood better by examining the full range of behavior (i.e., impulsivity) from normal to abnormal is increasingly supported in recent years (Insel et al., 2010). Second, those who are developing interventions to reduce steep TD could be informed by these findings and could develop neurofeedback or cognitive training programs that specifically target the regions I found to be involved in steep TD.

Advantages of a Multidisciplinary Approach

In the present thesis, a multidisciplinary approach to studying impulsivity in adolescents was used. I used peer status (popularity and acceptance) and peer relationship (best friendship) measures, self-reports of daily life impulsivity (substance use), decision-making tasks from behavioral economics (TD tasks, gambling tasks), measures of brain activation (fMRI), and measures of sex steroid hormones (testosterone and estradiol).

This multidisciplinary approach of studying behavior has two main advantages: 1) one will gain a more detailed and comprehensive understanding of the behavior of interest by studying its multiple aspects, including cognitive, neural, hormonal, and social; 2) each method has strengths and weaknesses and by combining different methods, the strengths of each are combined, while the weaknesses of one method may be supplemented by the strengths of the others.

Self-report measures of daily life impulsivity and peer-report measures of peer status both have high ecological validity, since they directly measure the behaviors and constructs of interest as they occur in everyday life. Peer-report measures have the further advantage that they involve multiple informants from a relevant peer group (classmates) who report on the peer status of an individual in that peer group.

However, while these measures provide important information on general behaviors, they do not provide information on the fundamental underlying mechanisms of these behaviors. Experimental tasks, such as gambling or TD tasks, do provide information on underlying mechanisms of behavior. These measures arguably are less sensitive to social desirability biases than self-report measures and provide excellent experimental control. For instance, in Chapter 3, I systematically varied the immediate reward amounts and delays preceding the larger reward in a TD task, so that I could determine the contribution of amount sensitivity and delay sensitivity to TD choice. Experimental tasks also can be used in combination with neuroimaging methods (as was done in Chapters 3, 4 and 6) to examine the neural mechanisms underlying behavior. Nevertheless, while experimental tasks and neuroimaging methods provide optimal experimental control and allow for a detailed understanding of fundamental mechanisms underlying behavior, they are relatively indirect and abstract measures of everyday behavior. Thus, I argue that combining self-report measures of daily life impulsivity, peer-report measures of peer status, and experimental
tasks and neuroimaging provides the best of both worlds: high ecological validity and excellent experimental control.

Combining these different measures helped me gain unique insights. In Chapter 5, I used peer-report measures of best friendship and popularity to identify best friendship dyads that were distinguished based on their popularity. Using self-report measures of substance use, I replicated the best friendship similarity in alcohol and tobacco use that was reported in prior research (Burk et al., 2012; de Vries et al., 2003; Fujimoto & Valente, 2012; Knecht et al., 2011). In addition, by using experimental tasks of risky and impulsive decision-making, I showed that risky decision-making might play a role in this similarity and in peer influence effects on alcohol use. This finding is particularly relevant for intervention studies, as risky decision-making can be altered through training (Reyna, Weldon, & McCormick, 2015) and alcohol use may therefore be reduced by training adolescents to reduce their risky decision-making. In Chapter 6, the use of Cyberball, an experimental paradigm of social exclusion, allowed me to study behavioral and neural responses to social exclusion in an experimentally controlled setting. These measures were combined with peer-report measures of popularity and acceptance, which allowed me to examine participants’ status in the peer group, which is highly relevant to participation in social exclusion in daily life (Cillessen & Mayeux, 2004). Importantly, I found that participants’ popularity and acceptance were not associated with their behavioral responses to social exclusion (i.e., self-reported social distress). However, I did observe significant associations between participants’ popularity and acceptance and their neural responses to social exclusion. These neural responses implied that acceptance and popularity may be differentially associated with the use of certain cognitive and emotional strategies (e.g., emotion-regulation, emotional salience processing) following social exclusion, which should be explored more directly in future research. Thus, by combining peer-report measures with experimental tasks and neuroimaging, I was able to identify potential differences between popular and accepted adolescents in underlying mechanisms of behavior, even in the absence of self-reported behavioral differences.
Future Directions

Adolescents with Impulse-control Problems

In the studies of this thesis, participants were typically developing adolescents. Nevertheless, steep discounting of delayed rewards is observed not only in typically developing adolescents, but particularly in adolescents with impulse-control problems, such as those with ADHD, substance abuse, conduct disorder, and risky sexual behaviors (Audrain-McGovern et al., 2009; Chesson et al., 2006; Demurie, Roevers, Baeyens, & Sonuga-Barke, 2012; Field, Christiansen, Cole, & Goudie, 2007; Patros et al., 2016; Reynolds, 2006; Reynolds & Fields, 2012; Scheres, Tontsch, Thoeny, & Kaczkurkin, 2010; White et al., 2014). Therefore, my findings regarding the neural mechanisms underlying individual differences in TD might be used to generate hypotheses about neural dysfunction in adolescents with impulse-control problems. Future researchers should feel emboldened to test these hypotheses directly by comparing the neural mechanisms of TD in adolescents with impulse-control problems and typically developing adolescents, as some researchers have started to do recently (Mies et al., 2016).

Life-span Development of Impulsivity

I focused on the developmental period of adolescence (extending into young adulthood in one study), as it is characterized by heightened impulsivity (Steinberg, 2008), profound changes in hormone levels and brain function and structure (Peper & Dahl, 2013), and a social re-orientation towards peers (Steinberg & Morris, 2001). Thus, adolescence is perfectly suited to study the cognitive, neural, hormonal, and social factors that contribute to heightened impulsivity. Still, heightened impulsivity is certainly not limited to adolescence, and changes in TD with age are also observed later in life beyond adolescence and young adulthood (Green, Fry, & Myerson, 1994). Future research should adopt a life-span approach to the development of impulsivity by including participants from a wide age range across childhood, adolescence, young adulthood, and older adulthood. Further, longitudinal studies should include multiple assessments (more than two) that cover multiple developmental periods (e.g., late childhood, adolescence, young adulthood). Including three or more assessments in a longitudinal study also makes it possible to examine non-linear developmental trajectories.

Cognitive and Neurofeedback Interventions

Engaging in high levels of impulsive behaviors poses an increased risk to both impulsive adolescents and their environment (Steinberg, 2004). Developing interventions to reduce TD based on the insights gained in this thesis is therefore an important future goal. For instance, I showed that increased activation of the lateral and medial PFC, VS, and parietal cortex was associated with increased TD. Recently developed neurofeedback methods could be used to alter activation of these brain areas. One promising and non-invasive method is real-time fMRI neurofeedback (Sulzer et al., 2013), in which individuals
are trained to increase or decrease activation of specific brain areas. This is done by providing feedback on the activity of these areas and by training individuals to use mental strategies while being scanned with fMRI. This method has been implemented successfully in adolescents to modulate activation of brain areas involved in emotion regulation (Cohen Kadosh et al., 2016).

Alternatively, cognitive training programs could be administered that have been shown to reduce TD by altering PFC activity in adults. These include working memory training (Bickel, Yi, Landes, Hill, & Baxter, 2011; Wesley & Bickel, 2014) and episodic prospection (Benoit, Gilbert, & Burgess, 2011; Peters & Buchel, 2010). Episodic prospection, which involves vividly imagining positive future events, has been shown to decrease both TD and unhealthy food intake in children and adolescents who are overweight (Daniel, Said, Stanton, & Epstein, 2015). Ideally, these cognitive training programs should be administered in a fun and engaging way in order to optimally motivate adolescents, for example by implementing the training in a videogame (Granic, Lobel, & Engels, 2014).

In addition to the neural mechanisms underlying steep TD, I also showed that risky decision-making is positively associated with alcohol use and tobacco use, and that popular adolescents’ risky decision-making is positively associated with the alcohol use of their less popular best friends. Cognitive interventions have been developed to reduce risky decision-making as well (Reyna et al., 2015). Future studies should examine whether reducing risky decision-making through these interventions also reduces daily-life risk-taking, such as substance use in adolescents.

Varying Task Characteristics

I used both monetary and primary rewards in the TD tasks to optimally mirror daily-life choices between immediate and delayed rewards, which often include primary, consumable rewards (e.g., food or illicit substances). However, other important task characteristics might be varied in future research as well. The TD tasks I used were potentially real in that one choice was randomly selected and paid to participants. Future studies should examine developmental and individual differences and their neural mechanisms using real or experiential TD tasks in which all rewards and delays are experienced (cf. Scheres et al., 2006). Such designs make it possible to examine neural activity associated with not only the decision-making phase, but also the delay-enduring and reward processing phases (Mies et al., 2016; Wittmann et al., 2010).

I studied risky decision-making with gambling tasks with monetary rewards. These tasks have been widely used in developmental populations (Defoe et al., 2015) and have been found to be sensitive to daily life risk-taking in adolescents, both in this thesis (Chapter 5) and in prior studies (Lejuez et al., 2005; Lejuez et al., 2003b; Xiao et al., 2008, 2009). However, in daily life, risky behavior is typically associated with social rewards (e.g., peer approval, gains in popularity) instead of monetary rewards. Thus, future studies should design risky decision-making tasks that incorporate such social rewards. Social rewards may
include visual rewards (happy faces of peers, videos of a smiling peer giving a “thumbs up”),
verbal rewards (compliments from peers), or feedback on how an individual compares to a
peer group in terms of risky decisions or rewards gained.

Social-contextual and Environmental Influences on Impulsivity

In this thesis, I focused on peer influences on impulsivity, since adolescents spend
a large amount of time interacting with peers. However, there are also other important
influences in adolescents’ environment that have received very little attention in past
research. Parents are still an important part of adolescents’ lives. They influence the
impulsive behavior of their children both by passing on genes that might predispose towards
heightened impulsivity and by serving as models of impulsive or self-controlled behavior
(Kandel, 1996). These influences deserve more attention in future research.

Physical characteristics of the early-life environment of children might also affect
their impulsivity, even well into adolescence. Prenatal exposure to chemical toxicants –
such as tobacco smoke during pregnancy, or lead and pesticides – has been shown to have
detrimental effects on the structure of several brain areas that I showed to be involved
in steep TD (i.e., lateral PFC, dACC, parietal cortex) (Horton, Margolis, Tang, & Wright,
2014). Little is known about the long-term effects of exposure to these toxicants on the
development of these brain areas and on impulsive behavior, but researchers should be
couraged to examine this highly relevant research question.

Conclusions

To conclude, I found that a wide array of factors contributed to heightened
impulsivity in adolescents:

1. Cognitive factors: steep discounting of delayed rewards compared to adults,
even when controlling for age differences in reward valuation. In contrast, risky decision-
making was not correlated with age or TD in adolescents and young adults, indicating that
TD and risky decision-making are separate constructs.

2. Neural factors: differential functioning of brain areas implicated in cognitive
control and reward valuation in adolescents who show relatively steep TD compared to their
peers. Specifically, adolescents who showed relatively steep discounting of delayed rewards
activated the lateral PFC, VS, and parietal cortex more during delayed reward choices and
activated the vmPFC more during immediate reward choices. I also examined individual
differences in the contribution of the amount of the immediate reward (amount sensitivity)
and the delay preceding the larger reward (delay sensitivity) to TD choices. Adolescents’
amount sensitivity was positively associated with VS and dACC activity during immediate
reward choices. Adolescents’ delay sensitivity was positively associated with parietal cortex
activity during delayed reward choices. Across a 1-year interval, I observed longitudinal
declines in DLPFC and mOFC activity during TD choices in adolescents. Longitudinal
decreases in DLPFC activity and increases in superior parietal cortex activity during delayed reward choices were associated with decreases in TD.

3. **Hormonal factors**: neither sex steroid hormone levels (testosterone and estradiol) nor self-reported physical changes driven by these hormones were associated with TD or its neural correlates. Thus, while hormone levels consistently have been linked to impulsive daily-life behaviors (e.g., alcohol use), they do not seem to stimulate these behaviors by influencing impulsive decision-making.

4. **Social factors**: adolescents’ own peer status and their best friends’ behavior and decision-making played an important role in impulsive behavior in daily life. Adolescent best friends were similar in their alcohol and tobacco use and risky decision-making. For the more popular friends, their risky decision-making was positively associated with their own alcohol use, while for the less popular friends their risky decision-making was positively associated with their own tobacco use. Popular friends’ risky decision-making was positively associated with the alcohol use of their less popular friends.

Peer status influenced adolescents’ neural responses to social exclusion by virtual players in the ball-tossing game Cyberball. Adolescents showed increased rACC activity during inclusion by virtual players who were average in popularity, but rated as more accepted than popular virtual players. Participants’ own popularity and acceptance were differentially associated with neural responses to exclusion. Acceptance was positively associated with dACC activity during exclusion. Participants’ popularity showed an interaction with the popularity of the virtual players in the mPFC and VS: these regions were positively associated with participants’ popularity during exclusion by popular players, compared to exclusion by players who were average in popularity.

Future studies should extend these findings by studying the neural mechanisms of heightened impulsivity in adolescents with impulse-control problems, by studying impulsivity across the lifespan, by varying the task characteristics of experimental measures of impulsivity, by examining interventions to reduce impulsivity in adolescents, and by investigating social-contextual and environmental influences on impulsivity.
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De adolescentie is de periode vanaf de start van de puberteit tot aan het begin van de volwassenheid, ongeveer van 9 tot en met 25 jaar in Westerse culturen. Adolescenten worden vaak gekenmerkt als impulsief, terwijl niet alle adolescenten even impulsief zijn. Adolescenten die zeer impulsief zijn, lopen echter een grotere kans om later gedragsproblemen (zoals verslaving) te ontwikkelen dan hun leeftijdsgenoten die minder impulsief zijn. Daarom is het erg belangrijk om te onderzoeken waarom sommige adolescenten zeer impulsief zijn. In dit proefschrift onderzocht ik factoren die bijdragen aan impulsiviteit van adolescenten. Ik onderzocht het nemen van ongeduldige en risicovolle beslissingen (cognitieve factoren), hersenactiviteit en -structuur (neurale factoren), puberteit en puberteitshormonen (hormonale factoren) en sociale status en invloed (sociale factoren). Het construct impulsiviteit bestaat uit meerdere componenten. In dit proefschrift richtte ik me op drie componenten: 1) de voorkeur voor directe beloningen; 2) het maken van risicovolle keuzes; 3) agressie, in het bijzonder sociale buitensluiting, een vorm van relationele agressie.

Onderzoeksmethoden

Ik heb temporal discounting (TD) taken gebruikt om de voorkeur voor directe beloningen te onderzoeken. Een TD taak bestaat uit keuzes tussen een kleine, directe beloning (bijv. €2 vandaag) en een grotere, uitgestelde beloning (bijv. €10 over 30 dagen). De grootte van de directe beloning en de wachttijd tot de uitgestelde beloning worden systematisch gevarieerd in TD taken, zodat de subjectieve waarde van de uitgestelde beloning bij een bepaalde wachttijd bepaald kan worden. De subjectieve waarde is gelijk aan de grootte van de directe beloning waarbij iemand geen duidelijke voorkeur heeft voor de directe of uitgestelde beloning. TD verwijst naar het afnemen van de subjectieve waarde van de uitgestelde beloning, naarmate men langer moet wachten op deze beloning.

Ik heb een goktaak gebruikt om het maken van risicovolle keuzes te onderzoeken. In deze taak werden er keuzes gemaakt tussen een risicovolle optie en een veilige optie. Als je de risicovolle optie koos, had je een kleine kans op een relatief grote beloning (bijv. 33% kans op €8), en een grote kans om niets te winnen. Als je de veilige optie koos, had je een grote kans op een kleinere beloning (bijv. 67% kans op €4), en een kleinere kans om niets te winnen.

Om te onderzoeken hoe de hersenen van adolescenten reageren op sociale buitensluiting, heb ik gebruik gemaakt van Cyberball, een balspel waarbij deelnemers werden buitengesloten doordat zij de bal niet kregen van twee virtuele spelers. Om hersenactiviteit te meten, heb ik gebruik gemaakt van functional magnetic resonance imaging (fMRI). Dit is een techniek die meet hoeveel zuurstof er aanwezig is in verschillende hersendelen, op het moment dat iemand een taak (bijv. een TD taak) uitvoert in een MRI.
scanner. Als een hersengebied actief is, is er veel zuurstof nodig. Hoe meer zuurstof er is in een gebied, des te actiever dit gebied dus is tijdens de taak.

Ik zal eerst de onderzoeksdoelen en conclusies van ieder empirisch hoofdstuk (Hoofdstuk 2 t/m 6, Hoofdstukken 1 en 7 bevatten de inleiding en de algemene discussie) van dit proefschrift bespreken, gevolgd door de algemene conclusies en aanbevelingen voor toekomstig onderzoek.

**Hoofdstuk 2: Leeftijdsverschillen in TD en risicovolle keuzes**

Ik heb leeftijdsverschillen in TD en risicovolle keuzes, en hun samenhang, onderzocht bij 337 adolescenten en jongvolwassenen van 12-27 jaar oud. Daarnaast heb ik onderzocht was de rol is van waardering van geld (bij adolescenten en jongvolwassenen) en puberteit (bij adolescenten) bij TD en risicovolle keuzes. Deelnemers aan het onderzoek voerden een TD taak en een goktaak uit. Om de waardering van geld te meten, gaven deelnemers op een schaal van 1 tot 10 aan hoe leuk ze het zouden vinden om €2.50, €5, €7.50 en €10 te krijgen, wat overeenkwam met de beloningen die in de taken werden gebruikt. Adolescenten vulden de Pubertal Developmen Scale (PDS) in, een lijst met vragen over lichamelijke veranderingen die horen bij de puberteit (bijv. borstontwikkeling en ongesteld worden voor meisjes, en de baard in de keel krijgen en gezichtshaar krijgen voor jongens).

De resultaten lieten zien dat TD en het maken van risicovolle keuzes niet dezelfde leeftijdsverschillen vertoonden. TD nam af met leeftijd: jongvolwassenen hadden een minder sterke voorkeur voor directe beloningen dan adolescenten. Er was echter geen leeftijdsverschil in risicovolle keuzes, en deze keuzes hingen ook niet samen met keuzes in de TD taak. Adolescenten waardeerden kleinere beloningen meer dan jongvolwassenen, maar de waardering van geld hing niet samen met de keuzes in de TD taak en goktaak, en het leeftijdsverschil in TD bleef significant nadat er voor verschillen in de waardering van geld werd gecontroleerd. De puberteitsontwikkeling van adolescenten hing niet samen met TD of risicovolle keuzes.

Deze resultaten suggereren dat de voorkeur voor directe beloningen en het maken van risicovolle keuzes verschillende componenten van impulsiviteit zijn bij adolescenten en jongvolwassenen. Iemand die erg ongeduldig is, neemt dus niet per se meer risico’s.

**Hoofdstuk 3: Hersengebieden die bijdragen aan individuele verschillen in TD**

Ik heb onderzocht welke hersengebieden bijdragen aan individuele verschillen in TD van geld en snacks bij 58 adolescenten van 12 tot 16 jaar oud. Ook heb ik TD keuzes voor geld en snacks, en de hersenactiviteit tijdens deze keuzes, met elkaar vergeleken. Daarnaast heb ik onderzocht of puberteitshormonen - testosteron en oestradiol gemeten in speeksel - bijdragen aan TD keuzes en hersenactiviteit tijdens deze keuzes. Deelnemers aan het onderzoek voerden een TD taak uit terwijl ze gescand werden met fMRI. Bij deze taak maakten ze keuzes voor geld, en keuzes voor hun favoriete snack. Met een mixed-
effects model analyse heb ik individuele verschillen in 3 verschillende componenten van TD keuzes onderzocht: 1) gemiddelde ongeduldigheid (de algemene voorkeur voor directe beloningen); 2) gevoeligheid voor de grootte van de directe beloning; 3) gevoeligheid voor de wachttijd tot de uitgestelde beloning.

De resultaten lieten zien dat de verschillende componenten van TD keuzes samenhangen met activiteit van verschillende hersengebieden. Deelnemers die gemiddeld relatief ongeduldig waren, vertoonden tijdens keuzes voor uitgestelde beloningen meer activatie van de laterale prefrontale cortex (PFC), het ventraal striatum (VS), en de pariëtaal cortex, dan tijdens keuzes voor directe beloningen. Deelnemers die gemiddeld relatief ongeduldig waren, vertoonden tijdens keuzes voor directe beloningen juist meer activatie van de ventromediale PFC (vmPFC), dan tijdens keuzes voor uitgestelde beloningen. Deelnemers die relatief gevoelig waren voor de grootte van de directe beloning, vertoonden meer activiteit van de dorsale anterior cingulate cortex (dACC) en VS tijdens het maken van keuzes voor directe beloningen. Deelnemers die relatief gevoelig waren voor de wachttijd tot de uitgestelde beloning, vertoonden meer pariëtaal cortex activatie tijdens keuzes voor de uitgestelde beloning. Deelnemers kozen vaker voor de directe beloning als ze keuzes maakten voor snacks dan voor geld, en bij keuzes voor beide soorten beloningen was de inferiure pariëtaal cortex actief. Puberteitshormonen hingen niet samen met TD keuzes of hersenactiviteit tijdens deze keuzes.

Deze resultaten suggereren dat verschillen in het functioneren van hersengebieden die een rol spelen bij cognitieve controle en de verwerking van emoties en beloningen, bijdragen aan individuele verschillen in TD bij adolescenten. Cognitieve controle gebieden en emotie- en beloningsgebieden dragen bij aan de gemiddelde ongeduldigheid van adolescenten, terwijl gevoeligheid voor de grootte van de directe beloning alleen samenhangt met activatie van emotie- en beloningsgebieden, en gevoeligheid voor de wachttijd tot de uitgestelde beloning alleen samenhangt met activatie van cognitieve controle gebieden.

**Hoofdstuk 4: Longitudinale ontwikkeling van TD en de betrokken hersengebieden**

Aan dit onderzoek deden 41 adolescenten van 13-17 jaar oud mee die al hadden meegedaan aan het onderzoek dat in Hoofdstuk 3 wordt beschreven. Een jaar na dit eerste onderzoek, voerden deze deelnemers opnieuw de TD taak met geld en snacks als beloningen uit in een MRI scanner. Met dit longitudinale MRI onderzoek, was ik in staat om te onderzoeken: 1) hoe stabiel TD keuzes en de hersenactiviteit tijdens deze keuzes zijn; 2) veranderingen na verloop van tijd in hersenactivatie tijdens het maken van TD keuzes; 3) hoe veranderingen in hersenactivatie en -structuur samenhangen met veranderingen in TD keuzes.

De resultaten toonden aan dat TD keuzes zeer stabiel waren gedurende 1 jaar, terwijl de hersenactiviteit tijdens deze keuzes juist niet stabiel was. Tijdens het maken van TD keuzes nam de activatie van de dorsolaterale PFC (DLPFC) en de mediale orbitofrontale cortex (mOFC) af na verloop van tijd. Een `afname` van DLPFC activatie tijdens het kiezen voor...
uitgestelde beloningen hing samen met een toename van het vermogen om op uitgestelde beloningen te wachten, terwijl een *toename* van superieure pariëtaal cortex activatie samenhangt met een toename van het vermogen om op uitgestelde beloningen te wachten. Veranderingen in hersenstructuur hingen niet samen met veranderingen in TD keuzes.

Deze resultaten tonen aan dat de PFC mogelijk efficiënter gaat werken tijdens de ontwikkeling, aangezien er na verloop van tijd minder activatie nodig was om tot dezelfde TD keuzes te komen. Adolescenten die de sterkste afname in (DL)PFC activatie lieten zien, vertoonden ook de sterkste toename in zelfbeheersing.

**Hoofdstuk 5: Middelengebruik en het nemen van beslissingen van beste vrienden: de rol van populariteit.**

In dit hoofdstuk onderzocht ik: 1) of adolescenten die elkaars beste vrienden waren op elkaar leken qua middelengebruik en het nemen van ongeduldige en risicovolle beslissingen; 2) of de ongeduldige en risicovolle beslissingen van adolescenten samenhangen met hun eigen middelengebruik en dat van hun beste vriend(in); 3) of de relatiieve populariteit van de twee beste vrienden invloed had op deze associaties.

Aan dit onderzoek deden 172 adolescenten van 12 tot 18 jaar oud mee. Deelnemers gaven de naam van hun beste vriend(in) in hun klas, en deze informatie gebruikte ik om 49 wederzijdse beste vriend dyades (2 deelnemers van hetzelfde geslacht die elkaar allebei als beste vriend(in) noemden) te identificeren. Klasgenoten van elke deelnemer gaven op een schaal van 1 tot 10 aan hoe populair ze de deelnemer vonden, en op basis hiervan werd iedere dyade ingedeeld in een meest populaire vriend en een minst populaire vriend. Middelengebruik werd gemeten met een lijst met vragen over alcoholgebruik, roken en marihuanagebruik. Het nemen van ongeduldige beslissingen werd gemeten met een TD taak, en het nemen van risicovolle beslissingen werd gemeten met een goktaak.

Er werd gevonden dat beste vrienden sterk op elkaar leken qua alcoholgebruik en roken, en ook wat betreft het nemen van risicovolle beslissingen in de goktaak. Bij de meest populaire vrienden hing het nemen van risicovolle beslissingen in de goktaak samen met meer alcoholgebruik. Bij de minst populaire vrienden hing het nemen van risicovolle beslissingen in de goktaak samen met een grotere kans om te roken. De risicovolle beslissingen van de meest populaire vrienden hingen samen met meer alcoholgebruik van de minst populaire vrienden. De beslissingen van de minst populaire vrienden hingen echter niet samen met het middelengebruik van de meest populaire vrienden.

Deze resultaten suggereren dat populaire adolescenten het meest invloedrijk zijn wat betreft het alcoholgebruik van hun vrienden, en dat de voorkeur voor risico’s van populaire adolescenten hierbij een rol speelt.

**Hoofdstuk 6: Sociale buitensluiting in de hersenen: effecten van sociale status.**

In dit hoofdstuk onderzocht ik de reacties van de hersenen op sociale buitensluiting en inclusie van adolescenten beïnvloed worden door de populariteit van degenen die
hen buitensluiten, en door hun eigen populariteit en acceptatie door leeftijdsgenoten. Deelnemers waren 52 adolescenten van 12 tot 16 jaar oud die Cyberball speelden terwijl hun hersenenactivatie werd gemeten met fMRI. Cyberball is een balspel dat deelnemers speelden met twee virtuele spelers, en waarbij ze soms de bal kregen van de andere spelers (inclusie) en soms niet (exclusie). De deelnemers speelden het balspel twee keer: eenmaal tegen twee spelers die werden beschreven als zeer populair, en eenmaal tegen twee spelers die werden beschreven als gemiddeld populair. De populariteit en acceptatie door leeftijdsgenoten van de deelnemers werd gemeten door aan klasgenoten te vragen wie ze het meest en minst populair in hun klas vonden (populariteit) en wie ze het meest en minst aardig vonden (acceptatie).

De resultaten lieten zien dat inclusie door virtuele spelers die als gemiddeld populair waren beschreven, maar als aardiger werden beoordeeld, een sterkere activatie van de rostrale ACC opwekte dan inclusie door zeer populaire, maar minder aardige virtuele spelers. De eigen populariteit en acceptatie van deelnemers hingen verschillend samen met de reacties van de hersenen op exclusie: deelnemers die meer geaccepteerd waren door leeftijdsgenoten lieten meer dACC activatie zien, terwijl meer populaire deelnemers meer activatie van de mediale PFC en VS lieten zien, maar alleen als de buitensluiters ook zeer populair waren.

Deze resultaten laten zien dat sociale status invloed heeft op reacties van de hersenen op buitensluiting en inclusie. Een hersengebied dat belangrijk is voor de verwerking van emotionele informatie was met name actief wanneer adolescenten betrokken werden bij een spel door spelers die ze aardig vonden. Daarnaast hingen twee verschillende vormen van sociale status verschillend samen met hersenreacties op buitensluiting. Adolescenten die heel aardig werden gevonden door hun klasgenoten, activeerden hersengebieden die een rol spelen van het verwerken en beheersen van emoties wanneer ze werden buitengesloten. Populaire adolescenten activeerden tijdens buitensluiting hersengebieden die een rol spelen bij inlevingsvermogen en het verwerken van emoties, maar alleen als ze werden buitengesloten door spelers die zelf ook zeer populair waren.

**Conclusies**
Geconcludeerd kan gesteld worden dat meerdere factoren bijdragen aan impulsief gedrag van adolescenten:

1. **Cognitieve factoren**: adolescenten vertonen een sterkere voorkeur voor directe beloningen dan volwassenen, zelfs als er gecontroleerd wordt voor verschillen in de waardering van geld. Het nemen van risicovolle keuzes hangt niet samen met leeftijd of de voorkeur voor directe beloningen, wat suggereert dat ongeduldigheid en het nemen van risico’s aparte componenten van impulsiviteit zijn.

2. **Neurale factoren**: adolescenten die een relatief sterke voorkeur voor directe beloningen hadden, activeerden hersengebieden die een rol spelen bij cognitieve controle (de laterale PFC en pariëtaal cortex) en beloning (VS) sterker tijdens het maken van keuzes.
voor uitgestelde beloningen. De PFC werd minder actief na verloop van tijd, maar deze afname in activatie was minder sterk bij adolescenten die een relatief sterke voorkeur voor directe beloningen hadden.

3. **Hormonale factoren**: Puberteitshormonen (testosteron en oestradiol) en de lichamelijke veranderingen die door deze hormonen worden veroorzaakt, hingen niet samen met TD of hersenactivatie tijdens het maken van TD keuzes. Hoewel puberteitshormonen in eerder onderzoek wel samenhangen met impulsief gedrag (alcoholgebruik), lijken deze hormonen dit gedrag dus niet te bevorderen door het nemen van ongeduldige beslissingen te stimuleren.

4. **Sociale factoren**: adolescenten lijken sterk op hun beste vriend(in) qua alcoholgebruik, roken en het nemen van risicovolle beslissingen. Populaire vrienden zijn met name invloedrijk als het om het alcoholgebruik van hun minder populaire beste vriend(in) gaat, en dit komt mogelijk door de voorkeur voor het nemen van risicovolle beslissingen van populaire adolescenten.

De sociale status van adolescenten heeft ook invloed op hun hersenreacties op buitensluiting door anderen. Adolescenten die aardig worden gevonden door hun klasgenoten, activeren een hersengebied dat belangrijk is voor het verwerken en beheersen van emoties sterker dan adolescenten die minder aardig gevonden worden. Meer populaire adolescenten activeren hersengebieden die een rol spelen bij inlevingsvermogen en emoties sterker dan minder populaire adolescenten, maar alleen als ze worden buitengesloten door anderen die zelf ook populair zijn.

In de toekomst zouden onderzoekers de bevindingen van dit proefschrift uit kunnen breiden door te onderzoeken welke hersengebieden bijdragen aan zeer impulsief gedrag van adolescenten met een verstoorde impulsbeheersing (bijv. adolescenten met ADHD of een verslaving), door impulsiviteit over de hele levensloop te onderzoeken, door variaties aan te brengen in experimentele taken die impulsiviteit meten, door interventies te onderzoeken die impulsiviteit bij adolescenten zouden kunnen verminderen, en door sociaal-contextuele (bijv. ouders) en omgevingsinvloeden (bijv. giftige stoffen in de omgeving) op impulsiviteit te onderzoeken.
CV

Erik de Water was born on May 7th, 1987 in Den Haag, the Netherlands. He studied Psychology at Leiden University, where he obtained his B.Sc. in 2008 (cum laude) and his M.Sc. in Clinical Neuropsychology and M.Sc. in Developmental Psychology (research) in 2011 (cum laude). He started his PhD project in December 2011 at Radboud University, Nijmegen, under the supervision of professor Toon Cillessen and Dr. Anouk Scheres. 
Erik studied the cognitive, neural, hormonal and social factors underlying impulsivity in adolescents. From May-November 2015, he was a visiting researcher at the Child Study Center at New York University, directed by Professor Xavier Castellanos.
Erik is currently working as a postdoctoral research fellow at the Icahn School of Medicine at Mount Sinai in New York City. Under the supervision of Dr. Megan Horton and Dr. Cheuk Tang, he is studying the effects of early-life exposure to metals on children’s brain connectivity and emotion-regulation.
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Giancarlo, ya no veo la hora de estar juntos en Nueva York. Soy feliz cuando caminamos juntos por horas, comemos como chanchitos, o al verte en shock cuando algo inesperado sucede en Scandal. Compartimos el mismo sentido de humor y la alimentación “saludable”. Quiero llegar a viejo junto a ti. Tan viejos que ni el mejor cirujano plástico pueda arreglar nuestras caras, en nuestra mansión con piscina e incontables perritos. Te amo.