Risks, Rewards, and the Developing Brain in Childhood and Adolescence

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Abstract

Adolescence is a time of changes in physical, cognitive and social-emotional domains. Behaviorally one of the prominent features of adolescence is an increase in risk-taking. In this chapter we review current theories and research to explain risk-taking behavior from a neural perspective. After a general introduction in section 1, we start in section 2 by laying out behavioral findings focusing on risk-taking, followed in section 3 by a description of current models of adolescent brain development that provide possible explanations for the observed risk-taking. In section 4 we describe neuroimaging research and how these findings map to the described models. Finally, in section 5 we propose new directions for future research.

Section 1: Why do adolescents take risks?

Adolescence, defined as the transition phase between childhood and adulthood, is a time of many physical, cognitive and social-emotional changes. It is a natural time of exploring, thrill seeking, and for eventually setting long-term goals and aspirations (Dahl, 2004; Steinberg, 2008b). The first phase of adolescence (also defined as early-to-mid adolescence) starts with the onset of pubertal maturation around age of 10-11 years (but approximately 1.5 years earlier for girls than for boys) and lasts until approximately ages 15-16 (Shirtcliff, Dahl, & Pollak, 2009). At the onset of puberty, a dramatic increase in the secretion of adrenal androgens, gonadal steroids, and growth hormone causes many changes in physical appearance (e.g., facial and physical changes) and in brain regions with high receptor density for gonadal hormones such

as testosterone and estradiol (Scherf, Berman, & Dahl, 2012). Following pubertal maturation, (Op de Macks et al., 2011) the second phase of adolescence (also defined as mid-to-late adolescence) lasts from approximately ages 15-16 to 21-22 years, during which adolescents gradually reach independence from parents and obtain mature social goals (Steinberg, 2008b; Steinberg & Morris, 2001).

One of the most prominent findings in observational studies, (i.e. correlational studies) is that adolescents take more risks than children or adults (Beyth-Marom & Fischhoff, 1997; Boyer, 2006). Risks are defined as engagement in behaviors that are associated with potentially negative outcomes. For example, they are more likely to have casual sexual partners, engage in binge drinking, get into car accidents and seem to act without thinking about the long term consequences of their actions (Eaton et al., 2008; Steinberg, 2008b). In a striking juxtaposition, although adolescents are physically in the best condition of their lives, mortality rates go up by 200-300% compared to children (Dahl, 2004). This mortality is primarily due to preventable causes such as getting involved in accidents, driving under the influence and engaging in high risk behaviors under pressure from peers/with friends, such as driving with friends which encourages reckless driving (presumably to show off and impress peers but the mechanisms are not fully understood; see Steinberg, 2008b)

Yet, as we describe in section two of this chapter, the behavior observed in the laboratory does not always support the observation of increased risk-taking in adolescents' daily life. Given this, it is perhaps not surprising that programs that teach adolescents to engage in less risky behaviors or teach them the consequences of their

actions have doubtful efficacy on risk-taking; (but see Fischhoff, Bruine de Bruin, Parker, Millstein, & Halpern-Felsher, 2010).

We propose that the deficits in risky decision making observed during adolescence is most likely not only related to cognitive immaturities, but rather to a combination of cognitive, emotional and social factors that lead to increased risk-taking behavior (Crone & Dahl, 2012; Steinberg, 2008b). Understanding these factors is of great importance to eventually change behavior and preventing adverse consequences of risk-taking in the future.

There is a great need for an integrative approach focusing on contextual influences on behavior, brain maturation, hormonal investigation and genetic susceptibility, to understand this crucial phase in life.

In the present chapter, we argue for such an integrative approach. We start in section two of this chapter by reviewing the empirical evidence, both from daily, naturalistic settings and controlled laboratory settings, of whether adolescents show greater risky behaviors. We will show in section three that approaching the problem from a cognitive neuroscience perspective is a very promising way to advance understanding of when adolescents take risks, why they take risks and who is at risk. We will then focus in section four specifically on the neural responses to rewards, focusing on both reward anticipation and reward processing. These processes seem to show differential developmental trajectories in terms of neural activity, illuminating that brain imaging informs risk-taking understanding in a way that has additive value above behavioral observations only. Finally, we will lay out future directions in section five and

conclude with a new working model for studying the dynamics of adolescent risk-taking.

Section 2: Evidence for increases in risk-taking in adolescence

As described earlier, adolescents in particular are at risk of getting involved in accidents, and engaging in other risky behaviors such as experimenting with illicit substances and engaging in unprotected sex (Dahl, 2004; Eaton, et al., 2008; Steinberg, 2008a). The ability to identify and avoid immediate and long-term undesirable consequences of actions and avoid excessive risk is one of the key aspects of mature decision-making and its development has been studied by developmental psychologists and developmental cognitive neuroscientists using various approaches. Developmental neuroscience research is influenced most by studies using a cognitive perspective which try to explain risk-taking behavior in adolescence by examining the development of decision-making skills. In these studies, risk-taking behavior is defined as the consequence of immature decision-making abilities. While the epidemiological support for a peak in risky behavior in adolescence (Dahl, 2004; Eaton, et al., 2008; Steinberg, 2008a) seems clear, it has been difficult to capture in laboratory research, which poses a challenge for neuroscience studies that take place in a laboratory context.

In most cognitive theories of decision-making, decisions are seen as the result of an evaluative process in which both the value of an outcome and the probability with which it will be attained are considered. These concepts are described in terms of the Expected Value (EV) of choice alternatives. The EV is defined as the multiplication of the value of a possible outcome and the likelihood that that outcome will be

obtained. Mature, rational, decisions should favor the choice options with the higher EV, and decisions can be defined as risky, if these rules are not followed. Adolescents' risky behavior suggests that the evaluative process underlying decisions is immature in this developmental period, and, the curvilinear pattern with a peak in risky behavior specific to adolescence suggests that decision-making skills do not improve linearly with development.

However, numerous behavioral experimental studies have found linear patterns of change with development. That is, in several studies children's decisions were more risky compared to adolescents' and adults' decisions. Similarly, the ability to take the long term consequences of choices into account improves from childhood until late adolescence. In addition, several studies suggest that key components of decision-making are relatively mature in adolescence. For example, in our lab we used the Cake Gambling Task, in which the demands on learning and working memory are minimized by making outcome values and associated probabilities explicit (Van Leijenhorst, Westenberg, & Crone, 2008). Decision-making behavior did not differ from age 8 to 30 on this task, which suggests that from late childhood on participants are able to take both reward and probability information into account when making decisions. Other developmental studies have shown that children as young as four years of age already show these kinds of decision-making skills (Anderson, 1991, 1996; A. Schlottmann, 2001; A. Schlottmann & Anderson, 1994). This suggests that decision-making skills improve with age, but that the foundation is laid relatively early in childhood. These findings lead to the question of why the developmental trajectory of risky behaviors as identified in epidemiological work is curvilinear, whereas the developmental trajectory as identified with many lab-based measures

suggests that adolescents' decision making is relatively mature and comparable to those of adults. How can adolescent specific risk-taking behaviors be understood using laboratory tasks?

One approach has been to connect laboratory based findings to real-life risk taking or personality constructs linked to real-life risk taking by assessing both in the same participants. In the previously mentioned study by Van Leijenhorst, Westenberg & Crone (2008) decision-making did not differ between age groups. Yet, there were consistent differences within groups; participants scoring high on a self-report measure of sensation seeking, which is associated with a vulnerability for problematic behaviors (e.g. Horvath & Zuckerman, 1993), showed more risky behavior in the experiment. Similarly, a recent study by Reyna et al. (2011) found individual differences; a laboratory measure of (gist-based) reasoning and reward sensitivity (e.g., sensation seeking) were found to independently predict real-life risky sexual behavior in adolescent participants. These findings support the ecological validity of theory-driven laboratory based measures that assess causal mechanisms underlying risky decision-making.

A second direction of research that assists in resolving the apparent discrepancy between the epidemiological findings and the lab-based findings has been to develop lab-based measures of adolescents' decision-making skills that more closely mimic the complex context in which decisions are made outside of the laboratory. One aspect of context that is gaining attention is whether the choice context is affective ('hot') or neutral ('cool') (Metcalfe & Mischel, 1999). Recent studies have taken this dual-process (hot vs. cold) approach to studying adolescents' decision-making skills

and have found interesting results. For example, Figner et al. (2009) examined the effects of choice context on differences in risk-taking behavior between adolescents aged 13-16 years old, and adults in terms of risk preferences and the amount of information that is taken into account when decisions are made. This study used two versions of a card gambling paradigm, one version was emotionally arousing and the other was emotionally neutral. The arousing version was hypothesized to make more demands on cognitive resources and as a consequence would result in an immature and risky decision strategy. In contrast, the neutral version was hypothesized to result in a deliberative, reasoning based strategy. Indeed, adolescents were found to take more risks and base their decisions on less information in the emotionally arousing condition compared to the neutral condition in which their performance was similar to that of adults. Comparable results were found by Van Duijvenvoorde et al., (2010) who contrasted 13-15 year olds' behavior in an affective decision-making task, the Hungry Donkey Task, a child-adapted version of the IGT (Crone & van der Molen, 2004) in which participants receive reward and loss feedback on each trial to a neutral decision-making task, the Gambling Machine Task, in which no performance feedback is given. Both tasks involve a similar comparison of choice dimensions, and require equally complex reasoning capacities. Adolescents made suboptimal decisions in terms of EV in the affective compared to the neutral task. The authors explain this in terms of the complexity of the reasoning that adolescents used, which was reduced in the affective context in which adolescents focused on only one of three relevant choice dimensions. Finally, Burnett, Bault, Coricelli, & Blakemore (2010) examined risk preferences in 9-35 year old males using a paired gambles task in which choice alternatives differed in the degree of risk involved. While the ability to make optimal decisions in terms of EV showed a linear increase with age, the number of risky

gambles peaked around age 14. The findings from these studies suggest that an affective or 'hot' context more closely mimics the complex context in which decisions are made outside of the laboratory, and suggest that adolescents' are particularly influenced by reward and loss information.

Taken together, a body of research supports the ecological validity of lab-based measures of risk-taking. This work has shown increases in decision-making abilities with development, and importantly, individual differences in performance on these lab-based measures of decision-making ability are related to individual differences in risk-taking behavior outside the lab. Moreover, a second line of research that has focused on decision-making in affective contexts has shown the curvilinear trend that is characteristic of the development trajectory of risk-taking identified in epidemiological work. Collectively these results suggest that the difference between adolescents and adults in decision making is relatively weak or absent when assessed with neutral tasks, consistent with the idea that decision making skills in neutral contexts are relatively intact in adolescence. However, individuals do vary in reasoning abilities, and these neutral tasks appear to capture such within group individual differences. The latter findings indicate that age differences are more likely to be observed in "hot" affectively charged decision-making situations. These results highlight the need for a more integrative approach, which takes cognitive, emotional and social context factors into account, as well as the need for a more mechanistic understanding of risk-taking in adolescence. A better understanding of the mechanisms underlying decision-making and their change with development can help explain the interactions of the development of cognitive abilities and contextual factors, which will help understand risky behavior in adolescence. A promising

approach in this regard is to study components of risk-taking (e.g., reward sensitivity, inhibition) from a cognitive neuroscience perspective, an approach to which we turn in the next section.

Section 3: Neurobiological models of adolescent risk-taking: Promises and challenges

From a neuroscientific perspective, several partly overlapping and partly complementary theoretical models have been proposed about how trajectories of brain maturation may explain behavioral changes in adolescence. Even though the models have broader goals than solely understanding risk-taking in adolescence, they provide intriguing hypotheses with respect to the question of why adolescence may be a vulnerable period for risk-taking.

The model that is probably most explicit in hypothesizing about risk-taking in adolescence is the dual processing model postulated by Somerville, Jones and Casey (2010). According to this model, there is an imbalance between the development of subcortical brain regions, such as the ventral striatum and the amygdala, which are thought to precede the development of the prefrontal cortex. Among the subcortical areas, the ventral striatum is involved with reward processing and decision-making based on incentives (Delgado, 2007), whereas the amygdala is involved with processing highly salient and motivational emotional stimuli (Cunningham, Arbuckle, Jahn, Mowrer, & Abduljalil, 2010), such as potential threats and emotional states of others. Also, the role of the amygdala in fear and anxiety has been well established (LeDoux, 2007). The prefrontal cortex is involved with tasks such as planning, inhibition and cognitive control more generally (Miller & Cohen, 2001). The interplay between a not fully developed prefrontal cortex, which is therefore not fully capable

of executing control related functions, and further developed emotional areas such as the amygdala and the ventral striatum causes an imbalance resulting in a primarily emotion driven approach to rewards and risks in mid-adolescence.

A comparable model is the triadic model proposed by Ernst et al. (2006; Ernst & Fudge, 2009). The triadic model is based on the interplay between three systems. The first is the approach system, tailored to rewards, the second the avoidance system, tailored to prevent harm, and the last is the regulatory system. The neural correlates underlying these systems are the ventral striatum, amygdala and the prefrontal cortex, respectively. These three systems interact with each other and, when balanced, work together in a beneficial way facilitating learning and harm-avoidance. However, during adolescence the balance often tips towards the approach system, resulting in reward driven behavior. The model is comparable to the Somerville et al. (2010) dual processing model, although it differs with respect to the assumptions about speed of maturation. Where the dual processing approach predicts that the subcortical areas develop earlier than the prefrontal areas, the triadic model does not make assumptions about earlier or later maturation. Instead, this model suggests that there is a fragile balance, which may result in tipping to approach or avoidance more easily in adolescence.

Finally, the third model that is relevant for our discussion is the social information processing model proposed by Nelson et al. (2005). During adolescence social re-orientation takes place. This model provides a broad explanation for changes in social processing (social perception, social emotion and social cognition) in adolescence, but also makes predictions about brain regions involved in risk-taking. The social information processing network distinguishes three nodes: a detection node, an

affective node and a cognitive-regulation node (Nelson, et al., 2005). Although different information is being processed in the different nodes, they are also connected and influence each other. In this model, the amygdala and ventral striatum are considered to be part of the affective node, and the prefrontal cortex is part of the cognitive-regulatory node, mirroring the earlier described models. The detection node is involved in basic processing of social stimuli and includes the fusiform face area, superior temporal sulcus and anterior temporal cortex. The social information processing model differs from the earlier described models in that the developmental pattern seen in risk-taking is ascribed to hormonally induced changes to the affective node. Specifically, Nelson et al. (2005) propose that activation in the ventral striatum is elevated due to the rise in gonadal hormones at the onset of puberty, which causes a fragile balance with the slowly developing prefrontal cortex. Therefore, this model does not necessarily predict that the structural development of the ventral striatum preludes structural development of the prefrontal cortex, but instead that the ventral striatum is more sensitive to specific pubertal changes, and therefore becomes more active (see also Steinberg et al., 2008 for a similar dual processing hypothesis based on behavioral empirical evidence).

Together, these models provide excellent starting points for a more in-depth analysis of neural patterns related to risk-taking in adolescence, and as we will see below, they each have received empirical support. Yet, as we will also see in the next section is that the models are not very specific with respect to the sub processes that are involved in risk-taking, and how the striatum and prefrontal cortex are expected to respond to risks versus rewards.

Section 4: Putting the models to the test: How does brain imaging inform risk-taking research in adolescence?

The empirical studies available to date have mostly used functional Magnetic Resonance Imaging (fMRI), a safe and non-invasive technique, which allows for the study of neural activation during specific phases of a task. These studies have focused on two task-related processes that are important for risk-taking investigation: reward anticipation and responses to receiving a reward.

In such neuroimaging studies, responses to anticipated and received rewards are usually investigated using tasks in which participants can receive an outcome that is favorable to them. Outcomes can be points, money or primary rewards such as juice (Delgado, 2007). A consistent finding in these studies is involvement of the ventral striatum/nucleus accumbens in response to receipt of rewards. In addition, the amygdala, anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC), ventromedial prefrontal cortex (VMPFC) and orbitofrontal cortex (OFC) are also found to be active, although these findings are not consistent across studies and possibly depend on specific task demands. Here we will focus on the developmental pattern in the ventral striatum specifically, as this region is most consistently activated in response to reward anticipation and reward processing.

Ventral striatum responses to reward

In reward studies both under- and over recruitment of the ventral striatum have been reported in adolescents compared to children and adults. The most prominent finding, is an over recruitment of the ventral striatum in response to reward receipt for adolescents. These results have been found with different tasks and in a wide age

range, including participants between 7-40 years of age, strengthening the credibility of the results. Four of these studies used tasks with an aspect of gambling, passive or active. With passive gambling we refer to paradigms in which the participant cannot influence the outcome, whereas an active task means that the participant can choose to take a risk or not. Two studies with passive gambling tasks support the hypothesis of over recruitment of the ventral striatum to reward in adolescence. Van Leijenhorst et al. (2010) used a task in which participants are shown a slot machine that they can start with a button press. The slots can fill with three types of fruit. Only when all three slots show the same fruit, they win. Winning was associated with increased activation in the ventral striatum, and more so for mid adolescents. Similarly, Galvan et al. (2006) used a delayed response two-choice task. In this task, participants are presented with a cue, after which they need to respond by indicating the location of the cue when prompted. Correct responses within the time interval set for the response are rewarded. Each cue is paired with a distinct reward amount. Again, winning was associated with increased activation in the ventral striatum, and more so for middle adolescents.

Tasks with an active aspect of gambling, such as the wheel of fortune task (Ernst et al., 2005) and the cake gambling task (Van Leijenhorst, Gunther Moor, et al., 2010), similarly show greater activation of the ventral striatum in response to reward receipt. In the wheel of fortune task, participants are shown a circle divided into two colors. Only trials were analyzed in which both colors covered 50% of the circle in this case, but divisions and therefore probabilities of winning can differ. Participants choose one of the colors and if the computer randomly picks the same color, they win. The cake gambling task is a slightly modified version of the wheel of fortune task. To make the

task more suitable for children, the wheel is explained as a cake with different flavors. Participants can choose which flavor they would like to bet on and if the computer picks the same flavor they win. Participants can choose between a low-risk gamble with a 66% chance of winning 1 euro, and a high-risk gamble with a 33% chance of winning 2, 4, 6 or 8 euros. In these tasks, winning was associated with increased activation in the ventral striatum, and more so in middle adolescence. This pattern of elevated ventral striatum response in middle adolescence was further confirmed in other paradigms which have used reward conditions, such as a temporal discounting task (Christakou, Brammer, & Rubia, 2011) and an anti-saccade task (Geier, Terwilliger, Teslovich, Velanova, & Luna, 2010; Padmanabhan, Geier, Ordaz, Teslovich, & Luna, 2011). Smith et al. (2011) used a sustained attention task in which adolescents showed elevated ventral striatum responses to rewarded trials compared to adults, but not compared to the youngest group. The results from this set of studies seem to provide consistent evidence for enhanced activation in the ventral striatum in middle adolescence.

However, in work focusing on the *anticipation* of rewards, the results have in some studies been opposite to the pattern described above. Two studies have found *under* recruitment of the striatum in middle adolescence. Both of these studies used the Monetary Incentive Delay (MID) task (Bjork et al., 2004; Bjork, Smith, Chen, & Hommer, 2010). In the MID task, participants can win (or avoid losing) different amounts of money by pressing a button within a short interval after a target is presented. Failure to press within the response interval results in omission of gain (or loss), whereas pressing the button within the response interval results in winning (or avoidance of loss). Participants win in 66% of the trials. Individual response intervals

are determined based on response time on a response time task, assessed before the start of the MID task. The MID task has two distinguished phases, separated in time to allow for fMRI analyses for both phases. As such it has been specifically designed to enable testing for differences in brain activation during anticipation, as well as receipt, of a reward. Both studies (Bjork, et al., 2004; Bjork, et al., 2010) found under recruitment of the right ventral striatum for adolescents, compared to an adult group, during gain versus non-gain anticipation. Activation during reward receipt, in contrast, did not yield any significant differences between the groups. It should be noted that the MID task allows for the possibility that groups engage in differential strategies. For example, whether or not the participant will receive the outcome is dependent on behavior, pressing a button as fast as possible, and there is a 66% reward scheme. For some participants, this may lead to greater certainty about the anticipated reward (knowing that they can influence the outcome by behavior), whereas for others this may make the task more uncertain (learning that the reward is only given on 66% of the trials). Whether and how these tasks differ should be an avenue for future research, but it is clear that intriguing shifts in response patterns may occur depending on how the task is framed (Bjork, Lynne-Landsman, Sirocco, & Boyce, in press).

Based on the studies described above two general phases can be distinguished; the anticipation of reward and the receipt of the reward (feedback) (although others have also distinguished between others phases, such as cue-related response and anticipation of outcome, see Geier, et al., 2010). The apparent inconsistency of results might be a result of confounding anticipation of reward and receipt of reward. Taken together, and consistent with the dual processing model (Somerville, et al., 2010) as

well as the triadic model (Ernst & Fudge, 2009), the studies presented show that the ventral striatum is most likely differentially involved in adolescents and most studies point towards enhanced activity, at least for reward receipt (see Figure 1 for a meta-analysis; Christakou, et al., 2011; Ernst, et al., 2005; Galvan, et al., 2006; Van Leijenhorst, Gunther Moor, et al., 2010; Van Leijenhorst, Zanolie, et al., 2010). No studies found an under recruitment of the ventral striatum during reward receipt. However, during anticipation, findings are more mixed. Studies find over recruitment (Galvan, et al., 2006; Van Leijenhorst, Gunther Moor, et al., 2010) as well as under recruitment (Bjork, et al., 2004; Bjork, et al., 2010). Although the models proposed by Somerville et al. (2010) and Ernst et al.(2006) provide a framework by which some of the results can be explained, there may be other factors mediating the effects. Since adolescents go through major changes in hormonal levels as well as in the social domain, this leads to the hypothesis that emotional and social contextual factors may influence these developmental sensitivities, as proposed by the Social Information Processing Model (Nelson, et al., 2005).

Insert Figure 1 about here

Peers and pubertal hormones

The social influences on neural correlates of risk-taking have hardly been studied, even though it is well-known that peers have a large influence on the behavior of adolescents As already pointed out by the social information processing model (Nelson, et al., 2005), adolescence is a time when peers become very important (Dahl, 2004). Also, much risk-taking behavior takes place in groups (Steinberg, 2004).

Adolescents can assess risks and can reason logically when they are asked about risks or consequences (Boyer, 2006). When adolescents are asked to perform a task in the lab, they are usually alone or in the presence of an experimenter, not among their peers. The risk-taking behavior that is observed in a natural setting may therefore not be captured in the standard laboratory environment.

One very exciting new fMRI study investigated risk-taking in a setting with peers for three age groups: adolescents, aged 14-18; young adults, aged 19-22 and adults, aged 24-29. In this study by Chein et al. (2011; see also Gardner & Steinberg, 2005), participants were asked to play a game in which they were driving a simulated car. Their goal was to drive from A to B as fast as possible. On the way, they encountered several crossings. On some of these crossings a stoplight turned orange, just when they approached. On each crossing they could decide to (continue to) go and take a risk, or stop. When they decided to take a risk, this could result in a crash, setting them back further than deciding to wait would have. In one condition, participants were told that they were performing this task alone and that no one would see what they did. In the other condition, however, their peers were physically present and watching them. All groups showed elevated risk-taking in the peer-present condition, but adolescents took even more risks than young adults and adults. Intriguingly, adolescents also showed elevated ventral striatum responses in the peer present condition compared to the other age-groups (see Figure 2).

Insert Figure 2 about here

Peers are assumed to have a large influence on the behavior of adolescents in real life. One mediating factor, which may provide a mechanistic explanation for peer sensitivity, is the role of specific pubertal hormones. These hormones may not only trigger reproductive development, but also influence social behaviors and interest in peers, such as sensation seeking, seeking of social status, fear of social rejection and a drive towards social acceptance (Dahl, 2004; Nelson, et al., 2005). Preliminary evidence for this assumed role of pubertal hormones in adolescent decision making and reward processing, comes from two studies, which investigated the role of testosterone on reward processing and risk anticipation (Hermans et al., 2010; van Honk et al., 2004).

The influence of testosterone on risk taking has been mainly studied through the measurement of naturally fluctuating hormone levels, but recently, exciting new advances in testosterone research have focused on the administration of testosterone in healthy (mostly female) adult participants. Administering small doses of testosterone resulted in increased risk-taking on the IOWA gambling task (van Honk, et al., 2004). In addition, administration of the same dose of testosterone in females results in enhanced activation in the nucleus accumbens during reward anticipation in the MID task (Hermans, et al., 2010). It is well known that in puberty the increase in testosterone is orders of magnitude larger than the increase due to administration of testosterone in the examples described above. Therefore, an intriguing question is whether hormone level increases are predictive of neural responses to risk and reward in pubertal adolescents.

Two studies used this approach. A study by Op De Macks et al. (2011) found that boys and girls with higher natural testosterone levels also showed higher ventral striatum responses to reward receipt, thereby confirming prior studies which showed that testosterone administration in adults also leads to enhanced ventral striatal responses to reward (Hermans, et al., 2010) (see Figure 3). However, as described before, responses to reward anticipation and reward receipt may rely on different mechanisms. This is highlighted in a study by Forbes et al. (2010) in which testosterone levels correlated positively with striatum responses in boys during anticipation, but correlated negatively with striatum responses to reward receipt in both boys and girls. Taken together, these findings shed light on the link between social influence, hormones and decision making as described in the Social Information Processing Model (Nelson, et al., 2005). However, future research is necessary to unravel these apparently inconsistent findings and integrate different approached to understand the interaction between peer sensitivity and pubertal hormones.

Insert Figure 3 about here

Section 5: Future directions

In puberty major changes take place in the body and brain of adolescents. Behaviorally an increase in risk-taking behavior is evident in daily life. Findings from the laboratory show that greater risk-taking among adolescents, compared to other age groups, is only evident under specific contextually arousing conditions (high rewards, peer presence) (Burnett, et al., 2010; Figner, et al., 2009; Gardner & Steinberg, 2005; van Duijvenvoorde, et al., 2010). Brain research investigating the underlying neural

correlates of risk-taking behavior in adolescence has revealed partly consistent (elevated neural response to reward outcome) and partly inconsistent results (reduced and elevated neural responses to reward anticipation). To more fully understand risk-taking, future researchers should continue to disentangle neural responses to anticipation and receipt of reward, and to focus on sensitivities to social and emotional contexts (see also Reyna & Farley, 2006; Rivers, Reyna, & Mills, 2008). We propose that the exciting new advances in brain imaging research, integrated with different approaches, take us to another level of explanation of neural responses to risks and rewards in adolescence. Three of these advances are highlighted here.

Firstly, very few studies up until now have investigated testosterone levels and the influence on risk-taking and reward processing. Bodily changes during puberty are primarily driven by hormonal changes and therefore the influence of hormones is an important area to explore in future work. Testosterone administration studies in adult females show a relationship between nucleus accumbens activity as well as increased risk-taking (Hermans, et al., 2010; van Honk, et al., 2004). Individual measures of hormone levels as assessed by for instance morning saliva samples provide valuable information above and beyond the effects of puberty (Op de Macks, et al., 2011). Reliably investigating individual differences calls for large sample sizes and preferably spread over a wide age range. Participants who have not yet reached puberty, as well as mid-pubertal and post-pubertal participants should be included in order to unravel puberty effects independent of age changes (Quevedo, Benning, Gunnar, & Dahl, 2009). To track the developmental pattern, a longitudinal design would be optimal in order to investigate the combined influence of early or late puberty onset and how this interacts with social environmental influences.

Secondly, it is well known that most risk-taking behavior takes place when adolescents are in the presence of peers, yet social factors influencing neural responses to risks and rewards have hardly been studied. Only one study investigated the effects of peer presence on brain activity (Chein, et al., 2011). Especially for adolescents the presence of peers was found to have a significantly elevating effect on striatum responses. Due to the confined space and limitations provided by the MRI scanner, it is challenging to manipulate peer presence within an MRI setting. Instead of directly manipulating actual peer presence, two other possibilities are to investigate the influence of social stimuli on risk-taking and the relationship between real-life risk-taking and neural responses. Social stimuli could for instance be status within the peer group or the influence of emotional faces on risk taking (Casey et al., 2011). Similar to the approach described earlier in behavioral research, real-life risk-taking could be measured for instance by use of illicit substances such as alcohol or marihuana, or engagement in sexual behavior. Yet another possibility would be to investigate attitudes towards risk-taking, for instance how likely someone thinks it is that a certain risk will yield a positive outcome. For example, Galvan et al. (2007) reported a significant positive correlation between the self-reported likelihood of engaging in risky behavior and nucleus accumbens reactivity in response to winning. Similar correlations can possibly be found between social relations in real life (e.g. resistance to peer influence) and neural responses to risks and rewards in the laboratory (see also Paus, Keshavan, & Giedd, 2008 for a similar approach), providing us with more information about the underlying mechanism of risk-taking at the neural level and to disentangle who is at risk of showing exaggerated risk-taking in real life.

Thirdly, integrating different theoretical approaches as described in the literature so far, such as affective and social neuroscience, can potentially help unravel risk-taking behavior. For example, besides numerous behavioral models, only the neuroscientific model by Nelson et al. (2005) explicitly takes social information processing into account, but the model is not yet specific with respect to how developmental and individual differences in theory of mind or resistance to peer influence may interact with individual tendencies towards risk-taking. Recently, Blakemore and colleagues (Blakemore, 2008; Burnett, Thompson, Bird, & Blakemore, 2011) have demonstrated that adolescence is characterized by large changes in brain networks important for mentalizing about intentions of others. Especially regions in the social brain network, such as the medial prefrontal cortex, precuneus, temporal parietal junction and insula were shown to develop both functionally and structurally during adolescence (Blakemore, 2008; Gogtay et al., 2004). Thus, it is of great importance to examine neural responses to rewards not in isolation, but in an integrative approach with interaction between affective neuroscience (neural responses to risks and rewards) and social neuroscience (ability to take perspective, understand intentions and resist peer influence).

The approach for the future is therefore to study risk taking and neural structure and function in relation to pubertal development, sensitivity versus resistance to peer influences, and mentalizing about intentions of others. Ultimately, we would like to be able to assess individual differences to enable identification of adolescents who are most likely to exhibit excessive risk-taking behavior. This knowledge has far-reaching

implications for policy questions, and for developing interventions that are specific for adolescents who need them, focusing on developmentally specific sensitivities.

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Figure 1 – Meta-analysis of available reward processing studies in adolescence, with a specific focus on the ventral striatum.

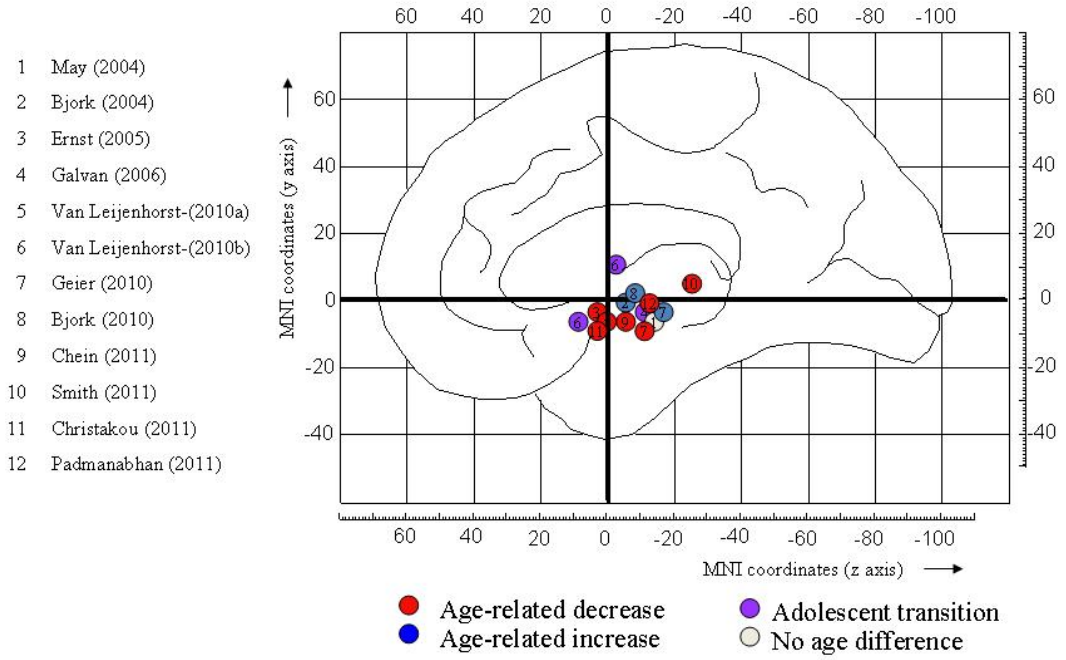

Figure 2 - Left panel: Age (adoles., YA, adults) x Social condition (peer present vs. alone) interaction in the right ventral striatum (VS. MNI peak coordinates: x = 9, y = 12, z =-8). Right panel: Mean estimated BOLD signal change (beta coefficients) in adolescents (adols.), young adults (YA), and adults under ALONE (blue bars) and PEER PRESENT (red bars) conditions. Error bars indicate standard error of the mean. Figure adapted from (Chein, et al., 2011), reprinted with permission.

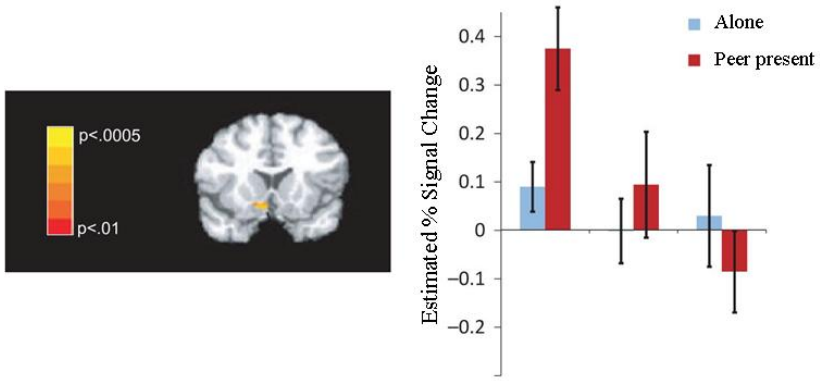

Figure 3 - Regions of activation for reward > loss with testosterone as predictor included the bilateral ventral striatum in boys (left), and left ventral striatum in girls (right), at a threshold of $p < .005$, unc. Colored bars represent t-values. Figure adapted from (Op de Macks, et al., 2011), reprinted with permission.